Brolucizumab/Beovu®

CRTH258B2301 (KESTREL) and CRTH258B2302 (KITE)

AMNOG Analysis

Week 100

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Table of contents

List of Tables and Figures

Tables

1 Patient disposition and baseline characteristics

Table 1.1 Patient disposition and compliance (RAN, FAS, SAF), week 100

	KESTREL			KITE		
Disposition/Reason (RAN, FAS, SAF)	**Brolucizumab n (%)**	**Aflibercept n (%)**	**Total n (%)**	**Brolucizumab n (%)**	**Aflibercept n (%)**	**Total n (%)**
Randomized (RAN)	**189**	**187**	**376**	**179**	**181**	**360**
Full Analysis Set (FAS)	**189 (100.0)**	**187 (100.0)**	**376 (100.0)**	**179 (100.0)**	**181 (100.0)**	**360 (100.0)**
Safety Set (SAF)	**189 (100.0)**	**187 (100.0)**	**376 (100.0)**	**179 (100.0)**	**181 (100.0)**	**360 (100.0)**
Study discontinuation (FAS)	**35 (18.5)**	**34 (18.2)**	**69 (18.4)**	**36 (20.1)**	**25 (13.8)**	**61 (16.9)**
Reason for study discontinuation						
Adverse event	3 (1.6)	7 (3.7)	10 (2.7)	5 (2.8)	4 (2.2)	9 (2.5)
Death	8 (4.2)	7 (3.7)	15 (4.0)	13 (7.3)	9 (5.0)	22 (6.1)
Lost to follow-up	4 (2.1)	4 (2.1)	8 (2.1)	2 (1.1)	2 (1.1)	4 (1.1)
Physician decision	0 (0.0)	1 (0.5)	1 (0.3)	2 (1.1)	3 (1.7)	5 (1.4)
Progressive disease	1 (0.5)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Protocol deviation	0 (0.0)	1 (0.5)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Subject decision	19 (10.1)	14 (7.5)	33 (8.8)	14 (7.8)	7 (3.9)	21 (5.8)
Study drug discontinuation (FAS)	**43 (22.8)**	**40 (21.4)**	**83 (22.1)**	**38 (21.2)**	**30 (16.6)**	**68 (18.9)**
Received alternative Anti-VEGF treatment	5 (2.6)	2 (1.1)	7 (1.9)	1 (0.6)	1 (0.6)	2 (0.6)
Reason for study drug discontinuation						
Adverse event	5 (2.6)	9 (4.8)	14 (3.7)	13 (7.3)	8 (4.4)	21 (5.8)
Death	6 (3.2)	6 (3.2)	12 (3.2)	11 (6.1)	8 (4.4)	19 (5.3)
Lost to follow-up	5 (2.6)	4 (2.1)	9 (2.4)	2 (1.1)	2 (1.1)	4 (1.1)
Physician decision	3 (1.6)	2 (1.1)	5 (1.3)	2 (1.1)	2 (1.1)	4 (1.1)
Pregnancy	1 (0.5)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Protocol deviation	2 (1.1)	2 (1.1)	4 (1.1)	1 (0.6)	3 (1.7)	4 (1.1)
Technical problems	0 (0.0)	1 (0.5)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Subject decision	21 (11.1)	16 (8.6)	37 (9.8)	9 (5.0)	7 (3.9)	16 (4.4)

n (%): Number and percentage of patients with event
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Percentages (%) are calculated based on 'n' from 'Randomized' category.

Table 1.2 Demographic characteristics at baseline (FAS)

	KESTREL			KITE		
Demographic Patient Characteristics (FAS)	**Brolucizumab N=189**	**Aflibercept N=187**	**Total N=376**	**Brolucizumab N=179**	**Aflibercept N=181**	**Total N=360**
Age (years)						
Mean ± SD	62.4 ± 10.14	63.9 ± 10.09	63.2 ± 10.13	62.3 ± 10.55	62.2 ± 9.48	62.2 ± 10.01
Median	64.0	65.0	64.0	64.0	63.0	63.0
Range	23 to 84	25 to 87	23 to 87	24 to 86	31 to 86	24 to 86
Age group (years), n (%)						
< 65 years	104 (55.0)	93 (49.7)	197 (52.4)	100 (55.9)	102 (56.4)	202 (56.1)
≥ 65 years	85 (45.0)	94 (50.3)	179 (47.6)	79 (44.1)	79 (43.6)	158 (43.9)
Sex, n (%)						
Male	110 (58.2)	126 (67.4)	236 (62.8)	120 (67.0)	115 (63.5)	235 (65.3)
Female	79 (41.8)	61 (32.6)	140 (37.2)	59 (33.0)	66 (36.5)	125 (34.7)
Race, n (%)						
White	158 (83.6)	152 (81.3)	310 (82.4)	133 (74.3)	132 (72.9)	265 (73.6)
Black or African American	4 (2.1)	7 (3.7)	11 (2.9)	3 (1.7)	1 (0.6)	4 (1.1)
Asian	25 (13.2)	26 (13.9)	51 (13.6)	43 (24.0)	48 (26.5)	91 (25.3)
Chinese	0 (0.0)	1 (0.5)	1 (0.3)	13 (7.3)	17 (9.4)	30 (8.3)
Indian	5 (2.6)	2 (1.1)	7 (1.9)	14 (7.8)	11 (6.1)	25 (6.9)
Japanese	20 (10.6)	22 (11.8)	42 (11.2)	0 (0.0)	0 (0.0)	0 (0.0)
Korean	0 (0.0)	0 (0.0)	0 (0.0)	9 (5.0)	10 (5.5)	19 (5.3)
Vietnamese	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.3)
Missing	0 (0.0)	1 (0.5)	1 (0.3)	7 (3.9)	9 (5.0)	16 (4.4)
Native Hawaiian or other Pacific Islander	2 (1.1)	0 (0.0)	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
American Indian or Alaska Native	0 (0.0)	1 (0.5)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Multiple	0 (0.0)	1 (0.5)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Ethnicity, n (%)						
Hispanic or Latino	61 (32.3)	55 (29.4)	116 (30.9)	3 (1.7)	4 (2.2)	7 (1.9)
Not Hispanic or Latino	118 (62.4)	129 (69.0)	247 (65.7)	163 (91.1)	170 (93.9)	333 (92.5)
Not reported	4 (2.1)	1 (0.5)	5 (1.3)	8 (4.5)	4 (2.2)	12 (3.3)
Unknown	6 (3.2)	2 (1.1)	8 (2.1)	5 (2.8)	3 (1.7)	8 (2.2)
Japanese Ancestry, n (%)						
Yes	19 (10.1)	22 (11.8)	41 (10.9)	0 (0.0)	0 (0.0)	0 (0.0)

	KESTREL			KITE		
Demographic Patient Characteristics (FAS)	**Brolucizumab N=189**	**Aflibercept N=187**	**Total N=376**	**Brolucizumab N=179**	**Aflibercept N=181**	**Total N=360**
No	170 (89.9)	165 (88.2)	335 (89.1)	179 (100.0)	181 (100.0)	360 (100.0)

N: Number of patients
n (%): Number and percentage of patients with event
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Table 1.3 Diabetes characteristics at baseline (FAS)

	KESTREL			KITE		
Diabetes characteristics (FAS)	**Brolucizumab N=189**	**Aflibercept N=187**	**Total N=376**	**Brolucizumab N=179**	**Aflibercept N=181**	**Total N=360**
Diabetes type, n (%)						
Type 1	12 (6.3)	6 (3.2)	18 (4.8)	19 (10.6)	7 (3.9)	26 (7.2)
Type 2	177 (93.7)	181 (96.8)	358 (95.2)	160 (89.4)	174 (96.1)	334 (92.8)
HbA1c						
Mean ± SD	7.7 ± 1.07	7.4 ± 1.13	7.6 ± 1.11	7.5 ± 1.17	7.5 ± 1.16	7.5 ± 1.17
Median	7.7	7.3	7.5	7.6	7.3	7.5
Range	5.0 to 10.0	4.3 to 10.2	4.3 to 10.2	5.0 to 10.0	5.2 to 10.0	5.0 to 10.0
HbA1c group, n (%)						
< 7.5 %	76 (40.2)	107 (57.2)	183 (48.7)	82 (45.8)	96 (53.0)	178 (49.4)
≥ 7.5 %	112 (59.3)	80 (42.8)	192 (51.1)	97 (54.2)	85 (47.0)	182 (50.6)
Missing	1 (0.5)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)

N: Number of patients
n (%): Number and percentage of patients with event
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Table 1.4 Baseline ocular characteristics for the study eye (FAS)

	KESTREL			KITE		
Baseline ocular characteristics for the study eye (FAS)	**Brolucizumab N=189**	**Aflibercept N=187**	**Total N=376**	**Brolucizumab N=179**	**Aflibercept N=181**	**Total N=360**
DME present (study eye), n (%)						
OS	98 (51.9)	95 (50.8)	193 (51.3)	95 (53.1)	97 (53.6)	192 (53.3)
OD	91 (48.1)	92 (49.2)	183 (48.7)	84 (46.9)	84 (46.4)	168 (46.7)
Time since DME diagnosis (months)						
Mean ± SD	9.4 ± 19.47	9.6 ± 24.17	9.5 ± 21.91	10.4 ± 16.56	9.9 ± 20.73	10.2 ± 18.75
Median	1.8	1.8	1.8	3.6	2.9	3.2
Range	0.1 to 115.9	0.1 to 238.0	0.1 to 238.0	0.1 to 99.2	0.1 to 180.4	0.1 to 180.4
Time since DME diagnosis group, n (%)						
≤ 3 months	120 (63.5)	110 (58.8)	230 (61.2)	85 (47.5)	92 (50.8)	177 (49.2)
> 3 - < 12 months	30 (15.9)	39 (20.9)	69 (18.4)	51 (28.5)	49 (27.1)	100 (27.8)
≥ 12 months	39 (20.6)	38 (20.3)	77 (20.5)	43 (24.0)	40 (22.1)	83 (23.1)
BCVA (letters)						
Mean ± SD	66.6 ± 9.67	65.2 ± 12.38	65.9 ± 11.11	66.0 ± 10.77	63.7 ± 11.70	64.9 ± 11.29
Median	69.0	69.0	69.0	70.0	65.0	68.0
Range	30 to 78	23 to 79	23 to 79	23 to 78	25 to 92	23 to 92
BCVA group, n (%)						
≤ 65 letters	74 (39.2)	64 (34.2)	138 (36.7)	65 (36.3)	91 (50.3)	156 (43.3)
> 65 letters	115 (60.8)	123 (65.8)	238 (63.3)	114 (63.7)	90 (49.7)	204 (56.7)
BCVA group, n (%)						
< 60 letters	36 (19.0)	41 (21.9)	77 (20.5)	42 (23.5)	50 (27.6)	92 (25.6)
≥ 60 - ≤ 70 letters	70 (37.0)	71 (38.0)	141 (37.5)	55 (30.7)	73 (40.3)	128 (35.6)
> 70 letters	83 (43.9)	75 (40.1)	158 (42.0)	82 (45.8)	58 (32.0)	140 (38.9)
Macular Edema Type, n (%)						
Focal	59 (31.2)	48 (25.7)	107 (28.5)	63 (35.2)	66 (36.5)	129 (35.8)
Diffuse	127 (67.2)	134 (71.7)	261 (69.4)	115 (64.2)	109 (60.2)	224 (62.2)
Missing	3 (1.6)	5 (2.7)	8 (2.1)	1 (0.6)	6 (3.3)	7 (1.9)
CSFT						
Mean ± SD	453.1 ± 123.42	475.6 ± 135.84	464.3 ± 130.06	481.1 ± 132.46	484.4 ± 134.58	482.7 ± 133.35
Median	428.0	448.0	438.0	455.0	461.0	456.0
Range	272 to 1023	258 to 1137	258 to 1137	299 to 992	264 to 1178	264 to 1178
CSFT group, n (%)						
< 450 µm	107 (56.6)	96 (51.3)	203 (54.0)	85 (47.5)	82 (45.3)	167 (46.4)

	KESTREL			KITE		
Baseline ocular characteristics for the study eye (FAS)	**Brolucizumab N=189**	**Aflibercept N=187**	**Total N=376**	**Brolucizumab N=179**	**Aflibercept N=181**	**Total N=360**
≥ 450 - < 650 µm	70 (37.0)	71 (38.0)	141 (37.5)	74 (41.3)	79 (43.6)	153 (42.5)
≥ 650 µm	12 (6.3)	20 (10.7)	32 (8.5)	20 (11.2)	19 (10.5)	39 (10.8)
Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.3)
Leakage on Fluorescein Angiography, n (%)						
Present	186 (98.4)	182 (97.3)	368 (97.9)	178 (99.4)	175 (96.7)	353 (98.1)
Absent	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	3 (1.6)	5 (2.7)	8 (2.1)	1 (0.6)	6 (3.3)	7 (1.9)
Intraretinal Fluid, n (%)						
Present	189 (100.0)	184 (98.4)	373 (99.2)	176 (98.3)	179 (98.9)	355 (98.6)
Absent	0 (0.0)	3 (1.6)	3 (0.8)	3 (1.7)	2 (1.1)	5 (1.4)
Subretinal Fluid, n (%)						
Present	62 (32.8)	61 (32.6)	123 (32.7)	56 (31.3)	67 (37.0)	123 (34.2)
Absent	127 (67.2)	126 (67.4)	253 (67.3)	123 (68.7)	114 (63.0)	237 (65.8)
Diabetic Retinopathy Severity Scale, n (%)						
DR absent	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.7)	1 (0.6)	4 (1.1)
Microaneurysms only	1 (0.5)	3 (1.6)	4 (1.1)	0 (0.0)	2 (1.1)	2 (0.6)
Mild NPDR	57 (30.2)	52 (27.8)	109 (29.0)	49 (27.4)	37 (20.4)	86 (23.9)
Moderate NPDR	54 (28.6)	59 (31.6)	113 (30.1)	55 (30.7)	68 (37.6)	123 (34.2)
Moderately severe NPDR	15 (7.9)	16 (8.6)	31 (8.2)	30 (16.8)	20 (11.0)	50 (13.9)
Severe NPDR	45 (23.8)	40 (21.4)	85 (22.6)	26 (14.5)	34 (18.8)	60 (16.7)
Mild PDR	3 (1.6)	7 (3.7)	10 (2.7)	9 (5.0)	7 (3.9)	16 (4.4)
Moderate PDR	8 (4.2)	5 (2.7)	13 (3.5)	3 (1.7)	5 (2.8)	8 (2.2)
High-risk PDR	3 (1.6)	2 (1.1)	5 (1.3)	1 (0.6)	2 (1.1)	3 (0.8)
Very high-risk PDR	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Advanced PDR	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.3)
Very advanced PDR	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	3 (1.6)	3 (1.6)	6 (1.6)	3 (1.7)	4 (2.2)	7 (1.9)

N: Number of patients
n (%): Number and percentage of patients with event
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Table 1.5 Overview subgroups (FAS)

	KESTREL			KITE		
Subgroups (FAS)	**Brolucizumab N=189**	**Aflibercept N=187**	**Total N=376**	**Brolucizumab N=179**	**Aflibercept N=181**	**Total N=360**
Age, n (%)						
< 65 years	104 (55.0)	93 (49.7)	197 (52.4)	100 (55.9)	102 (56.4)	202 (56.1)
≥ 65 years	85 (45.0)	94 (50.3)	179 (47.6)	79 (44.1)	79 (43.6)	158 (43.9)
Gender, n (%)						
Male	110 (58.2)	126 (67.4)	236 (62.8)	120 (67.0)	115 (63.5)	235 (65.3)
Female	79 (41.8)	61 (32.6)	140 (37.2)	59 (33.0)	66 (36.5)	125 (34.7)
Baseline BCVA categories, n (%)						
≤ 65 letters	74 (39.2)	64 (34.2)	138 (36.7)	65 (36.3)	91 (50.3)	156 (43.3)
> 65 letters	115 (60.8)	123 (65.8)	238 (63.3)	114 (63.7)	90 (49.7)	204 (56.7)
Region, n (%)						
Region of the Americas	90 (47.6)	83 (44.4)	173 (46.0)	0 (0.0)	0 (0.0)	0 (0.0)
South-East Asia Region and Eastern Mediterranean Region	0 (0.0)	0 (0.0)	0 (0.0)	26 (14.5)	21 (11.6)	47 (13.1)
European Region	69 (36.5)	75 (40.1)	144 (38.3)	135 (75.4)	132 (72.9)	267 (74.2)
Western Pacific Region	30 (15.9)	29 (15.5)	59 (15.7)	18 (10.1)	28 (15.5)	46 (12.8)
Diabetes type, n (%)						
Type 1	12 (6.3)	6 (3.2)	18 (4.8)	19 (10.6)	7 (3.9)	26 (7.2)
Type 2	177 (93.7)	181 (96.8)	358 (95.2)	160 (89.4)	174 (96.1)	334 (92.8)
Baseline HbA1c, n (%)						
< 7.5 %	76 (40.2)	107 (57.2)	183 (48.7)	82 (45.8)	96 (53.0)	178 (49.4)
≥ 7.5 %	112 (59.3)	80 (42.8)	192 (51.1)	97 (54.2)	85 (47.0)	182 (50.6)
Missing	1 (0.5)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Duration of DME, n (%)						
≤ 3 months	120 (63.5)	110 (58.8)	230 (61.2)	85 (47.5)	92 (50.8)	177 (49.2)
> 3 - < 12 months	30 (15.9)	39 (20.9)	69 (18.4)	51 (28.5)	49 (27.1)	100 (27.8)
≥ 12 months	39 (20.6)	38 (20.3)	77 (20.5)	43 (24.0)	40 (22.1)	83 (23.1)
DME type, n (%)						
focal	59 (31.2)	48 (25.7)	107 (28.5)	63 (35.2)	66 (36.5)	129 (35.8)
diffuse	127 (67.2)	134 (71.7)	261 (69.4)	115 (64.2)	109 (60.2)	224 (62.2)
Missing	3 (1.6)	5 (2.7)	8 (2.1)	1 (0.6)	6 (3.3)	7 (1.9)
Baseline CSFT - study eye, n (%)						
< 450 µm	107 (56.6)	96 (51.3)	203 (54.0)	85 (47.5)	82 (45.3)	167 (46.4)
≥ 450 - < 650 µm	70 (37.0)	71 (38.0)	141 (37.5)	74 (41.3)	79 (43.6)	153 (42.5)

	KESTREL			KITE		
Subgroups (FAS)	**Brolucizumab N=189**	**Aflibercept N=187**	**Total N=376**	**Brolucizumab N=179**	**Aflibercept N=181**	**Total N=360**
≥ 650 µm	12 (6.3)	20 (10.7)	32 (8.5)	20 (11.2)	19 (10.5)	39 (10.8)
Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.3)
Baseline status of IRF, n (%)						
presence	189 (100.0)	184 (98.4)	373 (99.2)	176 (98.3)	179 (98.9)	355 (98.6)
absence	0 (0.0)	3 (1.6)	3 (0.8)	3 (1.7)	2 (1.1)	5 (1.4)
Baseline status of SRF, n (%)						
presence	62 (32.8)	61 (32.6)	123 (32.7)	56 (31.3)	67 (37.0)	123 (34.2)
absence	127 (67.2)	126 (67.4)	253 (67.3)	123 (68.7)	114 (63.0)	237 (65.8)
Exposure to Covid-19 (Week 52), n (%)						
Non-exposed	71 (37.6)	75 (40.1)	146 (38.8)	85 (47.5)	90 (49.7)	175 (48.6)
Exposed	118 (62.4)	112 (59.9)	230 (61.2)	94 (52.5)	91 (50.3)	185 (51.4)
Exposure to Covid-19 (Week 100), n (%)						
Non-exposed	12 (6.3)	13 (7.0)	25 (6.6)	17 (9.5)	12 (6.6)	29 (8.1)
Exposed	177 (93.7)	174 (93.0)	351 (93.4)	162 (90.5)	169 (93.4)	331 (91.9)

N: Number of patients
n (%): Number and percentage of patients with event
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Table 1.6 Protocol deviations (FAS), week 100

	KESTREL			KITE		
Protocol deviations (FAS)	**Brolucizumab N=189 n (%)**	**Aflibercept N=187 n (%)**	**Total N=376 n (%)**	**Brolucizumab N=179 n (%)**	**Aflibercept N=181 n (%)**	**Total N=360 n (%)**
Subjects with at least one protocol deviation	**106 (56.1)**	**111 (59.4)**	**217 (57.7)**	**87 (48.6)**	**91 (50.3)**	**178 (49.4)**
Protocol deviation						
Selection criteria not met	2 (1.1)	5 (2.7)	7 (1.9)	3 (1.7)	7 (3.9)	10 (2.8)
Treatment deviation	51 (27.0)	61 (32.6)	112 (29.8)	50 (27.9)	71 (39.2)	121 (33.6)
Other	91 (48.1)	99 (52.9)	190 (50.5)	77 (43.0)	78 (43.1)	155 (43.1)
Subjects with at least one protocol deviation not related to Covid-19	**35 (18.5)**	**48 (25.7)**	**83 (22.1)**	**30 (16.8)**	**38 (21.0)**	**68 (18.9)**
Protocol deviation						
Selection criteria not met	2 (1.1)	5 (2.7)	7 (1.9)	3 (1.7)	7 (3.9)	10 (2.8)
Treatment deviation	29 (15.3)	33 (17.6)	62 (16.5)	22 (12.3)	27 (14.9)	49 (13.6)
Other	8 (4.2)	14 (7.5)	22 (5.9)	12 (6.7)	9 (5.0)	21 (5.8)
Subjects with at least one protocol deviation related to Covid-19	**87 (46.0)**	**97 (51.9)**	**184 (48.9)**	**72 (40.2)**	**72 (39.8)**	**144 (40.0)**
Protocol deviation						
Selection criteria not met	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Treatment deviation	30 (15.9)	44 (23.5)	74 (19.7)	36 (20.1)	56 (30.9)	92 (25.6)
Missed active treatment during loading phase	1 (0.5)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Missed active treatment after loading phase	29 (15.3)	44 (23.5)	73 (19.4)	36 (20.1)	56 (30.9)	92 (25.6)
Other	87 (46.0)	97 (51.9)	184 (48.9)	72 (40.2)	72 (39.8)	144 (40.0)
Missed visit	73 (38.6)	67 (35.8)	140 (37.2)	61 (34.1)	66 (36.5)	127 (35.3)
Changed/missed BCVA assessment	2 (1.1)	1 (0.5)	3 (0.8)	3 (1.7)	6 (3.3)	9 (2.5)
Changed/missed disease activity assessment	0 (0.0)	1 (0.5)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Changed/missed IOP assessment	15 (7.9)	22 (11.8)	37 (9.8)	0 (0.0)	4 (2.2)	4 (1.1)

	KESTREL			KITE		
Protocol deviations (FAS)	**Brolucizumab N=189 n (%)**	**Aflibercept N=187 n (%)**	**Total N=376 n (%)**	**Brolucizumab N=179 n (%)**	**Aflibercept N=181 n (%)**	**Total N=360 n (%)**
Changed/missed laboratory assessment	8 (4.2)	17 (9.1)	25 (6.6)	7 (3.9)	3 (1.7)	10 (2.8)
Changed/missed ophthalmic imaging	10 (5.3)	19 (10.2)	29 (7.7)	8 (4.5)	3 (1.7)	11 (3.1)
Changed/missed PK/ADA assessment	7 (3.7)	17 (9.1)	24 (6.4)	3 (1.7)	3 (1.7)	6 (1.7)
Changed/missed VFQ-25 assessment	3 (1.6)	2 (1.1)	5 (1.3)	1 (0.6)	0 (0.0)	1 (0.3)
Changed/missed vital signs assessment	4 (2.1)	12 (6.4)	16 (4.3)	1 (0.6)	4 (2.2)	5 (1.4)
Study discontinuation	4 (2.1)	3 (1.6)	7 (1.9)	4 (2.2)	2 (1.1)	6 (1.7)
Treatment discontinuation	0 (0.0)	1 (0.5)	1 (0.3)	0 (0.0)	1 (0.6)	1 (0.3)

N: Number of patients
n (%): Number and percentage of patients with event
.....

Table 1.7 Duration of study participation (FAS), week 100

	KESTREL			KITE		
Study participation (FAS)	**Brolucizumab N=189**	**Aflibercept N=187**	**Total N=376**	**Brolucizumab N=179**	**Aflibercept N=181**	**Total N=360**
Duration of study participation						
Mean ± SD (in days)	644.6 ± 139.9	648.3 ± 146.0	646.4 ± 142.8	643.2 ± 150.9	660.3 ± 135.2	651.8 ± 143.3
Median (in days)	701.0	701.0	701.0	701.0	702.0	701.0
Range (in days)	39 to 785	27 to 816	27 to 816	30 to 726	71 to 785	30 to 785
Patients ≥ 100 weeks in study, n (%)	154 (81.5)	153 (81.8)	307 (81.6)	143 (79.9)	156 (86.2)	299 (83.1)
Patients < 100 weeks in study, n (%)	35 (18.5)	34 (18.2)	69 (18.4)	36 (20.1)	25 (13.8)	61 (16.9)
Duration of study participation on study drug						
Mean ± SD (in days)	602.6 ± 151.1	610.7 ± 149.5	606.6 ± 150.1	611.8 ± 149.1	624.9 ± 137.9	618.4 ± 143.5
Median (in days)	673.0	673.0	673.0	673.0	673.0	673.0
Range (in days)	29 to 721	1 to 701	1 to 721	30 to 690	57 to 691	30 to 691
Patients ≥ 100 weeks in study, n (%)	146 (77.2)	147 (78.6)	293 (77.9)	141 (78.8)	151 (83.4)	292 (81.1)
Patients < 100 weeks in study, n (%)	43 (22.8)	40 (21.4)	83 (22.1)	38 (21.2)	30 (16.6)	68 (18.9)

N: Number of patients
n (%): Number and percentage of patients with event
.....

	KESTREL			KITE		
Study participation (FAS)	**Brolucizumab N=189**	**Aflibercept N=187**	**Total N=376**	**Brolucizumab N=179**	**Aflibercept N=181**	**Total N=360**
Duration of study participation						
Mean ± SD (in days)	644.6 ± 139.9	648.3 ± 146.0	646.4 ± 142.8	643.2 ± 150.9	660.3 ± 135.2	651.8 ± 143.3
Median (in days)	701.0	701.0	701.0	701.0	702.0	701.0
Range (in days)	39 to 785	27 to 816	27 to 816	30 to 726	71 to 785	30 to 785
Patients ≥ 100 weeks in study, n (%)	154 (81.5)	153 (81.8)	307 (81.6)	143 (79.9)	156 (86.2)	299 (83.1)
Patients < 100 weeks in study, n (%)	35 (18.5)	34 (18.2)	69 (18.4)	36 (20.1)	25 (13.8)	61 (16.9)
Duration of study participation on study drug						
Mean ± SD (in days)	602.6 ± 151.1	610.7 ± 149.5	606.6 ± 150.1	611.8 ± 149.1	624.9 ± 137.9	618.4 ± 143.5
Median (in days)	673.0	673.0	673.0	673.0	673.0	673.0
Range (in days)	29 to 721	1 to 701	1 to 721	30 to 690	57 to 691	30 to 691
Patients ≥ 100 weeks in study, n (%)	146 (77.2)	147 (78.6)	293 (77.9)	141 (78.8)	151 (83.4)	292 (81.1)
Patients < 100 weeks in study, n (%)	43 (22.8)	40 (21.4)	83 (22.1)	38 (21.2)	30 (16.6)	68 (18.9)

N: Number of patients
n (%): Number and percentage of patients with event
.....

2 Mortality

Table 2.1 All-cause mortality (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
All-cause mortality (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Death from all causes, Week 52					
KESTREL, N''/N'/N	189 / 189 / 189	187 / 187 / 187			
Death from all causes, n (%)	5 (2.6)	2 (1.1)	2.51 [0.48; 13.12] 0.274	2.47 [0.49; 12.59] 0.275	0.02 [-0.01; 0.04] 0.256
KITE, N''/N'/N	179 / 179 / 179	181 / 181 / 181			
Death from all causes, n (%)	3 (1.7)	2 (1.1)	1.53 [0.25; 9.24] 0.646	1.52 [0.26; 8.97] 0.646	0.01 [-0.02; 0.03] 0.644
Pooled Analysis, N''/N'/N	368 / 368 / 368	368 / 368 / 368			
Death from all causes, n (%) p_H=0.689	8 (2.2)	4 (1.1)	1.97 [0.58; 6.67] 0.277	2.00 [0.61; 6.58] 0.246	0.01 [-0.01; 0.03] 0.245
Death from all causes, Week 100					
KESTREL, N''/N'/N	189 / 189 / 189	187 / 187 / 187			
Death from all causes, n (%)	8 (4.2)	7 (3.7)	1.14 [0.40; 3.20] 0.809	1.13 [0.42; 3.06] 0.809	0.00 [-0.03; 0.04] 0.808
KITE, N''/N'/N	179 / 179 / 179	181 / 181 / 181			
Death from all causes, n (%)	13 (7.3)	9 (5.0)	1.50 [0.62; 3.59] 0.367	1.46 [0.64; 3.33] 0.368	0.02 [-0.03; 0.07] 0.364

	Treatment Groups		Comparison		
All-cause mortality (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N''/N'/N	368 / 368 / 368	368 / 368 / 368			
Death from all causes, n (%)	21 (5.7)	16 (4.3)	1.30 [0.66; 2.57] 0.449	1.32 [0.70; 2.48] 0.395	0.01 [-0.02; 0.05] 0.394
p_H=0.691					

N: Number of patients
N': Number of patients in the analysis
N'': Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 2.2 All-cause mortality by age (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
All-cause mortality by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Death from all causes, Week 100					
Test of heterogeneity in main analysis: **p_H=0.691**					
KESTREL: Death from all causes, Week 100					
Interaction Test:	p = 0.408				
< 65 years					
N"/N'/N	104 / 104 / 104	93 / 93 / 93			
Death from all causes, n (%)	3 (2.9)	1 (1.1)	2.73 [0.28; 26.73] 0.388	2.68 [0.28; 25.35] 0.389	0.02 [-0.02; 0.06] 0.356
≥ 65 years					
N"/N'/N	85 / 85 / 85	94 / 94 / 94			
Death from all causes, n (%)	5 (5.9)	6 (6.4)	0.92 [0.27; 3.12] 0.889	0.92 [0.29; 2.91] 0.889	-0.01 [-0.08; 0.07] 0.889
KITE: Death from all causes, Week 100					
Interaction Test:	p = 0.502				
< 65 years					
N"/N'/N	100 / 100 / 100	102 / 102 / 102			
Death from all causes, n (%)	4 (4.0)	4 (3.9)	1.02 [0.25; 4.20] 0.977	1.02 [0.26; 3.97] 0.977	0.00 [-0.05; 0.05] 0.977
≥ 65 years					
N"/N'/N	79 / 79 / 79	79 / 79 / 79			
Death from all causes, n (%)	9 (11.4)	5 (6.3)	1.90 [0.61; 5.96] 0.269	1.80 [0.63; 5.13] 0.272	0.05 [-0.04; 0.14] 0.261
Pooled Analysis: Death from all causes, Week 100					
Interaction Test:	p = 0.998				
< 65 years					
N"/N'/N	204 / 204 / 204	195 / 195 / 195			
Death from all causes, n (%)	7 (3.4)	5 (2.6)	1.33 [0.41; 4.33] 0.632	1.37 [0.44; 4.27] 0.587	0.01 [-0.02; 0.04] 0.583

	Treatment Groups		Comparison		
All-cause mortality by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N''/N'/N	164 / 164 / 164	173 / 173 / 173			
Death from all causes, n (%)	14 (8.5)	11 (6.4)	1.34 [0.58; 3.06] 0.494	1.33 [0.62; 2.86] 0.461	0.02 [-0.03; 0.08] 0.460

N: Number of patients
N': Number of patients in the analysis
N'': Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 2.3 All-cause mortality by gender (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
All-cause mortality by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Death from all causes, Week 100					
Test of heterogeneity in main analysis: **p_H=0.691**					
KESTREL: Death from all causes, Week 100					
Interaction Test:	N.E.				
Male					
N"/N'/N	110 / 110 / 110	126 / 126 / 126			
Death from all causes, n (%)	4 (3.6)	7 (5.6)	0.64 [0.18; 2.25] 0.488	0.65 [0.20; 2.18] 0.489	-0.02 [-0.07; 0.03] 0.479
Female					
N"/N'/N	79 / 79 / 79	61 / 61 / 61			
Death from all causes, n (%)	4 (5.1)	0 (0.0)	N.E.	6.98 [0.38; 127.13] 0.190	0.05 [0.00; 0.10] 0.040 *
KITE: Death from all causes, Week 100					
Interaction Test:	p = 0.363				
Male					
N"/N'/N	120 / 120 / 120	115 / 115 / 115			
Death from all causes, n (%)	10 (8.3)	5 (4.3)	2.00 [0.66; 6.04] 0.219	1.92 [0.68; 5.44] 0.221	0.04 [-0.02; 0.10] 0.207
Female					
N"/N'/N	59 / 59 / 59	66 / 66 / 66			
Death from all causes, n (%)	3 (5.1)	4 (6.1)	0.83 [0.18; 3.87] 0.813	0.84 [0.20; 3.60] 0.813	-0.01 [-0.09; 0.07] 0.812
Pooled Analysis: Death from all causes, Week 100					
Interaction Test:	p = 0.645				
Male					
N"/N'/N	230 / 230 / 230	241 / 241 / 241			
Death from all causes, n (%)	14 (6.1)	12 (5.0)	1.18 [0.53; 2.65] 0.684	1.21 [0.56; 2.59] 0.625	0.01 [-0.03; 0.05] 0.623

	Treatment Groups		Comparison		
All-cause mortality by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N''/N'/N	138 / 138 / 138	127 / 127 / 127			
Death from all causes, n (%)	7 (5.1)	4 (3.1)	1.68 [0.48; 5.91] 0.421	1.64 [0.50; 5.40] 0.414	0.02 [-0.02; 0.07] 0.360

N: Number of patients
N': Number of patients in the analysis
N'': Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
KESTREL / Week 100: logit(proportion) = treatment [by gender].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 2.4 All-cause mortality by BCVA (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
All-cause mortality by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Death from all causes, Week 100					
Test of heterogeneity in main analysis: **p_H=0.691**					
KESTREL: Death from all causes, Week 100					
Interaction Test:	p = 0.940				
≤ 65 letters					
N"/N'/N	74 / 74 / 74	64 / 64 / 64			
Death from all causes, n (%)	4 (5.4)	3 (4.7)	1.16 [0.25; 5.40] 0.848	1.15 [0.27; 4.96] 0.848	0.01 [-0.07; 0.08] 0.847
> 65 letters					
N"/N'/N	115 / 115 / 115	123 / 123 / 123			
Death from all causes, n (%)	4 (3.5)	4 (3.3)	1.07 [0.26; 4.39] 0.923	1.07 [0.27; 4.18] 0.923	0.00 [-0.04; 0.05] 0.923
KITE: Death from all causes, Week 100					
Interaction Test:	p = 0.127				
≤ 65 letters					
N"/N'/N	65 / 65 / 65	91 / 91 / 91			
Death from all causes, n (%)	4 (6.2)	7 (7.7)	0.79 [0.22; 2.81] 0.712	0.80 [0.24; 2.62] 0.712	-0.02 [-0.10; 0.06] 0.706
> 65 letters					
N"/N'/N	114 / 114 / 114	90 / 90 / 90			
Death from all causes, n (%)	9 (7.9)	2 (2.2)	3.77 [0.79; 17.91] 0.095	3.55 [0.79; 16.03] 0.099	0.06 [-0.00; 0.11] 0.056
Pooled Analysis: Death from all causes, Week 100					
Interaction Test:	p = 0.253				
≤ 65 letters					
N"/N'/N	139 / 139 / 139	155 / 155 / 155			
Death from all causes, n (%)	8 (5.8)	10 (6.5)	0.88 [0.33; 2.33] 0.799	0.93 [0.37; 2.32] 0.869	-0.00 [-0.06; 0.05] 0.868

	Treatment Groups		Comparison		
All-cause mortality by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N"/N'/N	229 / 229 / 229	213 / 213 / 213			
Death from all causes, n (%)	13 (5.7)	6 (2.8)	1.98 [0.73; 5.35] 0.179	1.98 [0.75; 5.25] 0.160	0.03 [-0.01; 0.06] 0.150

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 2.5 All-cause mortality by region (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
All-cause mortality by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Death from all causes, Week 100					
Test of heterogeneity in main analysis: **p_H=0.691**					
KESTREL: Death from all causes, Week 100					
Interaction Test:	N.E.				
Region of the Americas					
N"/N'/N	90 / 90 / 90	83 / 83 / 83			
Death from all causes, n (%)	6 (6.7)	4 (4.8)	1.41 [0.38; 5.19] 0.604	1.38 [0.40; 4.73] 0.605	0.02 [-0.05; 0.09] 0.600
European Region					
N"/N'/N	69 / 69 / 69	75 / 75 / 75			
Death from all causes, n (%)	2 (2.9)	3 (4.0)	0.72 [0.12; 4.42] 0.720	0.72 [0.12; 4.21] 0.720	-0.01 [-0.07; 0.05] 0.716
Western Pacific Region					
N"/N'/N	30 / 30 / 30	29 / 29 / 29			
Death from all causes, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE: Death from all causes, Week 100					
Interaction Test:	N.E.				
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	26 / 26 / 26	21 / 21 / 21			
Death from all causes, n (%)	0 (0.0)	2 (9.5)	N.E.	0.16 [0.01; 3.22] 0.233	-0.10 [-0.22; 0.03] 0.137
European Region					
N"/N'/N	135 / 135 / 135	132 / 132 / 132			
Death from all causes, n (%)	12 (8.9)	6 (4.5)	2.05 [0.75; 5.63] 0.164	1.96 [0.76; 5.06] 0.167	0.04 [-0.02; 0.10] 0.154
Western Pacific Region					
N"/N'/N	18 / 18 / 18	28 / 28 / 28			
Death from all causes, n (%)	1 (5.6)	1 (3.6)	1.59 [0.09; 27.11] 0.749	1.56 [0.10; 23.33] 0.749	0.02 [-0.11; 0.15] 0.758

	Treatment Groups		Comparison		
All-cause mortality by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis: Death from all causes, Week 100					
Interaction Test:	N.E.				
Region of the Americas					
N"/N'/N	90 / 90 / 90	83 / 83 / 83			
Death from all causes, n (%)	6 (6.7)	4 (4.8)	N.E.	1.38 [0.40; 4.73] 0.604	0.02 [-0.05; 0.09] 0.600
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	26 / 26 / 26	21 / 21 / 21			
Death from all causes, n (%)	0 (0.0)	2 (9.5)	N.E.	0.16 [0.01; 3.22] 0.172	-0.10 [-0.22; 0.03] 0.137
European Region					
N"/N'/N	204 / 204 / 204	207 / 207 / 207			
Death from all causes, n (%)	14 (6.9)	9 (4.3)	1.20 [0.42; 3.43] 0.735	1.56 [0.69; 3.54] 0.283	0.02 [-0.02; 0.07] 0.281
Western Pacific Region					
N"/N'/N	48 / 48 / 48	57 / 57 / 57			
Death from all causes, n (%)	1 (2.1)	1 (1.8)	N.E.	1.56 [0.10; 23.33] 0.750	0.01 [-0.04; 0.06] 0.755

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
KESTREL / Week 100, KITE / Week 100: logit(proportion) = treatment [by region].
Pooled Analysis / Week 100: logit(proportion) = treatment + study + treatment * study [by region].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 2.6 All-cause mortality by diabetes type (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
All-cause mortality by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Death from all causes, Week 52					
Test of heterogeneity in main analysis: **p_H=0.689**					
KESTREL: Death from all causes, Week 52					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	12 / 12 / 12	6 / 6 / 6			
Death from all causes, n (%)	1 (8.3)	0 (0.0)	N.E.	1.62 [0.08; 34.66] 0.759	0.08 [-0.07; 0.24] 0.296
Type 2					
N"/N'/N	177 / 177 / 177	181 / 181 / 181			
Death from all causes, n (%)	4 (2.3)	2 (1.1)	2.07 [0.37; 11.44] 0.405	2.05 [0.38; 11.03] 0.405	0.01 [-0.02; 0.04] 0.396
KITE: Death from all causes, Week 52					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	19 / 19 / 19	7 / 7 / 7			
Death from all causes, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N"/N'/N	160 / 160 / 160	174 / 174 / 174			
Death from all causes, n (%)	3 (1.9)	2 (1.1)	1.64 [0.27; 9.96] 0.589	1.63 [0.28; 9.64] 0.589	0.01 [-0.02; 0.03] 0.589
Pooled Analysis: Death from all causes, Week 52					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	31 / 31 / 31	13 / 13 / 13			
Death from all causes, n (%)	1 (3.2)	0 (0.0)	N.E.	1.62 [0.08; 34.66] 0.761	0.04 [-0.03; 0.10] 0.280
Type 2					
N"/N'/N	337 / 337 / 337	355 / 355 / 355			
Death from all causes, n (%)	7 (2.1)	4 (1.1)	1.85 [0.53; 6.39] 0.332	1.84 [0.54; 6.24] 0.320	0.01 [-0.01; 0.03] 0.322
Death from all causes, Week 100					
Test of heterogeneity in main analysis: **p_H=0.691**					

	Treatment Groups		Comparison		
All-cause mortality by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL: Death from all causes, Week 100					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	12 / 12 / 12	6 / 6 / 6			
Death from all causes, n (%)	1 (8.3)	0 (0.0)	N.E.	1.62 [0.08; 34.66] 0.759	0.08 [-0.07; 0.24] 0.296
Type 2					
N"/N'/N	177 / 177 / 177	181 / 181 / 181			
Death from all causes, n (%)	7 (4.0)	7 (3.9)	1.02 [0.35; 2.98] 0.966	1.02 [0.37; 2.86] 0.966	0.00 [-0.04; 0.04] 0.966
KITE: Death from all causes, Week 100					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	19 / 19 / 19	7 / 7 / 7			
Death from all causes, n (%)	1 (5.3)	0 (0.0)	N.E.	1.20 [0.05; 26.47] 0.908	0.05 [-0.05; 0.15] 0.304
Type 2					
N"/N'/N	160 / 160 / 160	174 / 174 / 174			
Death from all causes, n (%)	12 (7.5)	9 (5.2)	1.49 [0.61; 3.63] 0.384	1.45 [0.63; 3.35] 0.384	0.02 [-0.03; 0.08] 0.384
Pooled Analysis: Death from all causes, Week 100					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	31 / 31 / 31	13 / 13 / 13			
Death from all causes, n (%)	2 (6.5)	0 (0.0)	N.E.	1.40 [0.16; 12.27] 0.765	0.07 [-0.02; 0.15] 0.140

	Treatment Groups		Comparison		
All-cause mortality by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N''/N'/N	337 / 337 / 337	355 / 355 / 355			
Death from all causes, n (%)	19 (5.6)	16 (4.5)	1.23 [0.61; 2.47] 0.563	1.26 [0.66; 2.40] 0.484	0.01 [-0.02; 0.04] 0.484

N: Number of patients
N': Number of patients in the analysis
N'': Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
KESTREL / Week 52, KITE / Week 52, KESTREL / Week 100, KITE / Week 100: logit(proportion) = treatment [by diabetes type].
Pooled Analysis / Week 52, Pooled Analysis / Week 100: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 2.7 All-cause mortality by HbA1c (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
All-cause mortality by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Death from all causes, Week 52					
Test of heterogeneity in main analysis: **p_H=0.689**					
KESTREL: Death from all causes, Week 52					
Interaction Test:	N.E.				
< 7.5 %					
N"/N'/N	76 / 76 / 76	107 / 107 / 107			
Death from all causes, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
≥ 7.5 %					
N"/N'/N	112 / 112 / 112	80 / 80 / 80			
Death from all causes, n (%)	5 (4.5)	2 (2.5)	1.82 [0.34; 9.64] 0.480	1.79 [0.36; 8.97] 0.482	0.02 [-0.03; 0.07] 0.453
KITE: Death from all causes, Week 52					
Interaction Test:	N.E.				
< 7.5 %					
N"/N'/N	82 / 82 / 82	96 / 96 / 96			
Death from all causes, n (%)	2 (2.4)	0 (0.0)	N.E.	5.84 [0.28; 120.00] 0.252	0.02 [-0.01; 0.06] 0.152
≥ 7.5 %					
N"/N'/N	97 / 97 / 97	85 / 85 / 85			
Death from all causes, n (%)	1 (1.0)	2 (2.4)	0.43 [0.04; 4.85] 0.497	0.44 [0.04; 4.75] 0.497	-0.01 [-0.05; 0.02] 0.495
Pooled Analysis: Death from all causes, Week 52					
Interaction Test:	N.E.				
< 7.5 %					
N"/N'/N	158 / 158 / 158	203 / 203 / 203			
Death from all causes, n (%)	2 (1.3)	0 (0.0)	N.E.	5.84 [0.28; 120.00] 0.193	0.01 [-0.00; 0.03] 0.163
≥ 7.5 %					
N"/N'/N	209 / 209 / 209	165 / 165 / 165			
Death from all causes, n (%)	6 (2.9)	4 (2.4)	0.90 [0.21; 3.87] 0.888	1.14 [0.32; 4.06] 0.837	0.00 [-0.03; 0.04] 0.834
Death from all causes, Week 100					
Test of heterogeneity in main analysis: **p_H=0.691**					

	Treatment Groups		Comparison		
All-cause mortality by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL: Death from all causes, Week 100					
Interaction Test:	p = 0.666				
< 7.5 %					
N"/N'/N	76 / 76 / 76	107 / 107 / 107			
Death from all causes, n (%)	2 (2.6)	2 (1.9)	1.42 [0.20; 10.30] 0.730	1.41 [0.20; 9.78] 0.729	0.01 [-0.04; 0.05] 0.735
≥ 7.5 %					
N"/N'/N	112 / 112 / 112	80 / 80 / 80			
Death from all causes, n (%)	6 (5.4)	5 (6.3)	0.85 [0.25; 2.88] 0.793	0.86 [0.27; 2.71] 0.793	-0.01 [-0.08; 0.06] 0.795
KITE: Death from all causes, Week 100					
Interaction Test:	p = 0.527				
< 7.5 %					
N"/N'/N	82 / 82 / 82	96 / 96 / 96			
Death from all causes, n (%)	6 (7.3)	6 (6.3)	1.18 [0.37; 3.82] 0.777	1.17 [0.39; 3.49] 0.777	0.01 [-0.06; 0.08] 0.778
≥ 7.5 %					
N"/N'/N	97 / 97 / 97	85 / 85 / 85			
Death from all causes, n (%)	7 (7.2)	3 (3.5)	2.13 [0.53; 8.49] 0.286	2.04 [0.55; 7.66] 0.289	0.04 [-0.03; 0.10] 0.264
Pooled Analysis: Death from all causes, Week 100					
Interaction Test:	p = 0.947				
< 7.5 %					
N"/N'/N	158 / 158 / 158	203 / 203 / 203			
Death from all causes, n (%)	8 (5.1)	8 (3.9)	1.24 [0.45; 3.41] 0.681	1.23 [0.47; 3.17] 0.676	0.01 [-0.03; 0.05] 0.678

	Treatment Groups		Comparison		
All-cause mortality by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N"/N'/N	209 / 209 / 209	165 / 165 / 165			
Death from all causes, n (%)	13 (6.2)	8 (4.8)	1.30 [0.52; 3.24] 0.580	1.28 [0.55; 2.99] 0.571	0.01 [-0.03; 0.06] 0.567

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
KESTREL / Week 52, KITE / Week 52: logit(proportion) = treatment [by HbA1c].
Pooled Analysis / Week 52: logit(proportion) = treatment + study + treatment * study [by HbA1c].

Table 2.8 All-cause mortality by duration of DME (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
All-cause mortality by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Death from all causes, Week 100					
Test of heterogeneity in main analysis: **p_H=0.691**					
KESTREL: Death from all causes, Week 100					
Interaction Test:	N.E.				
≤ 3 months					
N"/N'/N	120 / 120 / 120	110 / 110 / 110			
Death from all causes, n (%)	5 (4.2)	6 (5.5)	0.75 [0.22; 2.54] 0.648	0.76 [0.24; 2.43] 0.649	-0.01 [-0.07; 0.04] 0.649
> 3 - < 12 months					
N"/N'/N	30 / 30 / 30	39 / 39 / 39			
Death from all causes, n (%)	1 (3.3)	0 (0.0)	N.E.	3.87 [0.16; 91.80] 0.402	0.03 [-0.03; 0.10] 0.309
≥ 12 months					
N"/N'/N	39 / 39 / 39	38 / 38 / 38			
Death from all causes, n (%)	2 (5.1)	1 (2.6)	2.00 [0.17; 23.02] 0.578	1.95 [0.18; 20.61] 0.579	0.02 [-0.06; 0.11] 0.569
KITE: Death from all causes, Week 100					
Interaction Test:	p = 0.700				
≤ 3 months					
N"/N'/N	85 / 85 / 85	92 / 92 / 92			
Death from all causes, n (%)	9 (10.6)	5 (5.4)	2.06 [0.66; 6.42] 0.212	1.95 [0.68; 5.58] 0.214	0.05 [-0.03; 0.13] 0.208
> 3 - < 12 months					
N"/N'/N	51 / 51 / 51	49 / 49 / 49			
Death from all causes, n (%)	2 (3.9)	2 (4.1)	0.96 [0.13; 7.09] 0.967	0.96 [0.14; 6.56] 0.967	-0.00 [-0.08; 0.08] 0.967
≥ 12 months					
N"/N'/N	43 / 43 / 43	40 / 40 / 40			
Death from all causes, n (%)	2 (4.7)	2 (5.0)	0.93 [0.12; 6.91] 0.941	0.93 [0.14; 6.30] 0.941	-0.00 [-0.10; 0.09] 0.941

	Treatment Groups		Comparison		
All-cause mortality by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis: Death from all causes, Week 100					
Interaction Test:	p = 0.985				
≤ 3 months					
N''/N'/N	205 / 205 / 205	202 / 202 / 202			
Death from all causes, n (%)	14 (6.8)	11 (5.4)	1.28 [0.56; 2.90] 0.558	1.28 [0.60; 2.73] 0.525	0.02 [-0.03; 0.06] 0.527
> 3 - < 12 months					
N''/N'/N	81 / 81 / 81	88 / 88 / 88			
Death from all causes, n (%)	3 (3.7)	2 (2.3)	1.49 [0.24; 9.39] 0.670	1.47 [0.31; 7.05] 0.627	0.01 [-0.04; 0.06] 0.638
≥ 12 months					
N''/N'/N	82 / 82 / 82	78 / 78 / 78			
Death from all causes, n (%)	4 (4.9)	3 (3.8)	1.22 [0.26; 5.71] 0.802	1.26 [0.29; 5.46] 0.754	0.01 [-0.05; 0.07] 0.752

N: Number of patients
N': Number of patients in the analysis
N'': Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
KESTREL / Week 100: logit(proportion) = treatment [by duration of DME].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 2.9 All-cause mortality by DME type (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
All-cause mortality by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Death from all causes, Week 100					
Test of heterogeneity in main analysis: **p_H=0.691**					
KESTREL: Death from all causes, Week 100					
Interaction Test:	N.E.				
focal					
N"/N'/N	59 / 59 / 59	48 / 48 / 48			
Death from all causes, n (%)	4 (6.8)	0 (0.0)	N.E.	7.35 [0.41; 133.22] 0.177	0.07 [0.00; 0.13] 0.038 *
diffuse					
N"/N'/N	127 / 127 / 127	134 / 134 / 134			
Death from all causes, n (%)	4 (3.1)	7 (5.2)	0.59 [0.17; 2.07] 0.409	0.60 [0.18; 2.01] 0.410	-0.02 [-0.07; 0.03] 0.401
KITE: Death from all causes, Week 100					
Interaction Test:	p = 0.238				
focal					
N"/N'/N	63 / 63 / 63	66 / 66 / 66			
Death from all causes, n (%)	3 (4.8)	4 (6.1)	0.78 [0.17; 3.61] 0.745	0.79 [0.18; 3.37] 0.746	-0.01 [-0.09; 0.06] 0.744
diffuse					
N"/N'/N	115 / 115 / 115	109 / 109 / 109			
Death from all causes, n (%)	10 (8.7)	4 (3.7)	2.50 [0.76; 8.22] 0.131	2.37 [0.77; 7.33] 0.134	0.05 [-0.01; 0.11] 0.115
Pooled Analysis: Death from all causes, Week 100					
Interaction Test:	p = 0.733				
focal					
N"/N'/N	122 / 122 / 122	114 / 114 / 114			
Death from all causes, n (%)	7 (5.7)	4 (3.5)	1.63 [0.46; 5.82] 0.451	1.60 [0.49; 5.19] 0.432	0.02 [-0.03; 0.08] 0.385

	Treatment Groups		Comparison		
All-cause mortality by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N''/N'/N	242 / 242 / 242	243 / 243 / 243			
Death from all causes, n (%)	14 (5.8)	11 (4.5)	1.26 [0.55; 2.85] 0.584	1.27 [0.58; 2.76] 0.549	0.01 [-0.03; 0.05] 0.548

N: Number of patients
N': Number of patients in the analysis
N'': Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
KESTREL / Week 100: logit(proportion) = treatment [by DME type].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 2.10 All-cause mortality by CSFT (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
All-cause mortality by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Death from all causes, Week 100					
Test of heterogeneity in main analysis: **p_H=0.691**					
KESTREL: Death from all causes, Week 100					
Interaction Test:	N.E.				
< 450 µm					
N"/N'/N	107 / 107 / 107	96 / 96 / 96			
Death from all causes, n (%)	4 (3.7)	3 (3.1)	1.20 [0.26; 5.52] 0.811	1.20 [0.27; 5.21] 0.811	0.01 [-0.04; 0.06] 0.810
≥ 450 - < 650 µm					
N"/N'/N	70 / 70 / 70	71 / 71 / 71			
Death from all causes, n (%)	4 (5.7)	3 (4.2)	1.37 [0.30; 6.37] 0.685	1.35 [0.31; 5.82] 0.685	0.01 [-0.06; 0.09] 0.684
≥ 650 µm					
N"/N'/N	12 / 12 / 12	20 / 20 / 20			
Death from all causes, n (%)	0 (0.0)	1 (5.0)	N.E.	0.54 [0.02; 12.26] 0.698	-0.05 [-0.15; 0.05] 0.305
KITE: Death from all causes, Week 100					
Interaction Test:	N.E.				
< 450 µm					
N"/N'/N	85 / 85 / 85	82 / 82 / 82			
Death from all causes, n (%)	9 (10.6)	3 (3.7)	3.12 [0.81; 11.96] 0.097	2.89 [0.81; 10.32] 0.101	0.07 [-0.01; 0.15] 0.078
≥ 450 - < 650 µm					
N"/N'/N	74 / 74 / 74	79 / 79 / 79			
Death from all causes, n (%)	3 (4.1)	6 (7.6)	0.51 [0.12; 2.14] 0.360	0.53 [0.14; 2.06] 0.362	-0.04 [-0.11; 0.04] 0.346
≥ 650 µm					
N"/N'/N	20 / 20 / 20	19 / 19 / 19			
Death from all causes, n (%)	1 (5.0)	0 (0.0)	N.E.	2.86 [0.12; 66.11] 0.512	0.05 [-0.05; 0.15] 0.305

	Treatment Groups		Comparison		
All-cause mortality by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis: Death from all causes, Week 100					
Interaction Test:	p = 0.396				
< 450 µm					
N''/N'/N	192 / 192 / 192	178 / 178 / 178			
Death from all causes, n (%)	13 (6.8)	6 (3.4)	2.06 [0.76; 5.56] 0.155	2.03 [0.79; 5.20] 0.131	0.03 [-0.01; 0.08] 0.126
≥ 450 - < 650 µm					
N''/N'/N	144 / 144 / 144	150 / 150 / 150			
Death from all causes, n (%)	7 (4.9)	9 (6.0)	0.77 [0.27; 2.16] 0.616	0.81 [0.31; 2.13] 0.671	-0.01 [-0.06; 0.04] 0.669
≥ 650 µm					
N''/N'/N	32 / 32 / 32	39 / 39 / 39			
Death from all causes, n (%)	1 (3.1)	1 (2.6)	1.09 [0.06; 18.36] 0.953	1.25 [0.16; 9.61] 0.828	0.01 [-0.07; 0.08] 0.865

N: Number of patients
N': Number of patients in the analysis
N'': Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
KESTREL / Week 100, KITE / Week 100: logit(proportion) = treatment [by CSFT].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 2.11 All-cause mortality by status of SRF (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
All-cause mortality by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Death from all causes, Week 100					
Test of heterogeneity in main analysis: **p_H=0.691**					
KESTREL: Death from all causes, Week 100					
Interaction Test:	p = 0.196				
presence					
N"/N'/N	62 / 62 / 62	61 / 61 / 61			
Death from all causes, n (%)	1 (1.6)	3 (4.9)	0.32 [0.03; 3.13] 0.326	0.33 [0.04; 3.07] 0.328	-0.03 [-0.10; 0.03] 0.301
absence					
N"/N'/N	127 / 127 / 127	126 / 126 / 126			
Death from all causes, n (%)	7 (5.5)	4 (3.2)	1.78 [0.51; 6.24] 0.368	1.74 [0.52; 5.78] 0.369	0.02 [-0.03; 0.07] 0.361
KITE: Death from all causes, Week 100					
Interaction Test:	p = 0.376				
presence					
N"/N'/N	56 / 56 / 56	67 / 67 / 67			
Death from all causes, n (%)	4 (7.1)	5 (7.5)	0.95 [0.24; 3.74] 0.946	0.96 [0.27; 3.39] 0.946	-0.00 [-0.10; 0.09] 0.946
absence					
N"/N'/N	123 / 123 / 123	114 / 114 / 114			
Death from all causes, n (%)	9 (7.3)	4 (3.5)	2.17 [0.65; 7.26] 0.208	2.09 [0.66; 6.59] 0.210	0.04 [-0.02; 0.10] 0.191
Pooled Analysis: Death from all causes, Week 100					
Interaction Test:	p = 0.144				
presence					
N"/N'/N	118 / 118 / 118	128 / 128 / 128			
Death from all causes, n (%)	5 (4.2)	8 (6.3)	0.66 [0.21; 2.09] 0.475	0.71 [0.24; 2.07] 0.524	-0.02 [-0.07; 0.04] 0.521

	Treatment Groups		Comparison		
All-cause mortality by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N''/N'/N	250 / 250 / 250	240 / 240 / 240			
Death from all causes, n (%)	16 (6.4)	8 (3.3)	1.92 [0.80; 4.62] 0.145	1.91 [0.83; 4.39] 0.119	0.03 [-0.01; 0.07] 0.115

N: Number of patients
N': Number of patients in the analysis
N'': Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 2.12 All-cause mortality by exposure (week 52) (FAS), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 2.13 All-cause mortality by exposure (week 100) (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
All-cause mortality by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Death from all causes, Week 100					
Test of heterogeneity in main analysis: **p_H=0.691**					
KESTREL: Death from all causes, Week 100					
Interaction Test:	p = 0.604				
Non-exposed					
N"/N'/N	12 / 12 / 12	13 / 13 / 13			
Death from all causes, n (%)	3 (25.0)	2 (15.4)	1.83 [0.25; 13.47] 0.551	1.63 [0.33; 8.11] 0.554	0.10 [-0.22; 0.41] 0.548
Exposed					
N"/N'/N	177 / 177 / 177	174 / 174 / 174			
Death from all causes, n (%)	5 (2.8)	5 (2.9)	0.98 [0.28; 3.46] 0.978	0.98 [0.29; 3.34] 0.978	-0.00 [-0.04; 0.03] 0.978
KITE: Death from all causes, Week 100					
Interaction Test:	p = 0.435				
Non-exposed					
N"/N'/N	17 / 17 / 17	12 / 12 / 12			
Death from all causes, n (%)	2 (11.8)	2 (16.7)	0.67 [0.08; 5.54] 0.707	0.71 [0.11; 4.34] 0.707	-0.05 [-0.31; 0.21] 0.712
Exposed					
N"/N'/N	162 / 162 / 162	169 / 169 / 169			
Death from all causes, n (%)	11 (6.8)	7 (4.1)	1.69 [0.64; 4.46] 0.293	1.64 [0.65; 4.13] 0.294	0.03 [-0.02; 0.08] 0.290
Pooled Analysis: Death from all causes, Week 100					
Interaction Test:	p = 0.741				
Non-exposed					
N"/N'/N	29 / 29 / 29	25 / 25 / 25			
Death from all causes, n (%)	5 (17.2)	4 (16.0)	1.03 [0.24; 4.38] 0.973	1.12 [0.34; 3.64] 0.853	0.02 [-0.18; 0.22] 0.852

	Treatment Groups		Comparison		
All-cause mortality by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N''/N'/N	339 / 339 / 339	343 / 343 / 343			
Death from all causes, n (%)	16 (4.7)	12 (3.5)	1.35 [0.62; 2.93] 0.446	1.36 [0.66; 2.83] 0.407	0.01 [-0.02; 0.04] 0.407

N: Number of patients
N': Number of patients in the analysis
N'': Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

3 BCVA: Continuous analysis

Table 3.0 BCVA (FAS), return rates, Week 100

	Treatment Groups		
BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Total**
KESTREL: BCVA			
N	189	187	376
Baseline Returns, n (%)	189 (100.0)	187 (100.0)	376 (100.0)
Week 4 Returns, n (%)	186 (98.4)	185 (98.9)	371 (98.7)
Week 6 Returns, n (%)	186 (98.4)	180 (96.3)	366 (97.3)
Week 8 Returns, n (%)	184 (97.4)	181 (96.8)	365 (97.1)
Week 12 Returns, n (%)	187 (98.9)	183 (97.9)	370 (98.4)
Week 16 Returns, n (%)	180 (95.2)	180 (96.3)	360 (95.7)
Week 18 Returns, n (%)	182 (96.3)	173 (92.5)	355 (94.4)
Week 20 Returns, n (%)	178 (94.2)	177 (94.7)	355 (94.4)
Week 24 Returns, n (%)	179 (94.7)	178 (95.2)	357 (94.9)
Week 28 Returns, n (%)	176 (93.1)	171 (91.4)	347 (92.3)
Week 32 Returns, n (%)	162 (85.7)	162 (86.6)	324 (86.2)
Week 36 Returns, n (%)	167 (88.4)	166 (88.8)	333 (88.6)
Week 40 Returns, n (%)	164 (86.8)	164 (87.7)	328 (87.2)
Week 44 Returns, n (%)	158 (83.6)	163 (87.2)	321 (85.4)
Week 48 Returns, n (%)	155 (82.0)	160 (85.6)	315 (83.8)
Week 52 Returns, n (%)	154 (81.5)	161 (86.1)	315 (83.8)
Week 56 Returns, n (%)	146 (77.2)	152 (81.3)	298 (79.3)
Week 60 Returns, n (%)	150 (79.4)	150 (80.2)	300 (79.8)
Week 64 Returns, n (%)	150 (79.4)	152 (81.3)	302 (80.3)
Week 68 Returns, n (%)	147 (77.8)	148 (79.1)	295 (78.5)
Week 72 Returns, n (%)	151 (79.9)	146 (78.1)	297 (79.0)
Week 76 Returns, n (%)	144 (76.2)	150 (80.2)	294 (78.2)
Week 80 Returns, n (%)	152 (80.4)	142 (75.9)	294 (78.2)
Week 84 Returns, n (%)	148 (78.3)	141 (75.4)	289 (76.9)
Week 88 Returns, n (%)	142 (75.1)	145 (77.5)	287 (76.3)
Week 92 Returns, n (%)	144 (76.2)	141 (75.4)	285 (75.8)
Week 96 Returns, n (%)	143 (75.7)	142 (75.9)	285 (75.8)
Week 100 Returns, n (%)	149 (78.8)	147 (78.6)	296 (78.7)
KITE: BCVA			
N	179	181	360
Baseline Returns, n (%)	179 (100.0)	181 (100.0)	360 (100.0)
Week 4 Returns, n (%)	177 (98.9)	181 (100.0)	358 (99.4)

Treatment Groups			
BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Total**
Week 6 Returns, n (%)	177 (98.9)	179 (98.9)	356 (98.9)
Week 8 Returns, n (%)	175 (97.8)	177 (97.8)	352 (97.8)
Week 12 Returns, n (%)	176 (98.3)	177 (97.8)	353 (98.1)
Week 16 Returns, n (%)	172 (96.1)	173 (95.6)	345 (95.8)
Week 18 Returns, n (%)	172 (96.1)	171 (94.5)	343 (95.3)
Week 20 Returns, n (%)	171 (95.5)	168 (92.8)	339 (94.2)
Week 24 Returns, n (%)	172 (96.1)	171 (94.5)	343 (95.3)
Week 28 Returns, n (%)	170 (95.0)	172 (95.0)	342 (95.0)
Week 32 Returns, n (%)	166 (92.7)	169 (93.4)	335 (93.1)
Week 36 Returns, n (%)	160 (89.4)	164 (90.6)	324 (90.0)
Week 40 Returns, n (%)	150 (83.8)	158 (87.3)	308 (85.6)
Week 44 Returns, n (%)	143 (79.9)	158 (87.3)	301 (83.6)
Week 48 Returns, n (%)	148 (82.7)	152 (84.0)	300 (83.3)
Week 52 Returns, n (%)	147 (82.1)	151 (83.4)	298 (82.8)
Week 56 Returns, n (%)	139 (77.7)	146 (80.7)	285 (79.2)
Week 60 Returns, n (%)	142 (79.3)	149 (82.3)	291 (80.8)
Week 64 Returns, n (%)	144 (80.4)	149 (82.3)	293 (81.4)
Week 68 Returns, n (%)	144 (80.4)	147 (81.2)	291 (80.8)
Week 72 Returns, n (%)	140 (78.2)	145 (80.1)	285 (79.2)
Week 76 Returns, n (%)	138 (77.1)	149 (82.3)	287 (79.7)
Week 80 Returns, n (%)	135 (75.4)	150 (82.9)	285 (79.2)
Week 84 Returns, n (%)	134 (74.9)	147 (81.2)	281 (78.1)
Week 88 Returns, n (%)	136 (76.0)	146 (80.7)	282 (78.3)
Week 92 Returns, n (%)	133 (74.3)	141 (77.9)	274 (76.1)
Week 96 Returns, n (%)	136 (76.0)	141 (77.9)	277 (76.9)
Week 100 Returns, n (%)	133 (74.3)	146 (80.7)	279 (77.5)
Pooled Analysis: BCVA			
N	368	368	736
Baseline Returns, n (%)	368 (100.0)	368 (100.0)	736 (100.0)
Week 4 Returns, n (%)	363 (98.6)	366 (99.5)	729 (99.0)
Week 6 Returns, n (%)	363 (98.6)	359 (97.6)	722 (98.1)
Week 8 Returns, n (%)	359 (97.6)	358 (97.3)	717 (97.4)
Week 12 Returns, n (%)	363 (98.6)	360 (97.8)	723 (98.2)
Week 16 Returns, n (%)	352 (95.7)	353 (95.9)	705 (95.8)
Week 18 Returns, n (%)	354 (96.2)	344 (93.5)	698 (94.8)
Week 20 Returns, n (%)	349 (94.8)	345 (93.8)	694 (94.3)
Week 24 Returns, n (%)	351 (95.4)	349 (94.8)	700 (95.1)
Week 28 Returns, n (%)	346 (94.0)	343 (93.2)	689 (93.6)

Treatment Groups			
BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Total**
Week 32 Returns, n (%)	328 (89.1)	331 (89.9)	659 (89.5)
Week 36 Returns, n (%)	327 (88.9)	330 (89.7)	657 (89.3)
Week 40 Returns, n (%)	314 (85.3)	322 (87.5)	636 (86.4)
Week 44 Returns, n (%)	301 (81.8)	321 (87.2)	622 (84.5)
Week 48 Returns, n (%)	303 (82.3)	312 (84.8)	615 (83.6)
Week 52 Returns, n (%)	301 (81.8)	312 (84.8)	613 (83.3)
Week 56 Returns, n (%)	285 (77.4)	298 (81.0)	583 (79.2)
Week 60 Returns, n (%)	292 (79.3)	299 (81.3)	591 (80.3)
Week 64 Returns, n (%)	294 (79.9)	301 (81.8)	595 (80.8)
Week 68 Returns, n (%)	291 (79.1)	295 (80.2)	586 (79.6)
Week 72 Returns, n (%)	291 (79.1)	291 (79.1)	582 (79.1)
Week 76 Returns, n (%)	282 (76.6)	299 (81.3)	581 (78.9)
Week 80 Returns, n (%)	287 (78.0)	292 (79.3)	579 (78.7)
Week 84 Returns, n (%)	282 (76.6)	288 (78.3)	570 (77.4)
Week 88 Returns, n (%)	278 (75.5)	291 (79.1)	569 (77.3)
Week 92 Returns, n (%)	277 (75.3)	282 (76.6)	559 (76.0)
Week 96 Returns, n (%)	279 (75.8)	283 (76.9)	562 (76.4)
Week 100 Returns, n (%)	282 (76.6)	293 (79.6)	575 (78.1)

N: Number of patients
n (%): Number and percentage of patients with available data for the total score
.....
The return rate is the proportion of patients with available data for the total score at the given visit based on the whole study population.

Table 3.1 BCVA (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KESTREL: Best Corrected Visual Acuity - Study Eye				
N'/ N	189 / 189	187 / 187		
Baseline Mean (SD)	66.61 (9.67)	65.17 (12.38)		
Week 52 Mean (SD)	77.41 (9.83)	75.98 (10.83)		
Week 100 Mean (SD)	77.33 (11.69)	76.04 (11.11)		
Week 52: Adjusted Mean Change (SE)	9.49 (0.58)	10.61 (0.58)	-1.12 [-2.73; 0.48]	0.170
Week 100: Adjusted Mean Change (SE)	9.39 (0.77)	10.77 (0.78)	-1.38 [-3.53; 0.78]	0.209
KITE: Best Corrected Visual Acuity - Study Eye				
N'/ N	179 / 179	181 / 181		
Baseline Mean (SD)	66.01 (10.77)	63.71 (11.70)		
Week 52 Mean (SD)	77.54 (10.82)	73.77 (11.93)		
Week 100 Mean (SD)	78.80 (10.07)	74.47 (12.96)		
Week 52: Adjusted Mean Change (SE)	11.19 (0.61)	9.44 (0.61)	1.76 [0.05; 3.46]	0.043 *
Week 100: Adjusted Mean Change (SE)	11.25 (0.94)	8.44 (0.92)	2.82 [0.23; 5.41]	0.033 *
Pooled Analysis: Best Corrected Visual Acuity - Study Eye p_H=0.011 *				
N'/ N	368 / 368	368 / 368		
Baseline Mean (SD)	66.32 (10.21)	64.45 (12.06)		
Week 52 Mean (SD)	77.48 (10.31)	74.91 (11.41)		
Week 100 Mean (SD)	78.02 (10.96)	75.26 (12.07)		
Week 52: Adjusted Mean Change (SE)	10.26 (0.42)	10.05 (0.42)	0.21 [-0.95; 1.38]	0.720
Week 100: Adjusted Mean Change (SE)	10.29 (0.60)	9.64 (0.59)	0.65 [-1.01; 2.30]	0.443

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study.

Table 3.2 BCVA by age (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
BCVA by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Best Corrected Visual Acuity - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.011 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.079			
< 65 years				
N'/ N	104 / 104	93 / 93		
Baseline Mean (SD)	65.48 (10.41)	65.83 (12.85)		
Week 52 Mean (SD)	79.22 (9.95)	77.35 (11.91)		
Week 100 Mean (SD)	78.57 (13.65)	78.26 (9.79)		
Week 52: Adjusted Mean Change (SE)	12.01 (0.83)	11.57 (0.86)	0.43 [-1.91; 2.78]	0.718
Week 100: Adjusted Mean Change (SE)	12.26 (0.88)	12.20 (0.91)	0.07 [-2.43; 2.56]	0.959
≥ 65 years				
N'/ N	85 / 85	94 / 94		
Baseline Mean (SD)	67.99 (8.53)	64.52 (11.94)		
Week 52 Mean (SD)	75.12 (9.24)	74.53 (9.41)		
Week 100 Mean (SD)	75.81 (8.56)	73.66 (11.98)		
Week 52: Adjusted Mean Change (SE)	6.55 (0.93)	9.78 (0.88)	-3.22 [-5.74; -0.71]	0.012 *
Week 100: Adjusted Mean Change (SE)	7.34 (0.98)	9.65 (0.94)	-2.30 [-4.97; 0.36]	0.090
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.093			
< 65 years				
N'/ N	100 / 100	102 / 102		
Baseline Mean (SD)	67.07 (10.11)	64.42 (10.50)		
Week 52 Mean (SD)	79.66 (10.51)	75.56 (11.68)		
Week 100 Mean (SD)	81.03 (9.77)	76.05 (13.00)		
Week 52: Adjusted Mean Change (SE)	13.04 (0.86)	10.70 (0.82)	2.34 [0.02; 4.66]	0.049 *
Week 100: Adjusted Mean Change (SE)	14.69 (0.91)	9.90 (0.83)	4.79 [2.38; 7.20]	<.001 *
≥ 65 years				
N'/ N	79 / 79	79 / 79		
Baseline Mean (SD)	64.66 (11.47)	62.78 (13.10)		
Week 52 Mean (SD)	75.09 (10.74)	71.54 (11.93)		
Week 100 Mean (SD)	76.10 (9.84)	72.15 (12.64)		
Week 52: Adjusted Mean Change (SE)	9.52 (0.91)	8.37 (0.93)	1.15 [-1.39; 3.69]	0.376
Week 100: Adjusted Mean Change (SE)	9.74 (0.99)	8.74 (1.00)	1.01 [-1.75; 3.76]	0.475

	Treatment Groups		Comparison	
BCVA by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.015 *			
< 65 years				
N'/ N	204 / 204	195 / 195		
Baseline Mean (SD)	66.26 (10.27)	65.09 (11.67)		
Week 52 Mean (SD)	79.43 (10.19)	76.45 (11.80)		
Week 100 Mean (SD)	79.73 (12.01)	77.08 (11.63)		
Week 52: Adjusted Mean Change (SE)	12.52 (0.59)	11.15 (0.59)	1.37 [-0.27; 3.01]	0.102
Week 100: Adjusted Mean Change (SE)	13.44 (0.63)	11.01 (0.61)	2.44 [0.71; 4.16]	0.006 *
≥ 65 years				
N'/ N	164 / 164	173 / 173		
Baseline Mean (SD)	66.38 (10.16)	63.73 (12.48)		
Week 52 Mean (SD)	75.10 (9.98)	73.14 (10.72)		
Week 100 Mean (SD)	75.94 (9.15)	72.98 (12.26)		
Week 52: Adjusted Mean Change (SE)	8.01 (0.65)	9.09 (0.64)	-1.08 [-2.86; 0.71]	0.237
Week 100: Adjusted Mean Change (SE)	8.52 (0.69)	9.19 (0.69)	-0.67 [-2.58; 1.24]	0.494

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + baseline category + age + treatment * age + visit * age + treatment * age * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + baseline category + study + treatment * study + age + treatment * age + visit * age + treatment * age * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL and KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix

Table 3.3 BCVA by gender (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
BCVA by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Best Corrected Visual Acuity - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.011 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.789			
Male				
N'/ N	110 / 110	126 / 126		
Baseline Mean (SD)	66.64 (10.70)	65.56 (12.01)		
Week 52 Mean (SD)	78.33 (10.83)	76.64 (10.96)		
Week 100 Mean (SD)	78.47 (13.47)	76.82 (10.66)		
Week 52: Adjusted Mean Change (SE)	10.62 (0.82)	11.31 (0.76)	-0.69 [-2.87; 1.49]	0.537
Week 100: Adjusted Mean Change (SE)	11.02 (0.86)	11.40 (0.81)	-0.38 [-2.70; 1.94]	0.749
Female				
N'/ N	79 / 79	61 / 61		
Baseline Mean (SD)	66.57 (8.08)	64.38 (13.19)		
Week 52 Mean (SD)	76.18 (8.22)	74.75 (10.58)		
Week 100 Mean (SD)	75.78 (8.56)	74.62 (11.86)		
Week 52: Adjusted Mean Change (SE)	7.96 (0.95)	9.65 (1.05)	-1.69 [-4.48; 1.09]	0.233
Week 100: Adjusted Mean Change (SE)	8.57 (1.00)	10.21 (1.10)	-1.64 [-4.56; 1.28]	0.271
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.670			
Male				
N'/ N	120 / 120	115 / 115		
Baseline Mean (SD)	66.46 (10.70)	65.63 (11.47)		
Week 52 Mean (SD)	78.17 (11.12)	74.67 (12.58)		
Week 100 Mean (SD)	79.64 (10.74)	76.55 (10.97)		
Week 52: Adjusted Mean Change (SE)	11.18 (0.76)	9.45 (0.77)	1.73 [-0.40; 3.85]	0.111
Week 100: Adjusted Mean Change (SE)	12.39 (0.81)	10.01 (0.80)	2.38 [0.15; 4.61]	0.037 *
Female				
N'/ N	59 / 59	66 / 66		
Baseline Mean (SD)	65.08 (10.95)	60.36 (11.42)		
Week 52 Mean (SD)	76.25 (10.18)	72.25 (10.65)		
Week 100 Mean (SD)	77.00 (8.27)	70.83 (15.30)		
Week 52: Adjusted Mean Change (SE)	12.09 (1.10)	10.07 (1.02)	2.03 [-0.90; 4.96]	0.175
Week 100: Adjusted Mean Change (SE)	12.64 (1.21)	8.17 (1.07)	4.47 [1.32; 7.63]	0.005 *

	Treatment Groups		Comparison	
BCVA by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.988			
Male				
N'/ N	230 / 230	241 / 241		
Baseline Mean (SD)	66.54 (10.68)	65.59 (11.73)		
Week 52 Mean (SD)	78.25 (10.95)	75.71 (11.77)		
Week 100 Mean (SD)	79.07 (12.12)	76.69 (10.78)		
Week 52: Adjusted Mean Change (SE)	10.86 (0.56)	10.40 (0.54)	0.46 [-1.06; 1.98]	0.556
Week 100: Adjusted Mean Change (SE)	11.69 (0.59)	10.71 (0.57)	0.98 [-0.63; 2.59]	0.233
Female				
N'/ N	138 / 138	127 / 127		
Baseline Mean (SD)	65.93 (9.41)	62.29 (12.41)		
Week 52 Mean (SD)	76.21 (9.06)	73.50 (10.64)		
Week 100 Mean (SD)	76.27 (8.43)	72.70 (13.77)		
Week 52: Adjusted Mean Change (SE)	9.82 (0.72)	9.86 (0.73)	-0.04 [-2.04; 1.97]	0.971
Week 100: Adjusted Mean Change (SE)	10.37 (0.77)	9.15 (0.76)	1.22 [-0.90; 3.35]	0.260

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + gender + treatment * gender + visit * gender + treatment * gender * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + gender + treatment * gender + visit * gender + treatment * gender * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL and KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix

Table 3.4 BCVA by BCVA (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
BCVA by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Best Corrected Visual Acuity - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.011 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.042 *			
≤ 65 letters				
N'/ N	74 / 74	64 / 64		
Baseline Mean (SD)	57.09 (8.65)	51.69 (12.30)		
Week 52 Mean (SD)	70.52 (11.06)	67.84 (12.87)		
Week 100 Mean (SD)	72.84 (11.10)	68.33 (13.80)		
Week 52: Adjusted Mean Change (SE)	11.68 (1.00)	15.99 (1.04)	-4.31 [-7.14; -1.47]	0.003 *
Week 100: Adjusted Mean Change (SE)	15.34 (1.06)	17.06 (1.10)	-1.72 [-4.73; 1.28]	0.261
> 65 letters				
N'/ N	115 / 115	123 / 123		
Baseline Mean (SD)	72.73 (3.11)	72.19 (3.27)		
Week 52 Mean (SD)	81.35 (6.31)	80.32 (6.18)		
Week 100 Mean (SD)	79.96 (11.27)	80.14 (6.36)		
Week 52: Adjusted Mean Change (SE)	8.25 (0.78)	7.78 (0.75)	0.47 [-1.65; 2.60]	0.662
Week 100: Adjusted Mean Change (SE)	6.82 (0.82)	7.57 (0.81)	-0.74 [-3.00; 1.51]	0.519
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.441			
≤ 65 letters				
N'/ N	65 / 65	91 / 91		
Baseline Mean (SD)	54.55 (9.74)	54.78 (9.72)		
Week 52 Mean (SD)	69.13 (11.77)	67.33 (12.62)		
Week 100 Mean (SD)	72.43 (11.87)	69.49 (12.64)		
Week 52: Adjusted Mean Change (SE)	14.89 (1.03)	12.46 (0.86)	2.42 [-0.21; 5.06]	0.071
Week 100: Adjusted Mean Change (SE)	16.52 (1.11)	13.86 (0.93)	2.65 [-0.18; 5.48]	0.066
> 65 letters				
N'/ N	114 / 114	90 / 90		
Baseline Mean (SD)	72.54 (3.24)	72.73 (4.18)		
Week 52 Mean (SD)	82.15 (6.81)	80.13 (6.70)		
Week 100 Mean (SD)	82.52 (6.46)	78.82 (11.66)		
Week 52: Adjusted Mean Change (SE)	8.91 (0.78)	7.65 (0.87)	1.26 [-1.03; 3.54]	0.280
Week 100: Adjusted Mean Change (SE)	9.54 (0.84)	5.70 (0.88)	3.85 [1.47; 6.22]	0.002 *

	Treatment Groups		Comparison	
BCVA by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.379			
≤ 65 letters				
N'/ N	139 / 139	155 / 155		
Baseline Mean (SD)	55.91 (9.23)	53.50 (10.93)		
Week 52 Mean (SD)	69.85 (11.37)	67.55 (12.68)		
Week 100 Mean (SD)	72.64 (11.41)	68.99 (13.10)		
Week 52: Adjusted Mean Change (SE)	13.28 (0.72)	14.05 (0.67)	-0.76 [-2.68; 1.15]	0.435
Week 100: Adjusted Mean Change (SE)	15.96 (0.76)	15.32 (0.71)	0.64 [-1.40; 2.69]	0.537
> 65 letters				
N'/ N	229 / 229	213 / 213		
Baseline Mean (SD)	72.63 (3.17)	72.42 (3.68)		
Week 52 Mean (SD)	81.74 (6.56)	80.24 (6.39)		
Week 100 Mean (SD)	81.17 (9.38)	79.55 (9.12)		
Week 52: Adjusted Mean Change (SE)	8.55 (0.55)	7.63 (0.57)	0.92 [-0.63; 2.47]	0.246
Week 100: Adjusted Mean Change (SE)	8.14 (0.59)	6.66 (0.59)	1.48 [-0.16; 3.12]	0.076

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + BCVA + treatment * BCVA + visit * BCVA + treatment * BCVA * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + study + treatment * study + BCVA + treatment * BCVA + visit * BCVA + treatment * BCVA * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL and KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix

Table 3.5 BCVA by region (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
BCVA by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Best Corrected Visual Acuity - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.011 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.338			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	66.17 (8.43)	64.24 (13.82)		
Week 52 Mean (SD)	76.82 (10.14)	75.29 (12.38)		
Week 100 Mean (SD)	77.55 (9.57)	76.42 (11.25)		
Week 52: Adjusted Mean Change (SE)	8.47 (0.90)	10.06 (0.92)	-1.59 [-4.12; 0.93]	0.216
Week 100: Adjusted Mean Change (SE)	9.81 (0.98)	11.10 (0.99)	-1.29 [-4.02; 1.43]	0.352
European Region				
N'/ N	69 / 69	75 / 75		
Baseline Mean (SD)	66.91 (9.83)	65.48 (12.17)		
Week 52 Mean (SD)	79.25 (8.58)	76.49 (10.05)		
Week 100 Mean (SD)	78.29 (14.67)	74.88 (11.99)		
Week 52: Adjusted Mean Change (SE)	11.03 (1.03)	11.21 (0.99)	-0.17 [-2.97; 2.63]	0.905
Week 100: Adjusted Mean Change (SE)	10.68 (1.07)	10.19 (1.05)	0.49 [-2.45; 3.43]	0.744
Western Pacific Region				
N'/ N	30 / 30	29 / 29		
Baseline Mean (SD)	67.23 (12.66)	67.03 (7.78)		
Week 52 Mean (SD)	75.08 (11.08)	76.70 (7.90)		
Week 100 Mean (SD)	74.69 (9.18)	77.75 (8.30)		
Week 52: Adjusted Mean Change (SE)	8.97 (1.54)	11.55 (1.56)	-2.58 [-6.88; 1.72]	0.239
Week 100: Adjusted Mean Change (SE)	8.86 (1.58)	12.56 (1.62)	-3.69 [-8.14; 0.75]	0.103
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.037 *			
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	63.00 (11.48)	66.14 (9.27)		
Week 52 Mean (SD)	76.47 (11.50)	77.79 (7.32)		
Week 100 Mean (SD)	77.69 (10.87)	80.80 (10.01)		
Week 52: Adjusted Mean Change (SE)	9.61 (1.76)	11.09 (1.91)	-1.48 [-6.57; 3.60]	0.567
Week 100: Adjusted Mean Change (SE)	9.98 (1.97)	13.10 (2.02)	-3.12 [-8.64; 2.40]	0.268

	Treatment Groups		Comparison	
BCVA by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
European Region				
N'/ N	135 / 135	132 / 132		
Baseline Mean (SD)	66.80 (10.49)	63.95 (11.51)		
Week 52 Mean (SD)	78.13 (10.46)	73.03 (12.43)		
Week 100 Mean (SD)	79.17 (9.96)	73.96 (11.64)		
Week 52: Adjusted Mean Change (SE)	11.96 (0.71)	9.17 (0.71)	2.80 [0.83; 4.77]	0.005 *
Week 100: Adjusted Mean Change (SE)	12.74 (0.75)	8.97 (0.74)	3.78 [1.71; 5.85]	<.001 *
Western Pacific Region				
N'/ N	18 / 18	28 / 28		
Baseline Mean (SD)	64.39 (11.43)	60.71 (13.84)		
Week 52 Mean (SD)	74.50 (12.67)	74.96 (11.42)		
Week 100 Mean (SD)	76.75 (10.70)	72.74 (18.77)		
Week 52: Adjusted Mean Change (SE)	10.01 (1.96)	11.13 (1.56)	-1.12 [-6.02; 3.78]	0.653
Week 100: Adjusted Mean Change (SE)	13.69 (2.25)	8.62 (1.60)	5.06 [-0.34; 10.47]	0.066
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.219			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	66.17 (8.43)	64.24 (13.82)		
Week 52 Mean (SD)	76.82 (10.14)	75.29 (12.38)		
Week 100 Mean (SD)	77.55 (9.57)	76.42 (11.25)		
Week 52: Adjusted Mean Change (SE)	9.37 (0.95)	9.46 (0.96)	-0.09 [-2.74; 2.56]	0.948
Week 100: Adjusted Mean Change (SE)	10.41 (0.96)	10.45 (0.98)	-0.05 [-2.74; 2.64]	0.972
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	63.00 (11.48)	66.14 (9.27)		
Week 52 Mean (SD)	76.47 (11.50)	77.79 (7.32)		
Week 100 Mean (SD)	77.69 (10.87)	80.80 (10.01)		
Week 52: Adjusted Mean Change (SE)	9.08 (1.73)	10.89 (1.90)	-1.81 [-6.85; 3.23]	0.482
Week 100: Adjusted Mean Change (SE)	9.81 (1.86)	11.75 (1.87)	-1.94 [-7.10; 3.22]	0.461
European Region				
N'/ N	204 / 204	207 / 207		
Baseline Mean (SD)	66.84 (10.25)	64.51 (11.75)		
Week 52 Mean (SD)	78.50 (9.87)	74.24 (11.74)		
Week 100 Mean (SD)	78.87 (11.75)	74.28 (11.73)		
Week 52: Adjusted Mean Change (SE)	11.34 (0.58)	10.04 (0.58)	1.30 [-0.30; 2.91]	0.111
Week 100: Adjusted Mean Change (SE)	11.47 (0.59)	9.50 (0.58)	1.97 [0.35; 3.59]	0.017 *

	Treatment Groups		Comparison	
BCVA by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Western Pacific Region				
N'/ N	48 / 48	57 / 57		
Baseline Mean (SD)	66.17 (12.17)	63.93 (11.53)		
Week 52 Mean (SD)	74.86 (11.56)	75.88 (9.65)		
Week 100 Mean (SD)	75.34 (9.58)	75.30 (14.47)		
Week 52: Adjusted Mean Change (SE)	9.22 (1.16)	11.13 (1.06)	-1.91 [-4.99; 1.18]	0.226
Week 100: Adjusted Mean Change (SE)	9.91 (1.19)	10.54 (1.08)	-0.63 [-3.77; 2.52]	0.696

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + region + treatment * region + visit * region + treatment * region * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + region + treatment * region + visit * region + treatment * region * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL and KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with compound symmetry covariance matrix

Table 3.6 BCVA by diabetes type (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
BCVA by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Best Corrected Visual Acuity - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.011 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.037 *			
Type 1				
N'/ N	12 / 12	6 / 6		
Baseline Mean (SD)	67.83 (8.27)	65.50 (15.57)		
Week 52 Mean (SD)	78.33 (8.43)	73.83 (10.68)		
Week 100 Mean (SD)	80.10 (8.50)	67.75 (14.31)		
Week 52: Adjusted Mean Change (SE)	10.77 (2.52)	9.55 (3.29)	1.22 [-6.91; 9.35]	0.768
Week 100: Adjusted Mean Change (SE)	11.45 (2.55)	5.72 (3.98)	5.73 [-3.53; 14.99]	0.225
Type 2				
N'/ N	177 / 177	181 / 181		
Baseline Mean (SD)	66.53 (9.77)	65.16 (12.32)		
Week 52 Mean (SD)	77.35 (9.93)	76.06 (10.86)		
Week 100 Mean (SD)	77.13 (11.88)	76.27 (10.98)		
Week 52: Adjusted Mean Change (SE)	9.41 (0.64)	10.77 (0.63)	-1.36 [-3.12; 0.39]	0.129
Week 100: Adjusted Mean Change (SE)	9.87 (0.68)	11.14 (0.66)	-1.26 [-3.12; 0.60]	0.183
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.558			
Type 1				
N'/ N	19 / 19	7 / 7		
Baseline Mean (SD)	67.00 (8.35)	65.14 (8.32)		
Week 52 Mean (SD)	80.22 (6.33)	77.00 (6.63)		
Week 100 Mean (SD)	82.41 (5.96)	81.20 (8.11)		
Week 52: Adjusted Mean Change (SE)	12.44 (1.83)	10.28 (2.98)	2.16 [-4.70; 9.02]	0.537
Week 100: Adjusted Mean Change (SE)	14.85 (1.91)	12.87 (3.25)	1.98 [-5.42; 9.38]	0.600
Type 2				
N'/ N	160 / 160	174 / 174		
Baseline Mean (SD)	65.89 (11.04)	63.65 (11.83)		
Week 52 Mean (SD)	77.17 (11.28)	73.62 (12.12)		
Week 100 Mean (SD)	78.28 (10.45)	74.23 (13.05)		
Week 52: Adjusted Mean Change (SE)	11.34 (0.67)	9.66 (0.63)	1.68 [-0.11; 3.48]	0.067
Week 100: Adjusted Mean Change (SE)	12.12 (0.72)	9.20 (0.65)	2.92 [1.02; 4.83]	0.003 *

	Treatment Groups		Comparison	
BCVA by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.069			
Type 1				
N'/ N	31 / 31	13 / 13		
Baseline Mean (SD)	67.32 (8.19)	65.31 (11.64)		
Week 52 Mean (SD)	79.59 (6.99)	75.54 (8.50)		
Week 100 Mean (SD)	81.56 (6.94)	75.22 (12.65)		
Week 52: Adjusted Mean Change (SE)	11.49 (1.48)	9.96 (2.21)	1.53 [-3.69; 6.75]	0.566
Week 100: Adjusted Mean Change (SE)	13.32 (1.54)	10.13 (2.51)	3.19 [-2.58; 8.96]	0.279
Type 2				
N'/ N	337 / 337	355 / 355		
Baseline Mean (SD)	66.22 (10.38)	64.42 (12.09)		
Week 52 Mean (SD)	77.27 (10.57)	74.89 (11.53)		
Week 100 Mean (SD)	77.65 (11.25)	75.26 (12.07)		
Week 52: Adjusted Mean Change (SE)	10.36 (0.46)	10.21 (0.44)	0.15 [-1.10; 1.40]	0.814
Week 100: Adjusted Mean Change (SE)	10.98 (0.49)	10.17 (0.47)	0.82 [-0.51; 2.14]	0.228

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + diabetes type + treatment * diabetes type + visit * diabetes type + treatment * diabetes type * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + diabetes type + treatment * diabetes type + visit * diabetes type + treatment * diabetes type * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL and KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix

Table 3.7 BCVA by HbA1c (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
BCVA by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Best Corrected Visual Acuity - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.011 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.600			
< 7.5 %				
N'/ N	76 / 76	107 / 107		
Baseline Mean (SD)	65.47 (11.76)	66.35 (11.23)		
Week 52 Mean (SD)	75.97 (11.16)	76.60 (11.50)		
Week 100 Mean (SD)	74.25 (14.97)	76.86 (11.26)		
Week 52: Adjusted Mean Change (SE)	9.23 (0.94)	10.86 (0.78)	-1.62 [-4.03; 0.78]	0.186
Week 100: Adjusted Mean Change (SE)	8.49 (0.96)	10.85 (0.79)	-2.36 [-4.80; 0.07]	0.057
≥ 7.5 %				
N'/ N	112 / 112	80 / 80		
Baseline Mean (SD)	67.37 (7.97)	63.60 (13.69)		
Week 52 Mean (SD)	78.41 (8.71)	75.09 (9.81)		
Week 100 Mean (SD)	79.47 (8.37)	74.71 (10.83)		
Week 52: Adjusted Mean Change (SE)	9.85 (0.78)	10.67 (0.92)	-0.82 [-3.20; 1.55]	0.498
Week 100: Adjusted Mean Change (SE)	10.56 (0.79)	11.16 (0.96)	-0.61 [-3.04; 1.82]	0.624
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.071			
< 7.5 %				
N'/ N	82 / 82	96 / 96		
Baseline Mean (SD)	64.70 (11.34)	62.72 (11.97)		
Week 52 Mean (SD)	77.52 (10.27)	72.24 (12.42)		
Week 100 Mean (SD)	78.79 (10.47)	73.68 (13.74)		
Week 52: Adjusted Mean Change (SE)	12.56 (0.92)	9.07 (0.84)	3.48 [1.04; 5.93]	0.005 *
Week 100: Adjusted Mean Change (SE)	13.99 (0.99)	8.92 (0.88)	5.08 [2.48; 7.67]	<.001 *
≥ 7.5 %				
N'/ N	97 / 97	85 / 85		
Baseline Mean (SD)	67.11 (10.18)	64.82 (11.35)		
Week 52 Mean (SD)	77.57 (11.32)	75.46 (11.20)		
Week 100 Mean (SD)	78.82 (9.79)	75.31 (12.11)		
Week 52: Adjusted Mean Change (SE)	10.56 (0.84)	10.37 (0.90)	0.19 [-2.23; 2.61]	0.880
Week 100: Adjusted Mean Change (SE)	11.17 (0.91)	9.80 (0.93)	1.37 [-1.17; 3.92]	0.290

	Treatment Groups		Comparison	
BCVA by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.574			
< 7.5 %				
N'/ N	158 / 158	203 / 203		
Baseline Mean (SD)	65.07 (11.51)	64.63 (11.70)		
Week 52 Mean (SD)	76.76 (10.70)	74.62 (12.09)		
Week 100 Mean (SD)	76.56 (13.03)	75.42 (12.50)		
Week 52: Adjusted Mean Change (SE)	10.87 (0.65)	9.92 (0.56)	0.95 [-0.73; 2.63]	0.269
Week 100: Adjusted Mean Change (SE)	10.95 (0.66)	9.79 (0.57)	1.17 [-0.54; 2.87]	0.181
≥ 7.5 %				
N'/ N	209 / 209	165 / 165		
Baseline Mean (SD)	67.25 (9.04)	64.23 (12.51)		
Week 52 Mean (SD)	78.01 (10.00)	75.28 (10.52)		
Week 100 Mean (SD)	79.18 (9.01)	75.05 (11.52)		
Week 52: Adjusted Mean Change (SE)	10.15 (0.56)	10.37 (0.63)	-0.22 [-1.88; 1.43]	0.792
Week 100: Adjusted Mean Change (SE)	10.93 (0.57)	10.26 (0.64)	0.66 [-1.02; 2.35]	0.440

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + HbA1c + treatment * HbA1c + visit * HbA1c + treatment * HbA1c * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + HbA1c + treatment * HbA1c + visit * HbA1c + treatment * HbA1c * visit.

Exceptionally applied model (due to nonconvergence):
KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
KESTREL: Adjusted mean change and mean difference obtained from MMRM with compound symmetry covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with compound symmetry covariance matrix

Table 3.8 BCVA by duration of DME (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
BCVA by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Best Corrected Visual Acuity - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.011 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.403			
≤ 3 months				
N'/ N	120 / 120	110 / 110		
Baseline Mean (SD)	67.23 (9.00)	65.36 (11.76)		
Week 52 Mean (SD)	78.60 (9.57)	77.21 (9.65)		
Week 100 Mean (SD)	77.69 (13.06)	77.31 (9.69)		
Week 52: Adjusted Mean Change (SE)	10.27 (0.76)	11.55 (0.79)	-1.28 [-3.44; 0.87]	0.242
Week 100: Adjusted Mean Change (SE)	9.87 (0.80)	11.47 (0.85)	-1.60 [-3.88; 0.68]	0.170
> 3 - < 12 months				
N'/ N	30 / 30	39 / 39		
Baseline Mean (SD)	65.57 (9.59)	63.85 (13.28)		
Week 52 Mean (SD)	76.58 (9.57)	74.97 (9.58)		
Week 100 Mean (SD)	79.18 (7.97)	75.15 (9.85)		
Week 52: Adjusted Mean Change (SE)	10.19 (1.56)	10.56 (1.37)	-0.37 [-4.45; 3.71]	0.858
Week 100: Adjusted Mean Change (SE)	13.68 (1.68)	11.96 (1.52)	1.73 [-2.72; 6.17]	0.446
≥ 12 months				
N'/ N	39 / 39	38 / 38		
Baseline Mean (SD)	65.51 (11.65)	65.97 (13.41)		
Week 52 Mean (SD)	73.59 (10.31)	73.33 (14.44)		
Week 100 Mean (SD)	74.61 (8.32)	73.53 (14.70)		
Week 52: Adjusted Mean Change (SE)	6.29 (1.43)	8.54 (1.34)	-2.25 [-6.09; 1.58]	0.250
Week 100: Adjusted Mean Change (SE)	7.40 (1.51)	8.93 (1.36)	-1.53 [-5.52; 2.45]	0.451
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.078			
≤ 3 months				
N'/ N	85 / 85	92 / 92		
Baseline Mean (SD)	67.52 (9.62)	64.09 (12.36)		
Week 52 Mean (SD)	78.82 (9.79)	72.60 (13.03)		
Week 100 Mean (SD)	80.09 (9.06)	74.70 (13.88)		
Week 52: Adjusted Mean Change (SE)	11.73 (0.91)	8.24 (0.86)	3.50 [1.03; 5.96]	0.005 *
Week 100: Adjusted Mean Change (SE)	12.69 (1.00)	8.83 (0.90)	3.87 [1.22; 6.51]	0.004 *

	Treatment Groups		Comparison	
BCVA by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 3 - < 12 months				
N'/ N	51 / 51	49 / 49		
Baseline Mean (SD)	62.65 (12.21)	61.90 (10.42)		
Week 52 Mean (SD)	75.41 (12.92)	74.31 (11.17)		
Week 100 Mean (SD)	77.05 (12.23)	73.47 (13.28)		
Week 52: Adjusted Mean Change (SE)	11.51 (1.14)	11.03 (1.18)	0.48 [-2.73; 3.70]	0.768
Week 100: Adjusted Mean Change (SE)	12.58 (1.18)	9.83 (1.26)	2.75 [-0.63; 6.13]	0.111
≥ 12 months				
N'/ N	43 / 43	40 / 40		
Baseline Mean (SD)	67.00 (10.46)	65.05 (11.63)		
Week 52 Mean (SD)	77.74 (9.69)	75.71 (10.16)		
Week 100 Mean (SD)	78.84 (8.41)	75.09 (10.70)		
Week 52: Adjusted Mean Change (SE)	10.90 (1.29)	11.37 (1.31)	-0.47 [-4.07; 3.12]	0.797
Week 100: Adjusted Mean Change (SE)	11.89 (1.38)	9.95 (1.33)	1.94 [-1.81; 5.70]	0.311
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.231			
≤ 3 months				
N'/ N	205 / 205	202 / 202		
Baseline Mean (SD)	67.35 (9.24)	64.78 (12.02)		
Week 52 Mean (SD)	78.69 (9.63)	75.20 (11.45)		
Week 100 Mean (SD)	78.57 (11.77)	76.11 (11.83)		
Week 52: Adjusted Mean Change (SE)	11.02 (0.59)	10.00 (0.58)	1.02 [-0.60; 2.64]	0.216
Week 100: Adjusted Mean Change (SE)	11.15 (0.63)	10.21 (0.62)	0.95 [-0.77; 2.67]	0.280
> 3 - < 12 months				
N'/ N	81 / 81	88 / 88		
Baseline Mean (SD)	63.73 (11.34)	62.76 (11.74)		
Week 52 Mean (SD)	75.82 (11.78)	74.59 (10.46)		
Week 100 Mean (SD)	77.77 (10.96)	74.17 (11.92)		
Week 52: Adjusted Mean Change (SE)	10.75 (0.93)	10.91 (0.90)	-0.16 [-2.68; 2.37]	0.904
Week 100: Adjusted Mean Change (SE)	12.62 (0.97)	10.78 (0.97)	1.84 [-0.85; 4.54]	0.180

	Treatment Groups		Comparison	
BCVA by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 12 months				
N'/ N	82 / 82	78 / 78		
Baseline Mean (SD)	66.29 (11.00)	65.50 (12.45)		
Week 52 Mean (SD)	75.94 (10.09)	74.54 (12.42)		
Week 100 Mean (SD)	76.87 (8.57)	74.32 (12.75)		
Week 52: Adjusted Mean Change (SE)	8.70 (0.96)	9.97 (0.94)	-1.26 [-3.89; 1.36]	0.345
Week 100: Adjusted Mean Change (SE)	9.74 (1.02)	9.44 (0.95)	0.31 [-2.43; 3.04]	0.827

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + duration of DME + treatment * duration of DME + visit * duration of DME + treatment * duration of DME * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + duration of DME + treatment * duration of DME + visit * duration of DME + treatment * duration of DME * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL and KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix

Table 3.9 BCVA by DME type (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
BCVA by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Best Corrected Visual Acuity - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.011 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.166			
focal				
N'/ N	59 / 59	48 / 48		
Baseline Mean (SD)	68.59 (9.34)	69.00 (9.11)		
Week 52 Mean (SD)	78.75 (8.93)	77.00 (9.16)		
Week 100 Mean (SD)	79.35 (10.02)	78.17 (9.42)		
Week 52: Adjusted Mean Change (SE)	9.61 (1.09)	8.84 (1.23)	0.77 [-2.45; 3.99]	0.639
Week 100: Adjusted Mean Change (SE)	10.96 (1.13)	9.96 (1.32)	1.00 [-2.40; 4.41]	0.564
diffuse				
N'/ N	127 / 127	134 / 134		
Baseline Mean (SD)	65.65 (9.77)	63.88 (13.24)		
Week 52 Mean (SD)	76.71 (10.31)	75.64 (11.51)		
Week 100 Mean (SD)	76.29 (12.51)	75.42 (11.63)		
Week 52: Adjusted Mean Change (SE)	9.38 (0.77)	11.33 (0.73)	-1.95 [-4.02; 0.12]	0.065
Week 100: Adjusted Mean Change (SE)	9.49 (0.82)	11.29 (0.77)	-1.80 [-4.00; 0.41]	0.111
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.483			
focal				
N'/ N	63 / 63	66 / 66		
Baseline Mean (SD)	67.02 (11.00)	66.06 (10.17)		
Week 52 Mean (SD)	79.71 (8.95)	76.00 (10.41)		
Week 100 Mean (SD)	80.33 (8.49)	75.11 (15.30)		
Week 52: Adjusted Mean Change (SE)	11.34 (1.07)	9.52 (1.02)	1.82 [-1.07; 4.71]	0.217
Week 100: Adjusted Mean Change (SE)	12.71 (1.13)	8.25 (1.05)	4.46 [1.45; 7.48]	0.004 *
diffuse				
N'/ N	115 / 115	109 / 109		
Baseline Mean (SD)	65.38 (10.66)	62.15 (12.51)		
Week 52 Mean (SD)	76.60 (11.53)	72.42 (12.67)		
Week 100 Mean (SD)	78.05 (10.82)	74.08 (11.33)		
Week 52: Adjusted Mean Change (SE)	11.68 (0.77)	9.78 (0.79)	1.90 [-0.26; 4.06]	0.085
Week 100: Adjusted Mean Change (SE)	12.44 (0.83)	10.04 (0.83)	2.40 [0.09; 4.70]	0.042 *

	Treatment Groups		Comparison	
BCVA by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.163			
focal				
N'/ N	122 / 122	114 / 114		
Baseline Mean (SD)	67.78 (10.22)	67.30 (9.81)		
Week 52 Mean (SD)	79.21 (8.91)	76.44 (9.84)		
Week 100 Mean (SD)	79.81 (9.29)	76.31 (13.32)		
Week 52: Adjusted Mean Change (SE)	10.45 (0.77)	9.29 (0.78)	1.16 [-0.99; 3.30]	0.289
Week 100: Adjusted Mean Change (SE)	11.84 (0.80)	9.05 (0.82)	2.80 [0.55; 5.04]	0.015 *
diffuse				
N'/ N	242 / 242	243 / 243		
Baseline Mean (SD)	65.52 (10.18)	63.10 (12.92)		
Week 52 Mean (SD)	76.66 (10.90)	74.19 (12.12)		
Week 100 Mean (SD)	77.12 (11.74)	74.82 (11.49)		
Week 52: Adjusted Mean Change (SE)	10.53 (0.54)	10.58 (0.53)	-0.05 [-1.54; 1.44]	0.945
Week 100: Adjusted Mean Change (SE)	10.94 (0.58)	10.65 (0.56)	0.29 [-1.30; 1.88]	0.724

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + DME type + treatment * DME type + visit * DME type + treatment * DME type * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + DME type + treatment * DME type + visit * DME type + treatment * DME type * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL and KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix

Table 3.10 BCVA by CSFT (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
BCVA by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Best Corrected Visual Acuity - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.011 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.285			
< 450 µm				
N'/ N	107 / 107	96 / 96		
Baseline Mean (SD)	68.29 (9.01)	68.98 (8.92)		
Week 52 Mean (SD)	79.69 (8.41)	78.57 (7.96)		
Week 100 Mean (SD)	78.37 (13.33)	78.84 (7.82)		
Week 52: Adjusted Mean Change (SE)	9.91 (0.72)	10.67 (0.76)	-0.76 [-2.81; 1.29]	0.466
Week 100: Adjusted Mean Change (SE)	10.02 (0.73)	10.86 (0.77)	-0.85 [-2.91; 1.22]	0.423
≥ 450 - < 650 µm				
N'/ N	70 / 70	71 / 71		
Baseline Mean (SD)	66.24 (8.92)	63.61 (11.87)		
Week 52 Mean (SD)	75.55 (10.33)	74.49 (11.26)		
Week 100 Mean (SD)	76.20 (8.64)	74.56 (11.73)		
Week 52: Adjusted Mean Change (SE)	9.18 (0.86)	10.17 (0.84)	-0.99 [-3.34; 1.36]	0.409
Week 100: Adjusted Mean Change (SE)	9.28 (0.86)	10.35 (0.85)	-1.07 [-3.44; 1.29]	0.374
≥ 650 µm				
N'/ N	12 / 12	20 / 20		
Baseline Mean (SD)	53.75 (10.38)	52.45 (18.19)		
Week 52 Mean (SD)	67.33 (11.36)	68.71 (16.55)		
Week 100 Mean (SD)	73.88 (10.83)	67.81 (16.71)		
Week 52: Adjusted Mean Change (SE)	8.73 (1.92)	13.42 (1.48)	-4.69 [-9.37; -0.00]	0.050 *
Week 100: Adjusted Mean Change (SE)	8.84 (1.92)	13.61 (1.49)	-4.77 [-9.46; -0.07]	0.046 *
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.092			
< 450 µm				
N'/ N	85 / 85	82 / 82		
Baseline Mean (SD)	69.41 (7.91)	67.15 (10.95)		
Week 52 Mean (SD)	78.97 (9.17)	76.68 (8.37)		
Week 100 Mean (SD)	80.74 (7.43)	77.43 (9.09)		
Week 52: Adjusted Mean Change (SE)	10.22 (0.93)	9.39 (0.93)	0.83 [-1.74; 3.41]	0.526
Week 100: Adjusted Mean Change (SE)	11.89 (0.99)	9.88 (0.98)	2.01 [-0.71; 4.73]	0.147

	Treatment Groups		Comparison	
BCVA by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 450 - < 650 µm				
N'/ N	74 / 74	79 / 79		
Baseline Mean (SD)	64.96 (11.09)	62.27 (11.27)		
Week 52 Mean (SD)	78.00 (9.92)	72.51 (13.91)		
Week 100 Mean (SD)	78.30 (10.58)	73.45 (15.29)		
Week 52: Adjusted Mean Change (SE)	13.01 (0.94)	9.58 (0.91)	3.44 [0.87; 6.00]	0.009 *
Week 100: Adjusted Mean Change (SE)	13.04 (1.02)	8.49 (0.95)	4.55 [1.82; 7.28]	0.001 *
≥ 650 µm				
N'/ N	20 / 20	19 / 19		
Baseline Mean (SD)	55.40 (12.74)	54.21 (10.59)		
Week 52 Mean (SD)	69.88 (16.80)	67.50 (11.89)		
Week 100 Mean (SD)	72.67 (14.73)	66.13 (12.15)		
Week 52: Adjusted Mean Change (SE)	10.49 (1.87)	11.83 (1.93)	-1.34 [-6.59; 3.91]	0.617
Week 100: Adjusted Mean Change (SE)	12.61 (2.01)	11.20 (1.99)	1.41 [-4.12; 6.95]	0.616
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.277			
< 450 µm				
N'/ N	192 / 192	178 / 178		
Baseline Mean (SD)	68.79 (8.54)	68.13 (9.92)		
Week 52 Mean (SD)	79.38 (8.72)	77.75 (8.16)		
Week 100 Mean (SD)	79.36 (11.27)	78.20 (8.42)		
Week 52: Adjusted Mean Change (SE)	10.19 (0.59)	9.72 (0.61)	0.47 [-1.20; 2.13]	0.583
Week 100: Adjusted Mean Change (SE)	10.12 (0.60)	10.06 (0.62)	0.07 [-1.61; 1.75]	0.939
≥ 450 - < 650 µm				
N'/ N	144 / 144	150 / 150		
Baseline Mean (SD)	65.58 (10.08)	62.90 (11.54)		
Week 52 Mean (SD)	76.85 (10.15)	73.42 (12.75)		
Week 100 Mean (SD)	77.26 (9.68)	73.95 (13.76)		
Week 52: Adjusted Mean Change (SE)	10.94 (0.67)	9.93 (0.65)	1.00 [-0.83; 2.83]	0.284
Week 100: Adjusted Mean Change (SE)	11.51 (0.69)	9.74 (0.66)	1.77 [-0.10; 3.64]	0.063

	Treatment Groups		Comparison	
BCVA by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 650 µm				
N'/ N	32 / 32	39 / 39		
Baseline Mean (SD)	54.78 (11.76)	53.31 (14.81)		
Week 52 Mean (SD)	68.96 (14.87)	68.12 (14.27)		
Week 100 Mean (SD)	73.09 (13.26)	67.00 (14.47)		
Week 52: Adjusted Mean Change (SE)	9.65 (1.46)	12.73 (1.30)	-3.09 [-6.89; 0.71]	0.111
Week 100: Adjusted Mean Change (SE)	12.99 (1.49)	10.76 (1.32)	2.23 [-1.64; 6.09]	0.259

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + CSFT + treatment * CSFT + visit * CSFT + treatment * CSFT * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + CSFT + treatment * CSFT + visit * CSFT + treatment * CSFT * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL: Adjusted mean change and mean difference obtained from MMRM with compound symmetry covariance matrix: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + CSFT + treatment * CSFT
KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with compound symmetry covariance matrix

Table 3.11 BCVA by status of SRF (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
BCVA by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Best Corrected Visual Acuity - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.011 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.898			
presence				
N'/ N	62 / 62	61 / 61		
Baseline Mean (SD)	64.03 (9.73)	62.05 (13.43)		
Week 52 Mean (SD)	76.67 (11.17)	75.06 (11.41)		
Week 100 Mean (SD)	77.52 (9.96)	73.73 (13.41)		
Week 52: Adjusted Mean Change (SE)	10.53 (1.08)	12.27 (1.07)	-1.74 [-4.69; 1.22]	0.249
Week 100: Adjusted Mean Change (SE)	12.06 (1.11)	11.86 (1.15)	0.21 [-2.91; 3.33]	0.897
absence				
N'/ N	127 / 127	126 / 126		
Baseline Mean (SD)	67.87 (9.42)	66.68 (11.60)		
Week 52 Mean (SD)	77.75 (9.17)	76.44 (10.56)		
Week 100 Mean (SD)	77.23 (12.56)	77.16 (9.68)		
Week 52: Adjusted Mean Change (SE)	8.97 (0.76)	9.95 (0.75)	-0.98 [-3.07; 1.11]	0.359
Week 100: Adjusted Mean Change (SE)	8.88 (0.81)	10.55 (0.80)	-1.67 [-3.90; 0.55]	0.141
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.391			
presence				
N'/ N	56 / 56	67 / 67		
Baseline Mean (SD)	61.96 (11.63)	61.33 (11.26)		
Week 52 Mean (SD)	76.04 (10.78)	73.72 (13.15)		
Week 100 Mean (SD)	78.64 (10.06)	74.41 (13.25)		
Week 52: Adjusted Mean Change (SE)	12.87 (1.11)	11.15 (1.00)	1.73 [-1.20; 4.65]	0.247
Week 100: Adjusted Mean Change (SE)	14.56 (1.21)	10.24 (1.04)	4.33 [1.20; 7.45]	0.007 *
absence				
N'/ N	123 / 123	114 / 114		
Baseline Mean (SD)	67.85 (9.86)	65.11 (11.78)		
Week 52 Mean (SD)	78.21 (10.83)	73.81 (11.17)		
Week 100 Mean (SD)	78.87 (10.13)	74.51 (12.85)		
Week 52: Adjusted Mean Change (SE)	10.78 (0.75)	8.86 (0.77)	1.92 [-0.18; 4.03]	0.073
Week 100: Adjusted Mean Change (SE)	11.51 (0.80)	8.86 (0.80)	2.65 [0.44; 4.87]	0.019 *

	Treatment Groups		Comparison	
BCVA by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.525			
presence				
N'/ N	118 / 118	128 / 128		
Baseline Mean (SD)	63.05 (10.68)	61.67 (12.30)		
Week 52 Mean (SD)	76.37 (10.93)	74.36 (12.31)		
Week 100 Mean (SD)	78.00 (9.96)	74.09 (13.27)		
Week 52: Adjusted Mean Change (SE)	11.68 (0.77)	11.72 (0.73)	-0.04 [-2.11; 2.03]	0.971
Week 100: Adjusted Mean Change (SE)	13.27 (0.82)	11.00 (0.77)	2.27 [0.07; 4.47]	0.043 *
absence				
N'/ N	250 / 250	240 / 240		
Baseline Mean (SD)	67.86 (9.62)	65.93 (11.68)		
Week 52 Mean (SD)	77.98 (10.00)	75.22 (10.90)		
Week 100 Mean (SD)	78.04 (11.43)	75.88 (11.37)		
Week 52: Adjusted Mean Change (SE)	9.87 (0.53)	9.40 (0.54)	0.46 [-1.02; 1.94]	0.539
Week 100: Adjusted Mean Change (SE)	10.19 (0.57)	9.71 (0.57)	0.48 [-1.09; 2.04]	0.552

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + status of SRF + treatment * status of SRF + visit * status of SRF + treatment * status of SRF * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + status of SRF + treatment * status of SRF + visit * status of SRF + treatment * status of SRF * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL and KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix

Table 3.13 BCVA by exposure (week 100) (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
BCVA by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Best Corrected Visual Acuity - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.011 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.515			
Non-exposed				
N'/ N	12 / 12	13 / 13		
Baseline Mean (SD)	63.00 (12.48)	63.15 (15.39)		
Week 52 Mean (SD)	74.00 (1.41)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 52: Adjusted Mean Change (SE)	3.93 (4.70)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	177 / 177	174 / 174		
Baseline Mean (SD)	66.85 (9.45)	65.32 (12.17)		
Week 52 Mean (SD)	77.45 (9.88)	75.98 (10.83)		
Week 100 Mean (SD)	77.33 (11.69)	76.04 (11.11)		
Week 52: Adjusted Mean Change (SE)	9.60 (0.63)	10.73 (0.62)	-1.13 [-2.86; 0.60]	0.199
Week 100: Adjusted Mean Change (SE)	10.01 (0.66)	11.00 (0.66)	-0.98 [-2.80; 0.83]	0.289
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.090			
Non-exposed				
N'/ N	17 / 17	12 / 12		
Baseline Mean (SD)	66.71 (12.94)	62.75 (14.48)		
Week 52 Mean (SD)	74.67 (21.39)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 52: Adjusted Mean Change (SE)	9.98 (4.18)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	162 / 162	169 / 169		
Baseline Mean (SD)	65.93 (10.56)	63.78 (11.53)		
Week 52 Mean (SD)	77.60 (10.63)	73.77 (11.93)		
Week 100 Mean (SD)	78.80 (10.07)	74.47 (12.96)		
Week 52: Adjusted Mean Change (SE)	11.67 (0.63)	9.73 (0.61)	1.94 [0.21; 3.67]	0.028 *
Week 100: Adjusted Mean Change (SE)	12.49 (0.67)	9.34 (0.64)	3.16 [1.35; 4.97]	<.001 *

	Treatment Groups		Comparison	
BCVA by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.077			
Non-exposed				
N'/ N	29 / 29	25 / 25		
Baseline Mean (SD)	65.17 (12.66)	62.96 (14.65)		
Week 52 Mean (SD)	74.40 (15.14)	N.E.		
Week 52: Adjusted Mean Change (SE)	7.35 (3.11)	N.E.	N.E.	N.E.
Exposed				
N'/ N	339 / 339	343 / 343		
Baseline Mean (SD)	66.41 (9.99)	64.56 (11.86)		
Week 52 Mean (SD)	77.53 (10.24)	74.91 (11.41)		
Week 100 Mean (SD)	78.02 (10.96)	75.26 (12.07)		
Week 52: Adjusted Mean Change (SE)	10.62 (0.44)	10.23 (0.44)	0.39 [-0.83; 1.61]	0.530
Week 100: Adjusted Mean Change (SE)	11.24 (0.47)	10.16 (0.46)	1.08 [-0.20; 2.36]	0.099

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + exposure (week 100) + treatment * exposure (week 100) + visit * exposure (week 100) + treatment * exposure (week 100) * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + exposure (week 100) + treatment * exposure (week 100) + visit * exposure (week 100) + treatment * exposure (week 100) * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL and KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix

4 BCVA: Binary analysis (Gain)

Table 4.1 BCVA - Gain of 10 respectively 15 letters (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in BCVA of ≥ 10 Letters, Week 52					
KESTREL, N''/N'/N	154 / 189 / 189	161 / 187 / 187			
Gain in BCVA of ≥ 10 Letters, n (%)	99 (52.4)	107 (57.2)	0.74 [0.48; 1.13] 0.165	0.92 [0.76; 1.10] 0.347	-0.05 [-0.15; 0.05] 0.345
KITE, N''/N'/N	147 / 179 / 179	151 / 181 / 181			
Gain in BCVA of ≥ 10 Letters, n (%)	110 (61.5)	106 (58.6)	1.27 [0.82; 1.96] 0.291	1.05 [0.89; 1.24] 0.576	0.03 [-0.07; 0.13] 0.576
Pooled Analysis, N''/N'/N	301 / 368 / 368	312 / 368 / 368			
Gain in BCVA of ≥ 10 Letters, n (%) p_H=0.085	209 (56.8)	213 (57.9)	0.98 [0.72; 1.32] 0.885	0.98 [0.87; 1.11] 0.772	-0.01 [-0.08; 0.06] 0.771
Gain in BCVA of ≥ 10 Letters, Week 100					
KESTREL, N''/N'/N	149 / 189 / 189	147 / 187 / 187			
Gain in BCVA of ≥ 10 Letters, n (%)	105 (55.6)	113 (60.4)	0.75 [0.49; 1.15] 0.181	0.92 [0.77; 1.09] 0.339	-0.05 [-0.15; 0.05] 0.338
KITE, N''/N'/N	133 / 179 / 179	146 / 181 / 181			
Gain in BCVA of ≥ 10 Letters, n (%)	110 (61.5)	98 (54.1)	1.54 [0.99; 2.39] 0.053	1.13 [0.95; 1.36] 0.162	0.07 [-0.03; 0.17] 0.159
Pooled Analysis, N''/N'/N	282 / 368 / 368	293 / 368 / 368			
Gain in BCVA of ≥ 10 Letters, n (%) p_H=0.019 *	215 (58.4)	211 (57.3)	1.07 [0.79; 1.45] 0.648	1.02 [0.90; 1.15] 0.766	0.01 [-0.06; 0.08] 0.766
Gain in BCVA of ≥ 15 Letters, Week 52					
KESTREL, N''/N'/N	154 / 189 / 189	161 / 187 / 187			
Gain in BCVA of ≥ 15 Letters, n (%)	70 (37.0)	74 (39.6)	0.81 [0.53; 1.25] 0.350	0.94 [0.72; 1.21] 0.613	-0.03 [-0.12; 0.07] 0.613
KITE, N''/N'/N	147 / 179 / 179	151 / 181 / 181			
Gain in BCVA of ≥ 15 Letters, n (%)	83 (46.4)	68 (37.6)	1.50 [0.98; 2.32] 0.065	1.23 [0.97; 1.58] 0.092	0.09 [-0.01; 0.19] 0.089

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N''/N'/N	301 / 368 / 368	312 / 368 / 368			
Gain in BCVA of ≥ 15 Letters, n (%)	153 (41.6)	142 (38.6)	1.13 [0.84; 1.53] 0.418	1.08 [0.90; 1.29] 0.405	0.03 [-0.04; 0.10] 0.405
p_H=0.043 *					
Gain in BCVA of ≥ 15 Letters, Week 100					
KESTREL, N''/N'/N	149 / 189 / 189	147 / 187 / 187			
Gain in BCVA of ≥ 15 Letters, n (%)	77 (40.7)	78 (41.7)	0.88 [0.57; 1.34] 0.545	0.98 [0.77; 1.24] 0.848	-0.01 [-0.11; 0.09] 0.848
KITE, N''/N'/N	133 / 179 / 179	146 / 181 / 181			
Gain in BCVA of ≥ 15 Letters, n (%)	89 (49.7)	67 (37.0)	1.83 [1.18; 2.82] 0.007 *	1.34 [1.06; 1.71] 0.016 *	0.13 [0.03; 0.23] 0.014 *
Pooled Analysis, N''/N'/N	282 / 368 / 368	293 / 368 / 368			
Gain in BCVA of ≥ 15 Letters, n (%)	166 (45.1)	145 (39.4)	1.30 [0.96; 1.75] 0.093	1.15 [0.97; 1.36] 0.117	0.06 [-0.01; 0.13] 0.117
p_H=0.013 *					

N: Number of patients
N': Number of patients in the analysis
N'': Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 4.2 BCVA - Gain of 10 respectively 15 letters by age (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in BCVA of ≥ 10 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.085**					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.046 *				
< 65 years					
N"/N'/N	86 / 104 / 104	83 / 93 / 93			
Gain in BCVA of ≥ 10 Letters, n (%)	70 (67.3)	57 (61.3)	1.13 [0.62; 2.07] 0.679	1.10 [0.89; 1.35] 0.382	0.06 [-0.07; 0.19] 0.378
≥ 65 years					
N"/N'/N	68 / 85 / 85	78 / 94 / 94			
Gain in BCVA of ≥ 10 Letters, n (%)	29 (34.1)	50 (53.2)	0.47 [0.25; 0.88] 0.017 *	0.64 [0.45; 0.91] 0.013 *	-0.19 [-0.33; -0.05] 0.009 *
KITE: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.557				
< 65 years					
N"/N'/N	79 / 100 / 100	84 / 102 / 102			
Gain in BCVA of ≥ 10 Letters, n (%)	66 (66.0)	63 (61.8)	1.43 [0.79; 2.58] 0.240	1.07 [0.87; 1.32] 0.531	0.04 [-0.09; 0.17] 0.531
≥ 65 years					
N"/N'/N	68 / 79 / 79	67 / 79 / 79			
Gain in BCVA of ≥ 10 Letters, n (%)	44 (55.7)	43 (54.4)	1.10 [0.58; 2.08] 0.772	1.02 [0.77; 1.36] 0.873	0.01 [-0.14; 0.17] 0.873
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.060				
< 65 years					
N"/N'/N	165 / 204 / 204	167 / 195 / 195			
Gain in BCVA of ≥ 10 Letters, n (%)	136 (66.7)	120 (61.5)	1.29 [0.85; 1.96] 0.235	1.08 [0.93; 1.26] 0.288	0.05 [-0.04; 0.15] 0.287

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N"/N'/N	136 / 164 / 164	145 / 173 / 173			
Gain in BCVA of ≥ 10 Letters, n (%)	73 (44.5)	93 (53.8)	0.72 [0.46; 1.12] 0.144	0.82 [0.66; 1.03] 0.080	-0.10 [-0.20; 0.01] 0.079
Gain in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.019 ***					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.138				
< 65 years					
N"/N'/N	82 / 104 / 104	76 / 93 / 93			
Gain in BCVA of ≥ 10 Letters, n (%)	70 (67.3)	59 (63.4)	1.03 [0.56; 1.89] 0.918	1.06 [0.86; 1.30] 0.570	0.04 [-0.09; 0.17] 0.569
≥ 65 years					
N"/N'/N	67 / 85 / 85	71 / 94 / 94			
Gain in BCVA of ≥ 10 Letters, n (%)	35 (41.2)	54 (57.4)	0.54 [0.29; 0.99] 0.047 *	0.72 [0.53; 0.98] 0.034 *	-0.16 [-0.31; -0.02] 0.028 *
KITE: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.334				
< 65 years					
N"/N'/N	73 / 100 / 100	87 / 102 / 102			
Gain in BCVA of ≥ 10 Letters, n (%)	69 (69.0)	60 (58.8)	1.88 [1.03; 3.42] 0.039 *	1.17 [0.95; 1.45] 0.134	0.10 [-0.03; 0.23] 0.130
≥ 65 years					
N"/N'/N	60 / 79 / 79	59 / 79 / 79			
Gain in BCVA of ≥ 10 Letters, n (%)	41 (51.9)	38 (48.1)	1.22 [0.65; 2.32] 0.535	1.08 [0.79; 1.47] 0.633	0.04 [-0.12; 0.19] 0.633
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.078				
< 65 years					
N"/N'/N	155 / 204 / 204	163 / 195 / 195			
Gain in BCVA of ≥ 10 Letters, n (%)	139 (68.1)	119 (61.0)	1.39 [0.92; 2.12] 0.122	1.12 [0.96; 1.29] 0.141	0.07 [-0.02; 0.16] 0.140

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N"/N'/N	127 / 164 / 164	130 / 173 / 173			
Gain in BCVA of ≥ 10 Letters, n (%)	76 (46.3)	92 (53.2)	0.81 [0.52; 1.25] 0.336	0.87 [0.70; 1.08] 0.210	-0.07 [-0.18; 0.04] 0.210
Gain in BCVA of ≥ 15 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.043 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.070				
< 65 years					
N"/N'/N	86 / 104 / 104	83 / 93 / 93			
Gain in BCVA of ≥ 15 Letters, n (%)	53 (51.0)	42 (45.2)	1.15 [0.65; 2.03] 0.638	1.13 [0.84; 1.51] 0.419	0.06 [-0.08; 0.20] 0.415
≥ 65 years					
N"/N'/N	68 / 85 / 85	78 / 94 / 94			
Gain in BCVA of ≥ 15 Letters, n (%)	17 (20.0)	32 (34.0)	0.50 [0.25; 1.00] 0.050 *	0.59 [0.35; 0.98] 0.041 *	-0.14 [-0.27; -0.01] 0.032 *
KITE: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.523				
< 65 years					
N"/N'/N	79 / 100 / 100	84 / 102 / 102			
Gain in BCVA of ≥ 15 Letters, n (%)	55 (55.0)	44 (43.1)	1.69 [0.96; 2.98] 0.068	1.28 [0.96; 1.69] 0.094	0.12 [-0.02; 0.26] 0.089
≥ 65 years					
N"/N'/N	68 / 79 / 79	67 / 79 / 79			
Gain in BCVA of ≥ 15 Letters, n (%)	28 (35.4)	24 (30.4)	1.27 [0.65; 2.48] 0.478	1.17 [0.75; 1.82] 0.499	0.05 [-0.10; 0.20] 0.498
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.067				
< 65 years					
N"/N'/N	165 / 204 / 204	167 / 195 / 195			
Gain in BCVA of ≥ 15 Letters, n (%)	108 (52.9)	86 (44.1)	1.44 [0.97; 2.14] 0.072	1.20 [0.98; 1.47] 0.077	0.09 [-0.01; 0.19] 0.075

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N"/N'/N	136 / 164 / 164	145 / 173 / 173			
Gain in BCVA of ≥ 15 Letters, n (%)	45 (27.4)	56 (32.4)	0.81 [0.50; 1.30] 0.376	0.84 [0.60; 1.18] 0.310	-0.05 [-0.15; 0.05] 0.309
Gain in BCVA of ≥ 15 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.013 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.047 *				
< 65 years					
N"/N'/N	82 / 104 / 104	76 / 93 / 93			
Gain in BCVA of ≥ 15 Letters, n (%)	55 (52.9)	40 (43.0)	1.30 [0.73; 2.32] 0.375	1.23 [0.91; 1.65] 0.171	0.10 [-0.04; 0.24] 0.164
≥ 65 years					
N"/N'/N	67 / 85 / 85	71 / 94 / 94			
Gain in BCVA of ≥ 15 Letters, n (%)	22 (25.9)	38 (40.4)	0.54 [0.28; 1.03] 0.062	0.64 [0.41; 0.99] 0.045 *	-0.15 [-0.28; -0.01] 0.036 *
KITE: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.108				
< 65 years					
N"/N'/N	73 / 100 / 100	87 / 102 / 102			
Gain in BCVA of ≥ 15 Letters, n (%)	60 (60.0)	41 (40.2)	2.48 [1.39; 4.42] 0.002 *	1.49 [1.12; 1.99] 0.006 *	0.20 [0.06; 0.33] 0.004 *
≥ 65 years					
N"/N'/N	60 / 79 / 79	59 / 79 / 79			
Gain in BCVA of ≥ 15 Letters, n (%)	29 (36.7)	26 (32.9)	1.21 [0.63; 2.35] 0.567	1.12 [0.73; 1.71] 0.617	0.04 [-0.11; 0.19] 0.616
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.007 *				
< 65 years					
N"/N'/N	155 / 204 / 204	163 / 195 / 195			
Gain in BCVA of ≥ 15 Letters, n (%)	115 (56.4)	81 (41.5)	1.87 [1.25; 2.80] 0.002 *	1.36 [1.11; 1.67] 0.003 *	0.15 [0.05; 0.25] 0.003 *

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N"/N'/N	127 / 164 / 164	130 / 173 / 173			
Gain in BCVA of ≥ 15 Letters, n (%)	51 (31.1)	64 (37.0)	0.80 [0.50; 1.27] 0.345	0.84 [0.62; 1.14] 0.252	-0.06 [-0.16; 0.04] 0.251

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + baseline category + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + baseline category + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 4.3 BCVA - Gain of 10 respectively 15 letters by gender (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in BCVA of ≥ 10 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.085**					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.420				
Male					
N"/N'/N	88 / 110 / 110	105 / 126 / 126			
Gain in BCVA of ≥ 10 Letters, n (%)	64 (58.2)	74 (58.7)	0.88 [0.51; 1.51] 0.642	0.99 [0.80; 1.23] 0.932	-0.01 [-0.13; 0.12] 0.932
Female					
N"/N'/N	66 / 79 / 79	56 / 61 / 61			
Gain in BCVA of ≥ 10 Letters, n (%)	35 (44.3)	33 (54.1)	0.61 [0.30; 1.24] 0.170	0.82 [0.58; 1.15] 0.247	-0.10 [-0.26; 0.07] 0.248
KITE: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.142				
Male					
N"/N'/N	99 / 120 / 120	95 / 115 / 115			
Gain in BCVA of ≥ 10 Letters, n (%)	70 (58.3)	68 (59.1)	1.01 [0.59; 1.71] 0.985	0.99 [0.80; 1.22] 0.901	-0.01 [-0.13; 0.12] 0.901
Female					
N"/N'/N	48 / 59 / 59	56 / 66 / 66			
Gain in BCVA of ≥ 10 Letters, n (%)	40 (67.8)	38 (57.6)	2.01 [0.94; 4.30] 0.072	1.18 [0.90; 1.55] 0.238	0.10 [-0.07; 0.27] 0.235
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.655				
Male					
N"/N'/N	187 / 230 / 230	200 / 241 / 241			
Gain in BCVA of ≥ 10 Letters, n (%)	134 (58.3)	142 (58.9)	0.93 [0.64; 1.37] 0.728	0.99 [0.85; 1.15] 0.883	-0.01 [-0.10; 0.08] 0.882

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N"/N'/N	114 / 138 / 138	112 / 127 / 127			
Gain in BCVA of ≥ 10 Letters, n (%)	75 (54.3)	71 (55.9)	1.08 [0.65; 1.79] 0.766	0.99 [0.80; 1.23] 0.963	-0.00 [-0.12; 0.12] 0.963
Gain in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.019 ***					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.965				
Male					
N"/N'/N	86 / 110 / 110	95 / 126 / 126			
Gain in BCVA of ≥ 10 Letters, n (%)	65 (59.1)	79 (62.7)	0.78 [0.45; 1.34] 0.365	0.94 [0.77; 1.16] 0.572	-0.04 [-0.16; 0.09] 0.571
Female					
N"/N'/N	63 / 79 / 79	52 / 61 / 61			
Gain in BCVA of ≥ 10 Letters, n (%)	40 (50.6)	34 (55.7)	0.76 [0.38; 1.53] 0.447	0.91 [0.66; 1.24] 0.546	-0.05 [-0.22; 0.12] 0.548
KITE: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.705				
Male					
N"/N'/N	91 / 120 / 120	93 / 115 / 115			
Gain in BCVA of ≥ 10 Letters, n (%)	75 (62.5)	63 (54.8)	1.45 [0.84; 2.48] 0.180	1.14 [0.92; 1.42] 0.232	0.08 [-0.05; 0.20] 0.229
Female					
N"/N'/N	42 / 59 / 59	53 / 66 / 66			
Gain in BCVA of ≥ 10 Letters, n (%)	35 (59.3)	35 (53.0)	1.72 [0.82; 3.62] 0.150	1.12 [0.82; 1.53] 0.479	0.06 [-0.11; 0.24] 0.478
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.827				
Male					
N"/N'/N	177 / 230 / 230	188 / 241 / 241			
Gain in BCVA of ≥ 10 Letters, n (%)	140 (60.9)	142 (58.9)	1.06 [0.72; 1.55] 0.777	1.03 [0.89; 1.20] 0.650	0.02 [-0.07; 0.11] 0.650

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N"/N'/N	105 / 138 / 138	105 / 127 / 127			
Gain in BCVA of ≥ 10 Letters, n (%)	75 (54.3)	69 (54.3)	1.13 [0.69; 1.88] 0.624	1.01 [0.81; 1.25] 0.960	0.00 [-0.12; 0.12] 0.960
Gain in BCVA of ≥ 15 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.043 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.578				
Male					
N"/N'/N	88 / 110 / 110	105 / 126 / 126			
Gain in BCVA of ≥ 15 Letters, n (%)	47 (42.7)	53 (42.1)	0.93 [0.54; 1.59] 0.782	1.02 [0.75; 1.37] 0.918	0.01 [-0.12; 0.13] 0.918
Female					
N"/N'/N	66 / 79 / 79	56 / 61 / 61			
Gain in BCVA of ≥ 15 Letters, n (%)	23 (29.1)	21 (34.4)	0.71 [0.34; 1.51] 0.376	0.85 [0.52; 1.38] 0.501	-0.05 [-0.21; 0.10] 0.504
KITE: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.818				
Male					
N"/N'/N	99 / 120 / 120	95 / 115 / 115			
Gain in BCVA of ≥ 15 Letters, n (%)	55 (45.8)	42 (36.5)	1.45 [0.85; 2.48] 0.168	1.25 [0.92; 1.71] 0.151	0.09 [-0.03; 0.22] 0.145
Female					
N"/N'/N	48 / 59 / 59	56 / 66 / 66			
Gain in BCVA of ≥ 15 Letters, n (%)	28 (47.5)	26 (39.4)	1.62 [0.78; 3.36] 0.199	1.20 [0.81; 1.80] 0.364	0.08 [-0.09; 0.25] 0.363
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.848				
Male					
N"/N'/N	187 / 230 / 230	200 / 241 / 241			
Gain in BCVA of ≥ 15 Letters, n (%)	102 (44.3)	95 (39.4)	1.17 [0.80; 1.70] 0.426	1.13 [0.91; 1.40] 0.274	0.05 [-0.04; 0.14] 0.273

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N"/N'/N	114 / 138 / 138	112 / 127 / 127			
Gain in BCVA of ≥ 15 Letters, n (%)	51 (37.0)	47 (37.0)	1.10 [0.66; 1.83] 0.728	1.03 [0.75; 1.40] 0.861	0.01 [-0.11; 0.13] 0.861
Gain in BCVA of ≥ 15 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.013 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.657				
Male					
N"/N'/N	86 / 110 / 110	95 / 126 / 126			
Gain in BCVA of ≥ 15 Letters, n (%)	52 (47.3)	57 (45.2)	0.99 [0.58; 1.69] 0.973	1.04 [0.79; 1.38] 0.754	0.02 [-0.11; 0.15] 0.754
Female					
N"/N'/N	63 / 79 / 79	52 / 61 / 61			
Gain in BCVA of ≥ 15 Letters, n (%)	25 (31.6)	21 (34.4)	0.81 [0.38; 1.69] 0.567	0.92 [0.57; 1.48] 0.728	-0.03 [-0.19; 0.13] 0.729
KITE: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.664				
Male					
N"/N'/N	91 / 120 / 120	93 / 115 / 115			
Gain in BCVA of ≥ 15 Letters, n (%)	62 (51.7)	45 (39.1)	1.70 [1.00; 2.89] 0.050 *	1.32 [0.99; 1.76] 0.057	0.13 [-0.00; 0.25] 0.052
Female					
N"/N'/N	42 / 59 / 59	53 / 66 / 66			
Gain in BCVA of ≥ 15 Letters, n (%)	27 (45.8)	22 (33.3)	2.08 [0.99; 4.40] 0.055	1.37 [0.88; 2.13] 0.158	0.12 [-0.05; 0.29] 0.153
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.982				
Male					
N"/N'/N	177 / 230 / 230	188 / 241 / 241			
Gain in BCVA of ≥ 15 Letters, n (%)	114 (49.6)	102 (42.3)	1.31 [0.90; 1.91] 0.156	1.17 [0.96; 1.43] 0.114	0.07 [-0.02; 0.16] 0.113

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N"/N'/N	105 / 138 / 138	105 / 127 / 127			
Gain in BCVA of ≥ 15 Letters, n (%)	52 (37.7)	43 (33.9)	1.32 [0.79; 2.22] 0.292	1.13 [0.82; 1.56] 0.454	0.04 [-0.07; 0.16] 0.453

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 4.4 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in BCVA of ≥ 10 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.085**					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.144				
≤ 65 letters					
N"/N'/N	56 / 74 / 74	56 / 64 / 64			
Gain in BCVA of ≥ 10 Letters, n (%)	47 (63.5)	48 (75.0)	0.46 [0.22; 0.99] 0.048 *	0.85 [0.68; 1.06] 0.144	-0.11 [-0.27; 0.04] 0.140
> 65 letters					
N"/N'/N	98 / 115 / 115	105 / 123 / 123			
Gain in BCVA of ≥ 10 Letters, n (%)	52 (45.2)	59 (48.0)	0.93 [0.55; 1.56] 0.771	0.94 [0.72; 1.24] 0.671	-0.03 [-0.15; 0.10] 0.671
KITE: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.845				
≤ 65 letters					
N"/N'/N	52 / 65 / 65	75 / 91 / 91			
Gain in BCVA of ≥ 10 Letters, n (%)	46 (70.8)	62 (68.1)	1.20 [0.60; 2.41] 0.613	1.04 [0.84; 1.28] 0.723	0.03 [-0.12; 0.17] 0.724
> 65 letters					
N"/N'/N	95 / 114 / 114	76 / 90 / 90			
Gain in BCVA of ≥ 10 Letters, n (%)	64 (56.1)	44 (48.9)	1.31 [0.75; 2.29] 0.343	1.15 [0.88; 1.50] 0.309	0.07 [-0.07; 0.21] 0.302
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.317				
≤ 65 letters					
N"/N'/N	108 / 139 / 139	131 / 155 / 155			
Gain in BCVA of ≥ 10 Letters, n (%)	93 (66.9)	110 (71.0)	0.80 [0.48; 1.32] 0.375	0.94 [0.81; 1.10] 0.456	-0.04 [-0.15; 0.07] 0.454

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N"/N'/N	193 / 229 / 229	181 / 213 / 213			
Gain in BCVA of ≥ 10 Letters, n (%)	116 (50.7)	103 (48.4)	1.10 [0.75; 1.61] 0.623	1.04 [0.86; 1.26] 0.701	0.02 [-0.08; 0.11] 0.701
Gain in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.019 ***					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.676				
≤ 65 letters					
N"/N'/N	55 / 74 / 74	51 / 64 / 64			
Gain in BCVA of ≥ 10 Letters, n (%)	53 (71.6)	46 (71.9)	0.85 [0.40; 1.82] 0.683	1.00 [0.81; 1.23] 0.974	-0.00 [-0.15; 0.15] 0.974
> 65 letters					
N"/N'/N	94 / 115 / 115	96 / 123 / 123			
Gain in BCVA of ≥ 10 Letters, n (%)	52 (45.2)	67 (54.5)	0.70 [0.42; 1.18] 0.181	0.83 [0.64; 1.07] 0.157	-0.09 [-0.22; 0.03] 0.152
KITE: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.592				
≤ 65 letters					
N"/N'/N	49 / 65 / 65	68 / 91 / 91			
Gain in BCVA of ≥ 10 Letters, n (%)	45 (69.2)	59 (64.8)	1.33 [0.67; 2.65] 0.419	1.07 [0.86; 1.33] 0.562	0.04 [-0.11; 0.19] 0.563
> 65 letters					
N"/N'/N	84 / 114 / 114	78 / 90 / 90			
Gain in BCVA of ≥ 10 Letters, n (%)	65 (57.0)	39 (43.3)	1.70 [0.96; 2.99] 0.067	1.32 [0.99; 1.75] 0.059	0.14 [-0.00; 0.27] 0.050
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.952				
≤ 65 letters					
N"/N'/N	104 / 139 / 139	119 / 155 / 155			
Gain in BCVA of ≥ 10 Letters, n (%)	98 (70.5)	105 (67.7)	1.06 [0.64; 1.76] 0.822	1.03 [0.89; 1.20] 0.688	0.02 [-0.08; 0.13] 0.687

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N"/N'/N	178 / 229 / 229	174 / 213 / 213			
Gain in BCVA of ≥ 10 Letters, n (%)	117 (51.1)	106 (49.8)	1.08 [0.74; 1.58] 0.690	1.03 [0.85; 1.24] 0.792	0.01 [-0.08; 0.11] 0.793
Gain in BCVA of ≥ 15 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.043 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.048 *				
≤ 65 letters					
N"/N'/N	56 / 74 / 74	56 / 64 / 64			
Gain in BCVA of ≥ 15 Letters, n (%)	31 (41.9)	35 (54.7)	0.46 [0.23; 0.94] 0.034 *	0.77 [0.54; 1.09] 0.134	-0.13 [-0.29; 0.04] 0.131
> 65 letters					
N"/N'/N	98 / 115 / 115	105 / 123 / 123			
Gain in BCVA of ≥ 15 Letters, n (%)	39 (33.9)	39 (31.7)	1.16 [0.66; 2.02] 0.605	1.07 [0.74; 1.54] 0.717	0.02 [-0.10; 0.14] 0.717
KITE: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.713				
≤ 65 letters					
N"/N'/N	52 / 65 / 65	75 / 91 / 91			
Gain in BCVA of ≥ 15 Letters, n (%)	30 (46.2)	37 (40.7)	1.37 [0.71; 2.64] 0.346	1.14 [0.79; 1.63] 0.492	0.05 [-0.10; 0.21] 0.495
> 65 letters					
N"/N'/N	95 / 114 / 114	76 / 90 / 90			
Gain in BCVA of ≥ 15 Letters, n (%)	53 (46.5)	31 (34.4)	1.61 [0.91; 2.88] 0.104	1.35 [0.95; 1.91] 0.090	0.12 [-0.01; 0.25] 0.079
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.121				
≤ 65 letters					
N"/N'/N	108 / 139 / 139	131 / 155 / 155			
Gain in BCVA of ≥ 15 Letters, n (%)	61 (43.9)	72 (46.5)	0.85 [0.53; 1.37] 0.504	0.93 [0.73; 1.20] 0.586	-0.03 [-0.15; 0.08] 0.586

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N"/N'/N	193 / 229 / 229	181 / 213 / 213			
Gain in BCVA of ≥ 15 Letters, n (%)	92 (40.2)	70 (32.9)	1.39 [0.93; 2.08] 0.105	1.20 [0.94; 1.55] 0.144	0.07 [-0.02; 0.16] 0.142
Gain in BCVA of ≥ 15 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.013 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.766				
≤ 65 letters					
N"/N'/N	55 / 74 / 74	51 / 64 / 64			
Gain in BCVA of ≥ 15 Letters, n (%)	42 (56.8)	35 (54.7)	0.95 [0.48; 1.89] 0.885	1.04 [0.77; 1.40] 0.808	0.02 [-0.15; 0.19] 0.807
> 65 letters					
N"/N'/N	94 / 115 / 115	96 / 123 / 123			
Gain in BCVA of ≥ 15 Letters, n (%)	35 (30.4)	43 (35.0)	0.83 [0.48; 1.44] 0.511	0.87 [0.60; 1.26] 0.459	-0.05 [-0.16; 0.07] 0.456
KITE: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.603				
≤ 65 letters					
N"/N'/N	49 / 65 / 65	68 / 91 / 91			
Gain in BCVA of ≥ 15 Letters, n (%)	34 (52.3)	39 (42.9)	1.61 [0.84; 3.09] 0.155	1.22 [0.88; 1.70] 0.239	0.09 [-0.06; 0.25] 0.242
> 65 letters					
N"/N'/N	84 / 114 / 114	78 / 90 / 90			
Gain in BCVA of ≥ 15 Letters, n (%)	55 (48.2)	28 (31.1)	2.03 [1.13; 3.64] 0.018 *	1.55 [1.08; 2.23] 0.017 *	0.17 [0.04; 0.30] 0.011 *
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.876				
≤ 65 letters					
N"/N'/N	104 / 139 / 139	119 / 155 / 155			
Gain in BCVA of ≥ 15 Letters, n (%)	76 (54.7)	74 (47.7)	1.26 [0.79; 2.01] 0.336	1.12 [0.90; 1.40] 0.312	0.06 [-0.06; 0.17] 0.310

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N''/N'/N	178 / 229 / 229	174 / 213 / 213			
Gain in BCVA of ≥ 15 Letters, n (%)	90 (39.3)	71 (33.3)	1.32 [0.89; 1.97] 0.170	1.16 [0.90; 1.50] 0.239	0.05 [-0.04; 0.14] 0.239

N: Number of patients
N': Number of patients in the analysis
N'': Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 4.5 BCVA - Gain of 10 respectively 15 letters by region (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in BCVA of ≥ 10 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.085**					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.353				
Region of the Americas					
N"/N'/N	72 / 90 / 90	73 / 83 / 83			
Gain in BCVA of ≥ 10 Letters, n (%)	46 (51.1)	46 (55.4)	0.84 [0.44; 1.58] 0.587	0.92 [0.70; 1.22] 0.570	-0.04 [-0.19; 0.11] 0.570
European Region					
N"/N'/N	56 / 69 / 69	61 / 75 / 75			
Gain in BCVA of ≥ 10 Letters, n (%)	42 (60.9)	45 (60.0)	0.88 [0.44; 1.78] 0.726	1.01 [0.78; 1.32] 0.915	0.01 [-0.15; 0.17] 0.915
Western Pacific Region					
N"/N'/N	26 / 30 / 30	27 / 29 / 29			
Gain in BCVA of ≥ 10 Letters, n (%)	11 (36.7)	16 (55.2)	0.36 [0.12; 1.07] 0.067	0.66 [0.37; 1.18] 0.163	-0.19 [-0.44; 0.06] 0.147
KITE: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.101				
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	17 / 26 / 26	14 / 21 / 21			
Gain in BCVA of ≥ 10 Letters, n (%)	12 (46.2)	14 (66.7)	0.43 [0.13; 1.45] 0.172	0.69 [0.41; 1.16] 0.161	-0.21 [-0.48; 0.07] 0.148
European Region					
N"/N'/N	114 / 135 / 135	113 / 132 / 132			
Gain in BCVA of ≥ 10 Letters, n (%)	87 (64.4)	73 (55.3)	1.67 [1.01; 2.79] 0.047 *	1.17 [0.96; 1.42] 0.130	0.09 [-0.03; 0.21] 0.126
Western Pacific Region					
N"/N'/N	16 / 18 / 18	24 / 28 / 28			
Gain in BCVA of ≥ 10 Letters, n (%)	11 (61.1)	19 (67.9)	0.85 [0.24; 3.00] 0.799	0.90 [0.58; 1.41] 0.647	-0.07 [-0.35; 0.22] 0.642

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.083				
Region of the Americas					
N"/N'/N	72 / 90 / 90	73 / 83 / 83			
Gain in BCVA of ≥ 10 Letters, n (%)	46 (51.1)	46 (55.4)	1.14 [0.55; 2.36] 0.726	0.92 [0.70; 1.22] 0.571	-0.04 [-0.19; 0.11] 0.570
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	17 / 26 / 26	14 / 21 / 21			
Gain in BCVA of ≥ 10 Letters, n (%)	12 (46.2)	14 (66.7)	0.30 [0.08; 1.09] 0.068	0.69 [0.41; 1.16] 0.164	-0.21 [-0.48; 0.07] 0.148
European Region					
N"/N'/N	170 / 204 / 204	174 / 207 / 207			
Gain in BCVA of ≥ 10 Letters, n (%)	129 (63.2)	118 (57.0)	1.23 [0.80; 1.89] 0.345	1.11 [0.95; 1.30] 0.197	0.06 [-0.03; 0.16] 0.196
Western Pacific Region					
N"/N'/N	42 / 48 / 48	51 / 57 / 57			
Gain in BCVA of ≥ 10 Letters, n (%)	22 (45.8)	35 (61.4)	0.55 [0.24; 1.25] 0.154	0.78 [0.54; 1.11] 0.166	-0.13 [-0.32; 0.05] 0.161
Gain in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.019 ***					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.010 *				
Region of the Americas					
N"/N'/N	67 / 90 / 90	66 / 83 / 83			
Gain in BCVA of ≥ 10 Letters, n (%)	48 (53.3)	52 (62.7)	0.65 [0.35; 1.24] 0.192	0.85 [0.66; 1.10] 0.216	-0.09 [-0.24; 0.05] 0.212
European Region					
N"/N'/N	56 / 69 / 69	57 / 75 / 75			
Gain in BCVA of ≥ 10 Letters, n (%)	48 (69.6)	43 (57.3)	1.56 [0.76; 3.17] 0.225	1.21 [0.95; 1.56] 0.129	0.12 [-0.03; 0.28] 0.124
Western Pacific Region					
N"/N'/N	26 / 30 / 30	24 / 29 / 29			
Gain in BCVA of ≥ 10 Letters, n (%)	9 (30.0)	18 (62.1)	0.21 [0.07; 0.64] 0.007 *	0.48 [0.26; 0.90] 0.021 *	-0.32 [-0.56; -0.08] 0.009 *

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.119				
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	13 / 26 / 26	15 / 21 / 21			
Gain in BCVA of ≥ 10 Letters, n (%)	14 (53.8)	15 (71.4)	0.46 [0.13; 1.62] 0.224	0.75 [0.48; 1.18] 0.215	-0.18 [-0.45; 0.10] 0.205
European Region					
N"/N'/N	108 / 135 / 135	108 / 132 / 132			
Gain in BCVA of ≥ 10 Letters, n (%)	85 (63.0)	67 (50.8)	1.91 [1.15; 3.18] 0.013 *	1.24 [1.00; 1.53] 0.046 *	0.12 [0.00; 0.24] 0.043 *
Western Pacific Region					
N"/N'/N	12 / 18 / 18	23 / 28 / 28			
Gain in BCVA of ≥ 10 Letters, n (%)	11 (61.1)	16 (57.1)	1.39 [0.40; 4.82] 0.602	1.07 [0.66; 1.74] 0.788	0.04 [-0.25; 0.33] 0.789
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.012 *				
Region of the Americas					
N"/N'/N	67 / 90 / 90	66 / 83 / 83			
Gain in BCVA of ≥ 10 Letters, n (%)	48 (53.3)	52 (62.7)	0.88 [0.42; 1.83] 0.726	0.85 [0.66; 1.10] 0.216	-0.09 [-0.24; 0.05] 0.212
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	13 / 26 / 26	15 / 21 / 21			
Gain in BCVA of ≥ 10 Letters, n (%)	14 (53.8)	15 (71.4)	0.34 [0.09; 1.28] 0.110	0.75 [0.48; 1.18] 0.223	-0.18 [-0.45; 0.10] 0.205
European Region					
N"/N'/N	164 / 204 / 204	165 / 207 / 207			
Gain in BCVA of ≥ 10 Letters, n (%)	133 (65.2)	110 (53.1)	1.62 [1.05; 2.50] 0.028 *	1.23 [1.05; 1.45] 0.012 *	0.12 [0.03; 0.22] 0.011 *
Western Pacific Region					
N"/N'/N	38 / 48 / 48	47 / 57 / 57			
Gain in BCVA of ≥ 10 Letters, n (%)	20 (41.7)	34 (59.6)	0.48 [0.21; 1.09] 0.080	0.72 [0.49; 1.06] 0.091	-0.17 [-0.36; 0.03] 0.089
Gain in BCVA of ≥ 15 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.043 ***					

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.673				
Region of the Americas					
N"/N'/N	72 / 90 / 90	73 / 83 / 83			
Gain in BCVA of ≥ 15 Letters, n (%)	32 (35.6)	32 (38.6)	0.90 [0.47; 1.72] 0.761	0.92 [0.63; 1.36] 0.683	-0.03 [-0.17; 0.11] 0.683
European Region					
N"/N'/N	56 / 69 / 69	61 / 75 / 75			
Gain in BCVA of ≥ 15 Letters, n (%)	30 (43.5)	32 (42.7)	0.86 [0.43; 1.73] 0.681	1.02 [0.70; 1.48] 0.922	0.01 [-0.15; 0.17] 0.922
Western Pacific Region					
N"/N'/N	26 / 30 / 30	27 / 29 / 29			
Gain in BCVA of ≥ 15 Letters, n (%)	8 (26.7)	10 (34.5)	0.50 [0.16; 1.61] 0.247	0.77 [0.36; 1.68] 0.517	-0.08 [-0.31; 0.16] 0.513
KITE: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.075				
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	17 / 26 / 26	14 / 21 / 21			
Gain in BCVA of ≥ 15 Letters, n (%)	8 (30.8)	9 (42.9)	0.59 [0.17; 1.99] 0.394	0.72 [0.34; 1.53] 0.392	-0.12 [-0.40; 0.16] 0.391
European Region					
N"/N'/N	114 / 135 / 135	113 / 132 / 132			
Gain in BCVA of ≥ 15 Letters, n (%)	67 (49.6)	44 (33.3)	2.08 [1.25; 3.45] 0.005 *	1.49 [1.11; 2.00] 0.008 *	0.16 [0.05; 0.28] 0.006 *
Western Pacific Region					
N"/N'/N	16 / 18 / 18	24 / 28 / 28			
Gain in BCVA of ≥ 15 Letters, n (%)	8 (44.4)	15 (53.6)	0.74 [0.22; 2.46] 0.618	0.83 [0.45; 1.54] 0.556	-0.09 [-0.39; 0.20] 0.544
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.113				
Region of the Americas					
N"/N'/N	72 / 90 / 90	73 / 83 / 83			
Gain in BCVA of ≥ 15 Letters, n (%)	32 (35.6)	32 (38.6)	1.34 [0.64; 2.80] 0.436	0.92 [0.63; 1.36] 0.684	-0.03 [-0.17; 0.11] 0.683

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	17 / 26 / 26	14 / 21 / 21			
Gain in BCVA of ≥ 15 Letters, n (%)	8 (30.8)	9 (42.9)	0.40 [0.11; 1.46] 0.165	0.72 [0.34; 1.53] 0.396	-0.12 [-0.40; 0.16] 0.391
European Region					
N"/N'/N	170 / 204 / 204	174 / 207 / 207			
Gain in BCVA of ≥ 15 Letters, n (%)	97 (47.5)	76 (36.7)	1.40 [0.91; 2.14] 0.122	1.30 [1.03; 1.63] 0.026 *	0.11 [0.01; 0.20] 0.025 *
Western Pacific Region					
N"/N'/N	42 / 48 / 48	51 / 57 / 57			
Gain in BCVA of ≥ 15 Letters, n (%)	16 (33.3)	25 (43.9)	0.62 [0.27; 1.40] 0.248	0.80 [0.49; 1.31] 0.379	-0.08 [-0.27; 0.10] 0.372
Gain in BCVA of ≥ 15 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.013 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.044 *				
Region of the Americas					
N"/N'/N	67 / 90 / 90	66 / 83 / 83			
Gain in BCVA of ≥ 15 Letters, n (%)	35 (38.9)	37 (44.6)	0.75 [0.40; 1.42] 0.377	0.87 [0.61; 1.24] 0.448	-0.06 [-0.20; 0.09] 0.448
European Region					
N"/N'/N	56 / 69 / 69	57 / 75 / 75			
Gain in BCVA of ≥ 15 Letters, n (%)	35 (50.7)	28 (37.3)	1.58 [0.79; 3.15] 0.197	1.36 [0.93; 1.98] 0.108	0.13 [-0.03; 0.29] 0.103
Western Pacific Region					
N"/N'/N	26 / 30 / 30	24 / 29 / 29			
Gain in BCVA of ≥ 15 Letters, n (%)	7 (23.3)	13 (44.8)	0.30 [0.09; 0.98] 0.045 *	0.52 [0.24; 1.12] 0.094	-0.21 [-0.45; 0.02] 0.074
KITE: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.050 *				
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	13 / 26 / 26	15 / 21 / 21			
Gain in BCVA of ≥ 15 Letters, n (%)	10 (38.5)	12 (57.1)	0.46 [0.14; 1.53] 0.208	0.67 [0.37; 1.24] 0.204	-0.19 [-0.47; 0.10] 0.195

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
European Region					
N"/N'/N	108 / 135 / 135	108 / 132 / 132			
Gain in BCVA of ≥ 15 Letters, n (%)	68 (50.4)	44 (33.3)	2.21 [1.33; 3.69] 0.002 *	1.51 [1.13; 2.03] 0.006 *	0.17 [0.05; 0.29] 0.004 *
Western Pacific Region					
N"/N'/N	12 / 18 / 18	23 / 28 / 28			
Gain in BCVA of ≥ 15 Letters, n (%)	11 (61.1)	11 (39.3)	2.74 [0.80; 9.43] 0.109	1.56 [0.86; 2.81] 0.142	0.22 [-0.07; 0.51] 0.139
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.031 *				
Region of the Americas					
N"/N'/N	67 / 90 / 90	66 / 83 / 83			
Gain in BCVA of ≥ 15 Letters, n (%)	35 (38.9)	37 (44.6)	1.14 [0.55; 2.36] 0.719	0.87 [0.61; 1.24] 0.449	-0.06 [-0.20; 0.09] 0.448
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	13 / 26 / 26	15 / 21 / 21			
Gain in BCVA of ≥ 15 Letters, n (%)	10 (38.5)	12 (57.1)	0.31 [0.09; 1.12] 0.073	0.67 [0.37; 1.24] 0.207	-0.19 [-0.47; 0.10] 0.195
European Region					
N"/N'/N	164 / 204 / 204	165 / 207 / 207			
Gain in BCVA of ≥ 15 Letters, n (%)	103 (50.5)	72 (34.8)	1.79 [1.17; 2.74] 0.007 *	1.45 [1.15; 1.83] 0.001 *	0.16 [0.06; 0.25] 0.001 *

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Western Pacific Region					
N''/N'/N	38 / 48 / 48	47 / 57 / 57			
Gain in BCVA of ≥ 15 Letters, n (%)	18 (37.5)	24 (42.1)	0.85 [0.38; 1.92] 0.698	0.93 [0.59; 1.47] 0.754	-0.03 [-0.22; 0.16] 0.757

N: Number of patients
N': Number of patients in the analysis
N'': Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 4.6 BCVA - Gain of 10 respectively 15 letters by diabetes type (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in BCVA of ≥ 10 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.085**					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.339				
Type 1					
N"/N'/N	9 / 12 / 12	6 / 6 / 6			
Gain in BCVA of ≥ 10 Letters, n (%)	7 (58.3)	2 (33.3)	2.02 [0.25; 16.53] 0.511	1.75 [0.51; 5.98] 0.372	0.25 [-0.22; 0.72] 0.296
Type 2					
N"/N'/N	145 / 177 / 177	155 / 181 / 181			
Gain in BCVA of ≥ 10 Letters, n (%)	92 (52.0)	105 (58.0)	0.71 [0.46; 1.10] 0.127	0.90 [0.74; 1.08] 0.253	-0.06 [-0.16; 0.04] 0.250
KITE: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.477				
Type 1					
N"/N'/N	18 / 19 / 19	7 / 7 / 7			
Gain in BCVA of ≥ 10 Letters, n (%)	14 (73.7)	6 (85.7)	0.52 [0.05; 5.64] 0.590	0.86 [0.57; 1.29] 0.464	-0.12 [-0.45; 0.21] 0.470
Type 2					
N"/N'/N	129 / 160 / 160	144 / 174 / 174			
Gain in BCVA of ≥ 10 Letters, n (%)	96 (60.0)	100 (57.5)	1.25 [0.80; 1.96] 0.327	1.04 [0.87; 1.25] 0.639	0.03 [-0.08; 0.13] 0.639
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.807				
Type 1					
N"/N'/N	27 / 31 / 31	13 / 13 / 13			
Gain in BCVA of ≥ 10 Letters, n (%)	21 (67.7)	8 (61.5)	1.14 [0.29; 4.58] 0.849	1.07 [0.67; 1.69] 0.786	0.04 [-0.26; 0.34] 0.781

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N"/N'/N	274 / 337 / 337	299 / 355 / 355			
Gain in BCVA of ≥ 10 Letters, n (%)	188 (55.8)	205 (57.7)	0.96 [0.70; 1.31] 0.790	0.97 [0.85; 1.10] 0.614	-0.02 [-0.09; 0.05] 0.613
Gain in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.019 ***					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.501				
Type 1					
N"/N'/N	10 / 12 / 12	4 / 6 / 6			
Gain in BCVA of ≥ 10 Letters, n (%)	8 (66.7)	3 (50.0)	1.48 [0.19; 11.43] 0.708	1.33 [0.55; 3.26] 0.529	0.17 [-0.31; 0.65] 0.497
Type 2					
N"/N'/N	139 / 177 / 177	143 / 181 / 181			
Gain in BCVA of ≥ 10 Letters, n (%)	97 (54.8)	110 (60.8)	0.72 [0.47; 1.12] 0.143	0.90 [0.75; 1.08] 0.254	-0.06 [-0.16; 0.04] 0.252
KITE: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.922				
Type 1					
N"/N'/N	17 / 19 / 19	5 / 7 / 7			
Gain in BCVA of ≥ 10 Letters, n (%)	15 (78.9)	5 (71.4)	1.63 [0.21; 12.36] 0.638	1.11 [0.66; 1.86] 0.708	0.08 [-0.31; 0.46] 0.699
Type 2					
N"/N'/N	116 / 160 / 160	141 / 174 / 174			
Gain in BCVA of ≥ 10 Letters, n (%)	95 (59.4)	93 (53.4)	1.47 [0.93; 2.30] 0.097	1.11 [0.92; 1.34] 0.275	0.06 [-0.05; 0.17] 0.274
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.554				
Type 1					
N"/N'/N	27 / 31 / 31	9 / 13 / 13			
Gain in BCVA of ≥ 10 Letters, n (%)	23 (74.2)	8 (61.5)	1.60 [0.39; 6.55] 0.516	1.19 [0.74; 1.89] 0.452	0.12 [-0.19; 0.42] 0.455

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N"/N'/N	255 / 337 / 337	284 / 355 / 355			
Gain in BCVA of ≥ 10 Letters, n (%)	192 (57.0)	203 (57.2)	1.03 [0.75; 1.41] 0.847	1.00 [0.88; 1.13] 0.951	-0.00 [-0.08; 0.07] 0.951
Gain in BCVA of ≥ 15 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.043 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.552				
Type 1					
N"/N'/N	9 / 12 / 12	6 / 6 / 6			
Gain in BCVA of ≥ 15 Letters, n (%)	6 (50.0)	2 (33.3)	1.50 [0.19; 12.06] 0.705	1.50 [0.42; 5.32] 0.530	0.17 [-0.30; 0.64] 0.488
Type 2					
N"/N'/N	145 / 177 / 177	155 / 181 / 181			
Gain in BCVA of ≥ 15 Letters, n (%)	64 (36.2)	72 (39.8)	0.78 [0.50; 1.22] 0.282	0.91 [0.70; 1.19] 0.481	-0.04 [-0.14; 0.06] 0.480
KITE: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.597				
Type 1					
N"/N'/N	18 / 19 / 19	7 / 7 / 7			
Gain in BCVA of ≥ 15 Letters, n (%)	11 (57.9)	4 (57.1)	0.91 [0.15; 5.43] 0.919	1.01 [0.48; 2.14] 0.973	0.01 [-0.42; 0.44] 0.973
Type 2					
N"/N'/N	129 / 160 / 160	144 / 174 / 174			
Gain in BCVA of ≥ 15 Letters, n (%)	72 (45.0)	64 (36.8)	1.50 [0.95; 2.35] 0.079	1.22 [0.94; 1.59] 0.128	0.08 [-0.02; 0.19] 0.126
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.960				
Type 1					
N"/N'/N	27 / 31 / 31	13 / 13 / 13			
Gain in BCVA of ≥ 15 Letters, n (%)	17 (54.8)	6 (46.2)	1.15 [0.30; 4.36] 0.836	1.17 [0.60; 2.25] 0.645	0.08 [-0.24; 0.40] 0.637

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N"/N'/N	274 / 337 / 337	299 / 355 / 355			
Gain in BCVA of ≥ 15 Letters, n (%)	136 (40.4)	136 (38.3)	1.11 [0.81; 1.52] 0.507	1.05 [0.88; 1.27] 0.574	0.02 [-0.05; 0.09] 0.575
Gain in BCVA of ≥ 15 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.013 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.142				
Type 1					
N"/N'/N	10 / 12 / 12	4 / 6 / 6			
Gain in BCVA of ≥ 15 Letters, n (%)	7 (58.3)	1 (16.7)	5.29 [0.45; 62.45] 0.186	3.50 [0.55; 22.30] 0.185	0.42 [0.01; 0.82] 0.046 *
Type 2					
N"/N'/N	139 / 177 / 177	143 / 181 / 181			
Gain in BCVA of ≥ 15 Letters, n (%)	70 (39.5)	77 (42.5)	0.81 [0.52; 1.26] 0.350	0.93 [0.72; 1.19] 0.565	-0.03 [-0.13; 0.07] 0.565
KITE: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.856				
Type 1					
N"/N'/N	17 / 19 / 19	5 / 7 / 7			
Gain in BCVA of ≥ 15 Letters, n (%)	14 (73.7)	4 (57.1)	2.03 [0.32; 12.88] 0.451	1.29 [0.64; 2.59] 0.474	0.17 [-0.25; 0.58] 0.436
Type 2					
N"/N'/N	116 / 160 / 160	141 / 174 / 174			
Gain in BCVA of ≥ 15 Letters, n (%)	75 (46.9)	63 (36.2)	1.71 [1.09; 2.68] 0.020 *	1.29 [1.00; 1.67] 0.049 *	0.11 [0.00; 0.21] 0.047 *
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.206				
Type 1					
N"/N'/N	27 / 31 / 31	9 / 13 / 13			
Gain in BCVA of ≥ 15 Letters, n (%)	21 (67.7)	5 (38.5)	2.99 [0.76; 11.83] 0.118	1.70 [0.85; 3.42] 0.089	0.28 [-0.03; 0.58] 0.076

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N"/N'/N	255 / 337 / 337	284 / 355 / 355			
Gain in BCVA of ≥ 15 Letters, n (%)	145 (43.0)	140 (39.4)	1.20 [0.88; 1.64] 0.243	1.09 [0.91; 1.30] 0.338	0.04 [-0.04; 0.11] 0.338

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 4.7 BCVA - Gain of 10 respectively 15 letters by HbA1c (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in BCVA of ≥ 10 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.085**					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.797				
< 7.5 %					
N"/N'/N	63 / 76 / 76	95 / 107 / 107			
Gain in BCVA of ≥ 10 Letters, n (%)	42 (55.3)	62 (57.9)	0.81 [0.43; 1.50] 0.499	0.95 [0.74; 1.24] 0.720	-0.03 [-0.17; 0.12] 0.718
≥ 7.5 %					
N"/N'/N	91 / 112 / 112	66 / 80 / 80			
Gain in BCVA of ≥ 10 Letters, n (%)	57 (50.9)	45 (56.3)	0.72 [0.39; 1.32] 0.290	0.90 [0.69; 1.18] 0.460	-0.05 [-0.20; 0.09] 0.462
KITE: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.821				
< 7.5 %					
N"/N'/N	66 / 82 / 82	79 / 96 / 96			
Gain in BCVA of ≥ 10 Letters, n (%)	48 (58.5)	52 (54.2)	1.30 [0.71; 2.40] 0.398	1.08 [0.83; 1.40] 0.557	0.04 [-0.10; 0.19] 0.557
≥ 7.5 %					
N"/N'/N	81 / 97 / 97	72 / 85 / 85			
Gain in BCVA of ≥ 10 Letters, n (%)	62 (63.9)	54 (63.5)	1.18 [0.63; 2.19] 0.608	1.01 [0.81; 1.25] 0.957	0.00 [-0.14; 0.14] 0.957
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.763				
< 7.5 %					
N"/N'/N	129 / 158 / 158	174 / 203 / 203			
Gain in BCVA of ≥ 10 Letters, n (%)	90 (57.0)	114 (56.2)	1.02 [0.66; 1.57] 0.941	1.01 [0.85; 1.22] 0.874	0.01 [-0.09; 0.11] 0.874

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N"/N'/N	172 / 209 / 209	138 / 165 / 165			
Gain in BCVA of ≥ 10 Letters, n (%)	119 (56.9)	99 (60.0)	0.93 [0.60; 1.42] 0.724	0.96 [0.81; 1.14] 0.622	-0.03 [-0.13; 0.07] 0.621
Gain in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.019 ***					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.116				
< 7.5 %					
N"/N'/N	59 / 76 / 76	91 / 107 / 107			
Gain in BCVA of ≥ 10 Letters, n (%)	38 (50.0)	67 (62.6)	0.52 [0.28; 0.97] 0.039 *	0.80 [0.61; 1.04] 0.100	-0.13 [-0.27; 0.02] 0.088
≥ 7.5 %					
N"/N'/N	89 / 112 / 112	56 / 80 / 80			
Gain in BCVA of ≥ 10 Letters, n (%)	67 (59.8)	46 (57.5)	1.04 [0.57; 1.92] 0.889	1.04 [0.82; 1.33] 0.748	0.02 [-0.12; 0.16] 0.748
KITE: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.974				
< 7.5 %					
N"/N'/N	61 / 82 / 82	75 / 96 / 96			
Gain in BCVA of ≥ 10 Letters, n (%)	51 (62.2)	52 (54.2)	1.53 [0.82; 2.84] 0.179	1.15 [0.89; 1.47] 0.278	0.08 [-0.06; 0.23] 0.277
≥ 7.5 %					
N"/N'/N	72 / 97 / 97	71 / 85 / 85			
Gain in BCVA of ≥ 10 Letters, n (%)	59 (60.8)	46 (54.1)	1.55 [0.84; 2.86] 0.160	1.12 [0.87; 1.45] 0.365	0.07 [-0.08; 0.21] 0.360
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.258				
< 7.5 %					
N"/N'/N	120 / 158 / 158	166 / 203 / 203			
Gain in BCVA of ≥ 10 Letters, n (%)	89 (56.3)	119 (58.6)	0.90 [0.58; 1.39] 0.622	0.96 [0.80; 1.15] 0.659	-0.02 [-0.13; 0.08] 0.661

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N"/N'/N	161 / 209 / 209	127 / 165 / 165			
Gain in BCVA of ≥ 10 Letters, n (%)	126 (60.3)	92 (55.8)	1.28 [0.83; 1.96] 0.267	1.08 [0.91; 1.29] 0.385	0.04 [-0.06; 0.15] 0.384
Gain in BCVA of ≥ 15 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.043 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.754				
< 7.5 %					
N"/N'/N	63 / 76 / 76	95 / 107 / 107			
Gain in BCVA of ≥ 15 Letters, n (%)	28 (36.8)	41 (38.3)	0.87 [0.46; 1.63] 0.657	0.96 [0.66; 1.41] 0.840	-0.01 [-0.16; 0.13] 0.839
≥ 7.5 %					
N"/N'/N	91 / 112 / 112	66 / 80 / 80			
Gain in BCVA of ≥ 15 Letters, n (%)	42 (37.5)	33 (41.3)	0.75 [0.41; 1.39] 0.364	0.91 [0.64; 1.30] 0.598	-0.04 [-0.18; 0.10] 0.600
KITE: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.385				
< 7.5 %					
N"/N'/N	66 / 82 / 82	79 / 96 / 96			
Gain in BCVA of ≥ 15 Letters, n (%)	37 (45.1)	31 (32.3)	1.80 [0.97; 3.36] 0.063	1.40 [0.96; 2.03] 0.081	0.13 [-0.01; 0.27] 0.078
≥ 7.5 %					
N"/N'/N	81 / 97 / 97	72 / 85 / 85			
Gain in BCVA of ≥ 15 Letters, n (%)	46 (47.4)	37 (43.5)	1.23 [0.68; 2.25] 0.492	1.09 [0.79; 1.50] 0.600	0.04 [-0.11; 0.18] 0.598
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.409				
< 7.5 %					
N"/N'/N	129 / 158 / 158	174 / 203 / 203			
Gain in BCVA of ≥ 15 Letters, n (%)	65 (41.1)	72 (35.5)	1.27 [0.82; 1.97] 0.285	1.16 [0.89; 1.51] 0.273	0.06 [-0.04; 0.16] 0.274

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N"/N'/N	172 / 209 / 209	138 / 165 / 165			
Gain in BCVA of ≥ 15 Letters, n (%)	88 (42.1)	70 (42.4)	0.98 [0.64; 1.50] 0.934	1.00 [0.79; 1.27] 0.998	0.00 [-0.10; 0.10] 0.998
Gain in BCVA of ≥ 15 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.013 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.659				
< 7.5 %					
N"/N'/N	59 / 76 / 76	91 / 107 / 107			
Gain in BCVA of ≥ 15 Letters, n (%)	29 (38.2)	44 (41.1)	0.78 [0.42; 1.46] 0.437	0.93 [0.64; 1.34] 0.688	-0.03 [-0.17; 0.11] 0.686
≥ 7.5 %					
N"/N'/N	89 / 112 / 112	56 / 80 / 80			
Gain in BCVA of ≥ 15 Letters, n (%)	48 (42.9)	34 (42.5)	0.95 [0.52; 1.74] 0.866	1.01 [0.72; 1.41] 0.961	0.00 [-0.14; 0.15] 0.961
KITE: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.935				
< 7.5 %					
N"/N'/N	61 / 82 / 82	75 / 96 / 96			
Gain in BCVA of ≥ 15 Letters, n (%)	42 (51.2)	36 (37.5)	1.87 [1.01; 3.45] 0.045 *	1.37 [0.98; 1.91] 0.067	0.14 [-0.01; 0.28] 0.064
≥ 7.5 %					
N"/N'/N	72 / 97 / 97	71 / 85 / 85			
Gain in BCVA of ≥ 15 Letters, n (%)	47 (48.5)	31 (36.5)	1.81 [0.98; 3.33] 0.058	1.33 [0.94; 1.88] 0.109	0.12 [-0.02; 0.26] 0.100
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.841				
< 7.5 %					
N"/N'/N	120 / 158 / 158	166 / 203 / 203			
Gain in BCVA of ≥ 15 Letters, n (%)	71 (44.9)	80 (39.4)	1.25 [0.81; 1.93] 0.307	1.14 [0.89; 1.45] 0.307	0.05 [-0.05; 0.16] 0.308

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N"/N'/N	161 / 209 / 209	127 / 165 / 165			
Gain in BCVA of ≥ 15 Letters, n (%)	95 (45.5)	65 (39.4)	1.33 [0.87; 2.05] 0.186	1.15 [0.91; 1.47] 0.240	0.06 [-0.04; 0.16] 0.237

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 4.8 BCVA - Gain of 10 respectively 15 letters by duration of DME (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in BCVA of ≥ 10 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.085**					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.458				
≤ 3 months					
N"/N'/N	103 / 120 / 120	97 / 110 / 110			
Gain in BCVA of ≥ 10 Letters, n (%)	71 (59.2)	68 (61.8)	0.82 [0.47; 1.42] 0.474	0.96 [0.78; 1.18] 0.681	-0.03 [-0.15; 0.10] 0.681
> 3 - < 12 months					
N"/N'/N	24 / 30 / 30	31 / 39 / 39			
Gain in BCVA of ≥ 10 Letters, n (%)	16 (53.3)	22 (56.4)	0.91 [0.33; 2.47] 0.846	0.95 [0.61; 1.46] 0.800	-0.03 [-0.27; 0.21] 0.799
≥ 12 months					
N"/N'/N	27 / 39 / 39	33 / 38 / 38			
Gain in BCVA of ≥ 10 Letters, n (%)	12 (30.8)	17 (44.7)	0.42 [0.16; 1.12] 0.083	0.69 [0.38; 1.24] 0.213	-0.14 [-0.35; 0.07] 0.202
KITE: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.153				
≤ 3 months					
N"/N'/N	68 / 85 / 85	75 / 92 / 92			
Gain in BCVA of ≥ 10 Letters, n (%)	50 (58.8)	44 (47.8)	1.90 [1.02; 3.53] 0.043 *	1.23 [0.93; 1.62] 0.144	0.11 [-0.04; 0.26] 0.140
> 3 - < 12 months					
N"/N'/N	44 / 51 / 51	42 / 49 / 49			
Gain in BCVA of ≥ 10 Letters, n (%)	33 (64.7)	35 (71.4)	0.76 [0.32; 1.81] 0.541	0.91 [0.69; 1.19] 0.472	-0.07 [-0.25; 0.11] 0.470
≥ 12 months					
N"/N'/N	35 / 43 / 43	34 / 40 / 40			
Gain in BCVA of ≥ 10 Letters, n (%)	27 (62.8)	27 (67.5)	0.83 [0.33; 2.08] 0.684	0.93 [0.68; 1.27] 0.653	-0.05 [-0.25; 0.16] 0.652

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.149				
≤ 3 months					
N"/N'/N	171 / 205 / 205	172 / 202 / 202			
Gain in BCVA of ≥ 10 Letters, n (%)	121 (59.0)	112 (55.4)	1.28 [0.85; 1.92] 0.242	1.06 [0.90; 1.25] 0.503	0.03 [-0.06; 0.13] 0.503
> 3 - < 12 months					
N"/N'/N	68 / 81 / 81	73 / 88 / 88			
Gain in BCVA of ≥ 10 Letters, n (%)	49 (60.5)	57 (64.8)	0.80 [0.42; 1.52] 0.492	0.92 [0.73; 1.16] 0.481	-0.05 [-0.20; 0.09] 0.477
≥ 12 months					
N"/N'/N	62 / 82 / 82	67 / 78 / 78			
Gain in BCVA of ≥ 10 Letters, n (%)	39 (47.6)	44 (56.4)	0.63 [0.33; 1.19] 0.155	0.84 [0.63; 1.12] 0.231	-0.09 [-0.24; 0.06] 0.226
Gain in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.019 ***					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.530				
≤ 3 months					
N"/N'/N	99 / 120 / 120	86 / 110 / 110			
Gain in BCVA of ≥ 10 Letters, n (%)	70 (58.3)	69 (62.7)	0.77 [0.44; 1.33] 0.342	0.93 [0.75; 1.15] 0.496	-0.04 [-0.17; 0.08] 0.495
> 3 - < 12 months					
N"/N'/N	22 / 30 / 30	27 / 39 / 39			
Gain in BCVA of ≥ 10 Letters, n (%)	19 (63.3)	24 (61.5)	1.11 [0.40; 3.09] 0.836	1.03 [0.71; 1.49] 0.878	0.02 [-0.21; 0.25] 0.879
≥ 12 months					
N"/N'/N	28 / 39 / 39	34 / 38 / 38			
Gain in BCVA of ≥ 10 Letters, n (%)	16 (41.0)	20 (52.6)	0.50 [0.20; 1.29] 0.153	0.78 [0.48; 1.26] 0.311	-0.12 [-0.34; 0.11] 0.304

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.981				
≤ 3 months					
N"/N'/N	58 / 85 / 85	73 / 92 / 92			
Gain in BCVA of ≥ 10 Letters, n (%)	49 (57.6)	48 (52.2)	1.52 [0.82; 2.83] 0.185	1.10 [0.85; 1.44] 0.465	0.05 [-0.09; 0.20] 0.464
> 3 - < 12 months					
N"/N'/N	43 / 51 / 51	38 / 49 / 49			
Gain in BCVA of ≥ 10 Letters, n (%)	36 (70.6)	30 (61.2)	1.61 [0.69; 3.79] 0.272	1.15 [0.87; 1.53] 0.327	0.09 [-0.09; 0.28] 0.321
≥ 12 months					
N"/N'/N	32 / 43 / 43	35 / 40 / 40			
Gain in BCVA of ≥ 10 Letters, n (%)	25 (58.1)	20 (50.0)	1.43 [0.59; 3.47] 0.435	1.16 [0.78; 1.74] 0.460	0.08 [-0.13; 0.30] 0.456
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.673				
≤ 3 months					
N"/N'/N	157 / 205 / 205	159 / 202 / 202			
Gain in BCVA of ≥ 10 Letters, n (%)	119 (58.0)	117 (57.9)	1.09 [0.72; 1.64] 0.678	1.00 [0.85; 1.18] 0.983	-0.00 [-0.10; 0.09] 0.983
> 3 - < 12 months					
N"/N'/N	65 / 81 / 81	65 / 88 / 88			
Gain in BCVA of ≥ 10 Letters, n (%)	55 (67.9)	54 (61.4)	1.31 [0.68; 2.53] 0.414	1.10 [0.88; 1.38] 0.396	0.06 [-0.08; 0.21] 0.392
≥ 12 months					
N"/N'/N	60 / 82 / 82	69 / 78 / 78			
Gain in BCVA of ≥ 10 Letters, n (%)	41 (50.0)	40 (51.3)	0.87 [0.46; 1.65] 0.666	0.97 [0.72; 1.32] 0.863	-0.01 [-0.17; 0.14] 0.863
Gain in BCVA of ≥ 15 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.043 ***					

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.452				
≤ 3 months					
N"/N'/N	103 / 120 / 120	97 / 110 / 110			
Gain in BCVA of ≥ 15 Letters, n (%)	53 (44.2)	49 (44.5)	0.89 [0.52; 1.53] 0.684	0.99 [0.74; 1.32] 0.954	-0.00 [-0.13; 0.12] 0.954
> 3 - < 12 months					
N"/N'/N	24 / 30 / 30	31 / 39 / 39			
Gain in BCVA of ≥ 15 Letters, n (%)	11 (36.7)	15 (38.5)	0.97 [0.35; 2.68] 0.946	0.95 [0.52; 1.76] 0.879	-0.02 [-0.25; 0.21] 0.879
≥ 12 months					
N"/N'/N	27 / 39 / 39	33 / 38 / 38			
Gain in BCVA of ≥ 15 Letters, n (%)	6 (15.4)	10 (26.3)	0.41 [0.13; 1.30] 0.131	0.58 [0.24; 1.45] 0.247	-0.11 [-0.29; 0.07] 0.234
KITE: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.077				
≤ 3 months					
N"/N'/N	68 / 85 / 85	75 / 92 / 92			
Gain in BCVA of ≥ 15 Letters, n (%)	41 (48.2)	29 (31.5)	2.32 [1.23; 4.38] 0.009 *	1.53 [1.05; 2.22] 0.025 *	0.17 [0.02; 0.31] 0.021 *
> 3 - < 12 months					
N"/N'/N	44 / 51 / 51	42 / 49 / 49			
Gain in BCVA of ≥ 15 Letters, n (%)	24 (47.1)	19 (38.8)	1.40 [0.62; 3.14] 0.420	1.21 [0.77; 1.92] 0.406	0.08 [-0.11; 0.28] 0.401
≥ 12 months					
N"/N'/N	35 / 43 / 43	34 / 40 / 40			
Gain in BCVA of ≥ 15 Letters, n (%)	18 (41.9)	20 (50.0)	0.66 [0.27; 1.61] 0.363	0.84 [0.52; 1.34] 0.458	-0.08 [-0.30; 0.13] 0.456
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.071				
≤ 3 months					
N"/N'/N	171 / 205 / 205	172 / 202 / 202			
Gain in BCVA of ≥ 15 Letters, n (%)	94 (45.9)	78 (38.6)	1.45 [0.97; 2.18] 0.072	1.18 [0.94; 1.48] 0.151	0.07 [-0.03; 0.17] 0.150

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 3 - < 12 months					
N"/N'/N	68 / 81 / 81	73 / 88 / 88			
Gain in BCVA of ≥ 15 Letters, n (%)	35 (43.2)	34 (38.6)	1.14 [0.60; 2.16] 0.685	1.11 [0.77; 1.60] 0.581	0.04 [-0.11; 0.19] 0.579
≥ 12 months					
N"/N'/N	62 / 82 / 82	67 / 78 / 78			
Gain in BCVA of ≥ 15 Letters, n (%)	24 (29.3)	30 (38.5)	0.57 [0.29; 1.13] 0.107	0.75 [0.49; 1.15] 0.191	-0.09 [-0.24; 0.05] 0.187
Gain in BCVA of ≥ 15 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.013 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.662				
≤ 3 months					
N"/N'/N	99 / 120 / 120	86 / 110 / 110			
Gain in BCVA of ≥ 15 Letters, n (%)	54 (45.0)	50 (45.5)	0.91 [0.53; 1.55] 0.720	0.99 [0.74; 1.32] 0.945	-0.00 [-0.13; 0.12] 0.945
> 3 - < 12 months					
N"/N'/N	22 / 30 / 30	27 / 39 / 39			
Gain in BCVA of ≥ 15 Letters, n (%)	14 (46.7)	17 (43.6)	1.15 [0.43; 3.12] 0.782	1.07 [0.63; 1.81] 0.798	0.03 [-0.21; 0.27] 0.799
≥ 12 months					
N"/N'/N	28 / 39 / 39	34 / 38 / 38			
Gain in BCVA of ≥ 15 Letters, n (%)	9 (23.1)	11 (28.9)	0.59 [0.21; 1.71] 0.333	0.80 [0.37; 1.70] 0.558	-0.06 [-0.25; 0.14] 0.556
KITE: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.990				
≤ 3 months					
N"/N'/N	58 / 85 / 85	73 / 92 / 92			
Gain in BCVA of ≥ 15 Letters, n (%)	42 (49.4)	35 (38.0)	1.86 [1.00; 3.46] 0.049 *	1.30 [0.93; 1.82] 0.130	0.11 [-0.03; 0.26] 0.125
> 3 - < 12 months					
N"/N'/N	43 / 51 / 51	38 / 49 / 49			
Gain in BCVA of ≥ 15 Letters, n (%)	25 (49.0)	17 (34.7)	1.88 [0.83; 4.27] 0.131	1.41 [0.88; 2.27] 0.154	0.14 [-0.05; 0.33] 0.142

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months					
N"/N'/N	32 / 43 / 43	35 / 40 / 40			
Gain in BCVA of ≥ 15 Letters, n (%)	22 (51.2)	15 (37.5)	1.74 [0.71; 4.24] 0.227	1.36 [0.83; 2.24] 0.219	0.14 [-0.08; 0.35] 0.206
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.866				
≤ 3 months					
N"/N'/N	157 / 205 / 205	159 / 202 / 202			
Gain in BCVA of ≥ 15 Letters, n (%)	96 (46.8)	85 (42.1)	1.32 [0.88; 1.98] 0.175	1.11 [0.89; 1.38] 0.343	0.05 [-0.05; 0.14] 0.342
> 3 - < 12 months					
N"/N'/N	65 / 81 / 81	65 / 88 / 88			
Gain in BCVA of ≥ 15 Letters, n (%)	39 (48.1)	34 (38.6)	1.42 [0.76; 2.68] 0.275	1.26 [0.88; 1.78] 0.204	0.10 [-0.05; 0.25] 0.199
≥ 12 months					
N"/N'/N	60 / 82 / 82	69 / 78 / 78			
Gain in BCVA of ≥ 15 Letters, n (%)	31 (37.8)	26 (33.3)	1.12 [0.57; 2.17] 0.746	1.13 [0.74; 1.71] 0.569	0.04 [-0.10; 0.19] 0.568

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 4.9 BCVA - Gain of 10 respectively 15 letters by DME type (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in BCVA of ≥ 10 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.085**					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.150				
focal					
N"/N'/N	51 / 59 / 59	41 / 48 / 48			
Gain in BCVA of ≥ 10 Letters, n (%)	31 (52.5)	23 (47.9)	1.21 [0.55; 2.68] 0.639	1.10 [0.75; 1.61] 0.636	0.05 [-0.14; 0.24] 0.634
diffuse					
N"/N'/N	101 / 127 / 127	116 / 134 / 134			
Gain in BCVA of ≥ 10 Letters, n (%)	66 (52.0)	81 (60.4)	0.60 [0.36; 1.01] 0.055	0.86 [0.69; 1.07] 0.171	-0.08 [-0.20; 0.04] 0.166
KITE: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.627				
focal					
N"/N'/N	48 / 63 / 63	52 / 66 / 66			
Gain in BCVA of ≥ 10 Letters, n (%)	35 (55.6)	36 (54.5)	1.10 [0.54; 2.23] 0.794	1.02 [0.75; 1.39] 0.908	0.01 [-0.16; 0.18] 0.908
diffuse					
N"/N'/N	98 / 115 / 115	95 / 109 / 109			
Gain in BCVA of ≥ 10 Letters, n (%)	75 (65.2)	67 (61.5)	1.37 [0.78; 2.41] 0.268	1.06 [0.87; 1.30] 0.561	0.04 [-0.09; 0.16] 0.560
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.563				
focal					
N"/N'/N	99 / 122 / 122	93 / 114 / 114			
Gain in BCVA of ≥ 10 Letters, n (%)	66 (54.1)	59 (51.8)	1.11 [0.66; 1.89] 0.692	1.05 [0.83; 1.34] 0.686	0.03 [-0.10; 0.15] 0.685

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N"/N'/N	199 / 242 / 242	211 / 243 / 243			
Gain in BCVA of ≥ 10 Letters, n (%)	141 (58.3)	148 (60.9)	0.92 [0.63; 1.34] 0.657	0.95 [0.82; 1.10] 0.525	-0.03 [-0.12; 0.06] 0.525
Gain in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.019 ***					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.377				
focal					
N"/N'/N	51 / 59 / 59	35 / 48 / 48			
Gain in BCVA of ≥ 10 Letters, n (%)	31 (52.5)	25 (52.1)	0.99 [0.45; 2.17] 0.974	1.01 [0.70; 1.45] 0.962	0.00 [-0.19; 0.19] 0.962
diffuse					
N"/N'/N	96 / 127 / 127	108 / 134 / 134			
Gain in BCVA of ≥ 10 Letters, n (%)	72 (56.7)	86 (64.2)	0.64 [0.38; 1.08] 0.097	0.88 [0.72; 1.08] 0.219	-0.07 [-0.19; 0.04] 0.215
KITE: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.040 *				
focal					
N"/N'/N	46 / 63 / 63	54 / 66 / 66			
Gain in BCVA of ≥ 10 Letters, n (%)	33 (52.4)	38 (57.6)	0.85 [0.41; 1.73] 0.648	0.91 [0.66; 1.24] 0.554	-0.05 [-0.22; 0.12] 0.553
diffuse					
N"/N'/N	86 / 115 / 115	88 / 109 / 109			
Gain in BCVA of ≥ 10 Letters, n (%)	77 (67.0)	58 (53.2)	2.20 [1.24; 3.88] 0.007 *	1.26 [1.01; 1.56] 0.039 *	0.14 [0.01; 0.26] 0.034 *
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.375				
focal					
N"/N'/N	97 / 122 / 122	89 / 114 / 114			
Gain in BCVA of ≥ 10 Letters, n (%)	64 (52.5)	63 (55.3)	0.87 [0.51; 1.47] 0.595	0.95 [0.75; 1.21] 0.685	-0.03 [-0.15; 0.10] 0.684

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N"/N'/N	182 / 242 / 242	196 / 243 / 243			
Gain in BCVA of ≥ 10 Letters, n (%)	149 (61.6)	144 (59.3)	1.16 [0.80; 1.70] 0.431	1.04 [0.90; 1.20] 0.602	0.02 [-0.06; 0.11] 0.604
Gain in BCVA of ≥ 15 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.043 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.436				
focal					
N"/N'/N	51 / 59 / 59	41 / 48 / 48			
Gain in BCVA of ≥ 15 Letters, n (%)	23 (39.0)	18 (37.5)	1.09 [0.48; 2.47] 0.828	1.04 [0.64; 1.69] 0.875	0.01 [-0.17; 0.20] 0.875
diffuse					
N"/N'/N	101 / 127 / 127	116 / 134 / 134			
Gain in BCVA of ≥ 15 Letters, n (%)	46 (36.2)	53 (39.6)	0.74 [0.44; 1.26] 0.269	0.92 [0.67; 1.25] 0.580	-0.03 [-0.15; 0.08] 0.579
KITE: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.943				
focal					
N"/N'/N	48 / 63 / 63	52 / 66 / 66			
Gain in BCVA of ≥ 15 Letters, n (%)	26 (41.3)	22 (33.3)	1.43 [0.69; 2.96] 0.334	1.24 [0.79; 1.94] 0.353	0.08 [-0.09; 0.25] 0.350
diffuse					
N"/N'/N	98 / 115 / 115	95 / 109 / 109			
Gain in BCVA of ≥ 15 Letters, n (%)	57 (49.6)	45 (41.3)	1.48 [0.86; 2.55] 0.158	1.20 [0.90; 1.60] 0.217	0.08 [-0.05; 0.21] 0.212
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.670				
focal					
N"/N'/N	99 / 122 / 122	93 / 114 / 114			
Gain in BCVA of ≥ 15 Letters, n (%)	49 (40.2)	40 (35.1)	1.26 [0.73; 2.17] 0.407	1.14 [0.82; 1.59] 0.429	0.05 [-0.07; 0.17] 0.426

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N"/N'/N	199 / 242 / 242	211 / 243 / 243			
Gain in BCVA of ≥ 15 Letters, n (%)	103 (42.6)	98 (40.3)	1.09 [0.75; 1.58] 0.649	1.05 [0.85; 1.30] 0.650	0.02 [-0.07; 0.11] 0.649
Gain in BCVA of ≥ 15 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.013 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.925				
focal					
N"/N'/N	51 / 59 / 59	35 / 48 / 48			
Gain in BCVA of ≥ 15 Letters, n (%)	23 (39.0)	20 (41.7)	0.85 [0.38; 1.89] 0.685	0.94 [0.59; 1.49] 0.778	-0.03 [-0.21; 0.16] 0.778
diffuse					
N"/N'/N	96 / 127 / 127	108 / 134 / 134			
Gain in BCVA of ≥ 15 Letters, n (%)	53 (41.7)	56 (41.8)	0.89 [0.53; 1.48] 0.645	1.00 [0.75; 1.33] 0.992	-0.00 [-0.12; 0.12] 0.992
KITE: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.423				
focal					
N"/N'/N	46 / 63 / 63	54 / 66 / 66			
Gain in BCVA of ≥ 15 Letters, n (%)	28 (44.4)	24 (36.4)	1.46 [0.71; 3.00] 0.302	1.22 [0.80; 1.86] 0.351	0.08 [-0.09; 0.25] 0.348
diffuse					
N"/N'/N	86 / 115 / 115	88 / 109 / 109			
Gain in BCVA of ≥ 15 Letters, n (%)	61 (53.0)	41 (37.6)	2.11 [1.22; 3.67] 0.008 *	1.41 [1.05; 1.90] 0.023 *	0.15 [0.03; 0.28] 0.019 *
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.512				
focal					
N"/N'/N	97 / 122 / 122	89 / 114 / 114			
Gain in BCVA of ≥ 15 Letters, n (%)	51 (41.8)	44 (38.6)	1.13 [0.66; 1.93] 0.664	1.08 [0.79; 1.48] 0.616	0.03 [-0.09; 0.16] 0.615

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N"/N'/N	182 / 242 / 242	196 / 243 / 243			
Gain in BCVA of ≥ 15 Letters, n (%)	114 (47.1)	97 (39.9)	1.40 [0.97; 2.03] 0.075	1.18 [0.96; 1.45] 0.116	0.07 [-0.02; 0.16] 0.115

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 4.10 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in BCVA of ≥ 10 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.085**					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.161				
< 450 µm					
N"/N'/N	87 / 107 / 107	83 / 96 / 96			
Gain in BCVA of ≥ 10 Letters, n (%)	60 (56.1)	50 (52.1)	1.02 [0.57; 1.82] 0.949	1.08 [0.83; 1.39] 0.570	0.04 [-0.10; 0.18] 0.569
≥ 450 - < 650 µm					
N"/N'/N	58 / 70 / 70	61 / 71 / 71			
Gain in BCVA of ≥ 10 Letters, n (%)	33 (47.1)	43 (60.6)	0.53 [0.26; 1.07] 0.078	0.78 [0.57; 1.06] 0.114	-0.13 [-0.30; 0.03] 0.107
≥ 650 µm					
N"/N'/N	9 / 12 / 12	17 / 20 / 20			
Gain in BCVA of ≥ 10 Letters, n (%)	6 (50.0)	14 (70.0)	0.27 [0.06; 1.27] 0.097	0.71 [0.38; 1.35] 0.299	-0.20 [-0.55; 0.15] 0.259
KITE: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.360				
< 450 µm					
N"/N'/N	65 / 85 / 85	63 / 82 / 82			
Gain in BCVA of ≥ 10 Letters, n (%)	45 (52.9)	41 (50.0)	1.15 [0.62; 2.14] 0.660	1.06 [0.79; 1.42] 0.704	0.03 [-0.12; 0.18] 0.704
≥ 450 - < 650 µm					
N"/N'/N	66 / 74 / 74	71 / 79 / 79			
Gain in BCVA of ≥ 10 Letters, n (%)	53 (71.6)	51 (64.6)	1.68 [0.83; 3.40] 0.146	1.11 [0.89; 1.38] 0.349	0.07 [-0.08; 0.22] 0.347
≥ 650 µm					
N"/N'/N	16 / 20 / 20	16 / 19 / 19			
Gain in BCVA of ≥ 10 Letters, n (%)	12 (60.0)	14 (73.7)	0.56 [0.14; 2.24] 0.414	0.81 [0.52; 1.27] 0.368	-0.14 [-0.43; 0.16] 0.358

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.222				
< 450 µm					
N"/N'/N	152 / 192 / 192	146 / 178 / 178			
Gain in BCVA of ≥ 10 Letters, n (%)	105 (54.7)	91 (51.1)	1.12 [0.73; 1.71] 0.597	1.07 [0.88; 1.30] 0.499	0.04 [-0.07; 0.14] 0.498
≥ 450 - < 650 µm					
N"/N'/N	124 / 144 / 144	132 / 150 / 150			
Gain in BCVA of ≥ 10 Letters, n (%)	86 (59.7)	94 (62.7)	0.98 [0.60; 1.59] 0.923	0.96 [0.80; 1.15] 0.624	-0.03 [-0.14; 0.08] 0.625
≥ 650 µm					
N"/N'/N	25 / 32 / 32	33 / 39 / 39			
Gain in BCVA of ≥ 10 Letters, n (%)	18 (56.3)	28 (71.8)	0.42 [0.15; 1.17] 0.097	0.77 [0.53; 1.12] 0.158	-0.16 [-0.39; 0.06] 0.150
Gain in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.019 ***					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.680				
< 450 µm					
N"/N'/N	86 / 107 / 107	76 / 96 / 96			
Gain in BCVA of ≥ 10 Letters, n (%)	59 (55.1)	54 (56.3)	0.83 [0.47; 1.48] 0.531	0.98 [0.77; 1.25] 0.874	-0.01 [-0.15; 0.13] 0.874
≥ 450 - < 650 µm					
N"/N'/N	55 / 70 / 70	55 / 71 / 71			
Gain in BCVA of ≥ 10 Letters, n (%)	39 (55.7)	45 (63.4)	0.70 [0.34; 1.41] 0.312	0.88 [0.67; 1.16] 0.356	-0.08 [-0.24; 0.08] 0.352
≥ 650 µm					
N"/N'/N	8 / 12 / 12	16 / 20 / 20			
Gain in BCVA of ≥ 10 Letters, n (%)	7 (58.3)	14 (70.0)	0.41 [0.09; 1.90] 0.253	0.83 [0.48; 1.46] 0.522	-0.12 [-0.46; 0.23] 0.506

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.433				
< 450 µm					
N"/N'/N	62 / 85 / 85	63 / 82 / 82			
Gain in BCVA of ≥ 10 Letters, n (%)	44 (51.8)	40 (48.8)	1.13 [0.60; 2.12] 0.701	1.06 [0.78; 1.44] 0.700	0.03 [-0.12; 0.18] 0.700
≥ 450 - < 650 µm					
N"/N'/N	56 / 74 / 74	67 / 79 / 79			
Gain in BCVA of ≥ 10 Letters, n (%)	52 (70.3)	47 (59.5)	2.06 [1.03; 4.14] 0.042 *	1.18 [0.93; 1.49] 0.164	0.11 [-0.04; 0.26] 0.160
≥ 650 µm					
N"/N'/N	15 / 20 / 20	15 / 19 / 19			
Gain in BCVA of ≥ 10 Letters, n (%)	14 (70.0)	11 (57.9)	1.85 [0.48; 7.15] 0.375	1.21 [0.75; 1.95] 0.437	0.12 [-0.18; 0.42] 0.428
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.832				
< 450 µm					
N"/N'/N	148 / 192 / 192	139 / 178 / 178			
Gain in BCVA of ≥ 10 Letters, n (%)	103 (53.6)	94 (52.8)	1.00 [0.65; 1.53] 0.995	1.01 [0.84; 1.23] 0.887	0.01 [-0.09; 0.11] 0.886
≥ 450 - < 650 µm					
N"/N'/N	111 / 144 / 144	122 / 150 / 150			
Gain in BCVA of ≥ 10 Letters, n (%)	91 (63.2)	92 (61.3)	1.20 [0.74; 1.96] 0.464	1.03 [0.86; 1.23] 0.734	0.02 [-0.09; 0.13] 0.734
≥ 650 µm					
N"/N'/N	23 / 32 / 32	31 / 39 / 39			
Gain in BCVA of ≥ 10 Letters, n (%)	21 (65.6)	25 (64.1)	0.95 [0.35; 2.60] 0.917	1.03 [0.72; 1.48] 0.880	0.02 [-0.21; 0.25] 0.879
Gain in BCVA of ≥ 15 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.043 ***					

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.133				
< 450 µm					
N"/N'/N	87 / 107 / 107	83 / 96 / 96			
Gain in BCVA of ≥ 15 Letters, n (%)	45 (42.1)	35 (36.5)	1.11 [0.62; 2.00] 0.726	1.15 [0.82; 1.63] 0.417	0.06 [-0.08; 0.19] 0.414
≥ 450 - < 650 µm					
N"/N'/N	58 / 70 / 70	61 / 71 / 71			
Gain in BCVA of ≥ 15 Letters, n (%)	21 (30.0)	27 (38.0)	0.64 [0.31; 1.32] 0.228	0.79 [0.50; 1.26] 0.318	-0.08 [-0.24; 0.08] 0.313
≥ 650 µm					
N"/N'/N	9 / 12 / 12	17 / 20 / 20			
Gain in BCVA of ≥ 15 Letters, n (%)	4 (33.3)	12 (60.0)	0.23 [0.05; 1.09] 0.065	0.56 [0.23; 1.33] 0.189	-0.27 [-0.61; 0.08] 0.127
KITE: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.299				
< 450 µm					
N"/N'/N	65 / 85 / 85	63 / 82 / 82			
Gain in BCVA of ≥ 15 Letters, n (%)	38 (44.7)	25 (30.5)	1.76 [0.92; 3.36] 0.088	1.47 [0.98; 2.19] 0.063	0.14 [-0.00; 0.29] 0.055
≥ 450 - < 650 µm					
N"/N'/N	66 / 74 / 74	71 / 79 / 79			
Gain in BCVA of ≥ 15 Letters, n (%)	37 (50.0)	33 (41.8)	1.60 [0.83; 3.10] 0.161	1.20 [0.85; 1.69] 0.308	0.08 [-0.08; 0.24] 0.306
≥ 650 µm					
N"/N'/N	16 / 20 / 20	16 / 19 / 19			
Gain in BCVA of ≥ 15 Letters, n (%)	8 (40.0)	10 (52.6)	0.57 [0.16; 2.08] 0.396	0.76 [0.38; 1.51] 0.433	-0.13 [-0.44; 0.18] 0.425
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.055				
< 450 µm					
N"/N'/N	152 / 192 / 192	146 / 178 / 178			
Gain in BCVA of ≥ 15 Letters, n (%)	83 (43.2)	60 (33.7)	1.45 [0.94; 2.23] 0.096	1.28 [0.99; 1.66] 0.062	0.09 [-0.00; 0.19] 0.060

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 450 - < 650 µm					
N"/N'/N	124 / 144 / 144	132 / 150 / 150			
Gain in BCVA of ≥ 15 Letters, n (%)	58 (40.3)	60 (40.0)	1.08 [0.67; 1.74] 0.756	1.01 [0.77; 1.33] 0.940	0.00 [-0.11; 0.12] 0.940
≥ 650 µm					
N"/N'/N	25 / 32 / 32	33 / 39 / 39			
Gain in BCVA of ≥ 15 Letters, n (%)	12 (37.5)	22 (56.4)	0.39 [0.15; 1.04] 0.060	0.66 [0.39; 1.14] 0.124	-0.19 [-0.42; 0.04] 0.113
Gain in BCVA of ≥ 15 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.013 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.790				
< 450 µm					
N"/N'/N	86 / 107 / 107	76 / 96 / 96			
Gain in BCVA of ≥ 15 Letters, n (%)	46 (43.0)	39 (40.6)	0.95 [0.53; 1.71] 0.877	1.06 [0.76; 1.47] 0.733	0.02 [-0.11; 0.16] 0.733
≥ 450 - < 650 µm					
N"/N'/N	55 / 70 / 70	55 / 71 / 71			
Gain in BCVA of ≥ 15 Letters, n (%)	24 (34.3)	29 (40.8)	0.70 [0.34; 1.44] 0.335	0.84 [0.55; 1.29] 0.423	-0.07 [-0.23; 0.09] 0.420
≥ 650 µm					
N"/N'/N	8 / 12 / 12	16 / 20 / 20			
Gain in BCVA of ≥ 15 Letters, n (%)	7 (58.3)	10 (50.0)	1.00 [0.23; 4.43] 0.996	1.17 [0.61; 2.23] 0.641	0.08 [-0.27; 0.44] 0.645
KITE: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.048 *				
< 450 µm					
N"/N'/N	62 / 85 / 85	63 / 82 / 82			
Gain in BCVA of ≥ 15 Letters, n (%)	37 (43.5)	30 (36.6)	1.30 [0.69; 2.46] 0.421	1.19 [0.82; 1.73] 0.362	0.07 [-0.08; 0.22] 0.359
≥ 450 - < 650 µm					
N"/N'/N	56 / 74 / 74	67 / 79 / 79			
Gain in BCVA of ≥ 15 Letters, n (%)	44 (59.5)	28 (35.4)	3.37 [1.70; 6.67] <.001 *	1.68 [1.18; 2.39] 0.004 *	0.24 [0.09; 0.39] 0.002 *

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm					
N"/N'/N	15 / 20 / 20	15 / 19 / 19			
Gain in BCVA of ≥ 15 Letters, n (%)	8 (40.0)	9 (47.4)	0.74 [0.20; 2.69] 0.642	0.84 [0.41; 1.73] 0.644	-0.07 [-0.38; 0.24] 0.642
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.377				
< 450 µm					
N"/N'/N	148 / 192 / 192	139 / 178 / 178			
Gain in BCVA of ≥ 15 Letters, n (%)	83 (43.2)	69 (38.8)	1.17 [0.76; 1.80] 0.474	1.11 [0.87; 1.42] 0.388	0.04 [-0.06; 0.14] 0.386
≥ 450 - < 650 µm					
N"/N'/N	111 / 144 / 144	122 / 150 / 150			
Gain in BCVA of ≥ 15 Letters, n (%)	68 (47.2)	57 (38.0)	1.62 [1.00; 2.61] 0.050 *	1.25 [0.95; 1.63] 0.105	0.09 [-0.02; 0.21] 0.106
≥ 650 µm					
N"/N'/N	23 / 32 / 32	31 / 39 / 39			
Gain in BCVA of ≥ 15 Letters, n (%)	15 (46.9)	19 (48.7)	0.81 [0.31; 2.12] 0.666	0.99 [0.61; 1.60] 0.965	-0.01 [-0.24; 0.23] 0.964

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 4.11 BCVA - Gain of 10 respectively 15 letters by status of SRF (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in BCVA of ≥ 10 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.085**					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.868				
presence					
N"/N'/N	49 / 62 / 62	53 / 61 / 61			
Gain in BCVA of ≥ 10 Letters, n (%)	39 (62.9)	41 (67.2)	0.78 [0.36; 1.70] 0.538	0.94 [0.72; 1.21] 0.616	-0.04 [-0.21; 0.13] 0.616
absence					
N"/N'/N	105 / 127 / 127	108 / 126 / 126			
Gain in BCVA of ≥ 10 Letters, n (%)	60 (47.2)	66 (52.4)	0.72 [0.43; 1.21] 0.219	0.90 [0.70; 1.16] 0.415	-0.05 [-0.17; 0.07] 0.413
KITE: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.530				
presence					
N"/N'/N	45 / 56 / 56	58 / 67 / 67			
Gain in BCVA of ≥ 10 Letters, n (%)	39 (69.6)	47 (70.1)	1.05 [0.48; 2.29] 0.910	0.99 [0.79; 1.25] 0.951	-0.01 [-0.17; 0.16] 0.951
absence					
N"/N'/N	102 / 123 / 123	93 / 114 / 114			
Gain in BCVA of ≥ 10 Letters, n (%)	71 (57.7)	59 (51.8)	1.41 [0.84; 2.40] 0.197	1.12 [0.88; 1.41] 0.358	0.06 [-0.07; 0.19] 0.356
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.722				
presence					
N"/N'/N	94 / 118 / 118	111 / 128 / 128			
Gain in BCVA of ≥ 10 Letters, n (%)	78 (66.1)	88 (68.8)	0.91 [0.52; 1.57] 0.732	0.96 [0.81; 1.15] 0.687	-0.02 [-0.14; 0.09] 0.686

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N"/N'/N	207 / 250 / 250	201 / 240 / 240			
Gain in BCVA of ≥ 10 Letters, n (%)	131 (52.4)	125 (52.1)	1.02 [0.71; 1.48] 0.898	1.00 [0.85; 1.19] 0.959	0.00 [-0.09; 0.09] 0.959
Gain in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.019 ***					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.200				
presence					
N"/N'/N	52 / 62 / 62	48 / 61 / 61			
Gain in BCVA of ≥ 10 Letters, n (%)	46 (74.2)	43 (70.5)	1.18 [0.52; 2.66] 0.693	1.05 [0.85; 1.31] 0.647	0.04 [-0.12; 0.20] 0.646
absence					
N"/N'/N	97 / 127 / 127	99 / 126 / 126			
Gain in BCVA of ≥ 10 Letters, n (%)	59 (46.5)	70 (55.6)	0.63 [0.38; 1.05] 0.075	0.84 [0.66; 1.07] 0.150	-0.09 [-0.21; 0.03] 0.146
KITE: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.425				
presence					
N"/N'/N	39 / 56 / 56	54 / 67 / 67			
Gain in BCVA of ≥ 10 Letters, n (%)	40 (71.4)	39 (58.2)	2.01 [0.93; 4.36] 0.078	1.23 [0.94; 1.59] 0.126	0.13 [-0.03; 0.30] 0.121
absence					
N"/N'/N	94 / 123 / 123	92 / 114 / 114			
Gain in BCVA of ≥ 10 Letters, n (%)	70 (56.9)	59 (51.8)	1.37 [0.81; 2.34] 0.242	1.10 [0.87; 1.39] 0.428	0.05 [-0.08; 0.18] 0.425
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.125				
presence					
N"/N'/N	91 / 118 / 118	102 / 128 / 128			
Gain in BCVA of ≥ 10 Letters, n (%)	86 (72.9)	82 (64.1)	1.56 [0.89; 2.74] 0.117	1.13 [0.96; 1.34] 0.156	0.08 [-0.03; 0.20] 0.152

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N"/N'/N	191 / 250 / 250	191 / 240 / 240			
Gain in BCVA of ≥ 10 Letters, n (%)	129 (51.6)	129 (53.8)	0.93 [0.64; 1.34] 0.681	0.96 [0.81; 1.14] 0.625	-0.02 [-0.11; 0.07] 0.625
Gain in BCVA of ≥ 15 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.043 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.854				
presence					
N"/N'/N	49 / 62 / 62	53 / 61 / 61			
Gain in BCVA of ≥ 15 Letters, n (%)	30 (48.4)	31 (50.8)	0.87 [0.42; 1.80] 0.705	0.95 [0.67; 1.36] 0.787	-0.02 [-0.20; 0.15] 0.787
absence					
N"/N'/N	105 / 127 / 127	108 / 126 / 126			
Gain in BCVA of ≥ 15 Letters, n (%)	40 (31.5)	43 (34.1)	0.80 [0.46; 1.37] 0.413	0.92 [0.65; 1.31] 0.656	-0.03 [-0.14; 0.09] 0.656
KITE: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.625				
presence					
N"/N'/N	45 / 56 / 56	58 / 67 / 67			
Gain in BCVA of ≥ 15 Letters, n (%)	31 (55.4)	33 (49.3)	1.33 [0.65; 2.75] 0.433	1.12 [0.80; 1.58] 0.498	0.06 [-0.12; 0.24] 0.499
absence					
N"/N'/N	102 / 123 / 123	93 / 114 / 114			
Gain in BCVA of ≥ 15 Letters, n (%)	52 (42.3)	35 (30.7)	1.67 [0.97; 2.88] 0.065	1.38 [0.98; 1.94] 0.069	0.12 [-0.01; 0.24] 0.062
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.815				
presence					
N"/N'/N	94 / 118 / 118	111 / 128 / 128			
Gain in BCVA of ≥ 15 Letters, n (%)	61 (51.7)	64 (50.0)	1.10 [0.66; 1.83] 0.727	1.04 [0.81; 1.32] 0.777	0.02 [-0.11; 0.14] 0.776

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N"/N'/N	207 / 250 / 250	201 / 240 / 240			
Gain in BCVA of ≥ 15 Letters, n (%)	92 (36.8)	78 (32.5)	1.18 [0.81; 1.73] 0.390	1.13 [0.88; 1.44] 0.326	0.04 [-0.04; 0.13] 0.325
Gain in BCVA of ≥ 15 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.013 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.755				
presence					
N"/N'/N	52 / 62 / 62	48 / 61 / 61			
Gain in BCVA of ≥ 15 Letters, n (%)	33 (53.2)	32 (52.5)	0.97 [0.47; 2.03] 0.941	1.01 [0.73; 1.42] 0.932	0.01 [-0.17; 0.18] 0.932
absence					
N"/N'/N	97 / 127 / 127	99 / 126 / 126			
Gain in BCVA of ≥ 15 Letters, n (%)	44 (34.6)	46 (36.5)	0.84 [0.50; 1.43] 0.526	0.95 [0.68; 1.32] 0.757	-0.02 [-0.14; 0.10] 0.757
KITE: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.924				
presence					
N"/N'/N	39 / 56 / 56	54 / 67 / 67			
Gain in BCVA of ≥ 15 Letters, n (%)	34 (60.7)	31 (46.3)	1.93 [0.93; 4.00] 0.079	1.31 [0.94; 1.83] 0.110	0.14 [-0.03; 0.32] 0.106
absence					
N"/N'/N	94 / 123 / 123	92 / 114 / 114			
Gain in BCVA of ≥ 15 Letters, n (%)	55 (44.7)	36 (31.6)	1.84 [1.07; 3.17] 0.028 *	1.42 [1.01; 1.98] 0.041 *	0.13 [0.01; 0.25] 0.036 *
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.784				
presence					
N"/N'/N	91 / 118 / 118	102 / 128 / 128			
Gain in BCVA of ≥ 15 Letters, n (%)	67 (56.8)	63 (49.2)	1.39 [0.83; 2.33] 0.208	1.15 [0.91; 1.46] 0.237	0.08 [-0.05; 0.20] 0.234

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N"/N'/N	191 / 250 / 250	191 / 240 / 240			
Gain in BCVA of ≥ 15 Letters, n (%)	99 (39.6)	82 (34.2)	1.27 [0.87; 1.86] 0.208	1.16 [0.92; 1.46] 0.218	0.05 [-0.03; 0.14] 0.217

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 4.12 BCVA - Gain of 10 respectively 15 letters by exposure (week 52) (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by exposure (week 52) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in BCVA of ≥ 10 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.085**					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.030 *				
Non-exposed					
N"/N'/N	58 / 71 / 71	62 / 75 / 75			
Gain in BCVA of ≥ 10 Letters, n (%)	38 (53.5)	50 (66.7)	0.40 [0.19; 0.82] 0.012 *	0.80 [0.61; 1.05] 0.110	-0.13 [-0.29; 0.03] 0.102
Exposed					
N"/N'/N	96 / 118 / 118	99 / 112 / 112			
Gain in BCVA of ≥ 10 Letters, n (%)	61 (51.7)	57 (50.9)	1.08 [0.63; 1.86] 0.778	1.02 [0.79; 1.31] 0.903	0.01 [-0.12; 0.14] 0.903
KITE: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.946				
Non-exposed					
N"/N'/N	71 / 85 / 85	76 / 90 / 90			
Gain in BCVA of ≥ 10 Letters, n (%)	55 (64.7)	54 (60.0)	1.29 [0.69; 2.43] 0.424	1.08 [0.86; 1.36] 0.521	0.05 [-0.10; 0.19] 0.520
Exposed					
N"/N'/N	76 / 94 / 94	75 / 91 / 91			
Gain in BCVA of ≥ 10 Letters, n (%)	55 (58.5)	52 (57.1)	1.25 [0.69; 2.29] 0.462	1.02 [0.80; 1.31] 0.851	0.01 [-0.13; 0.16] 0.851
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.139				
Non-exposed					
N"/N'/N	129 / 156 / 156	138 / 165 / 165			
Gain in BCVA of ≥ 10 Letters, n (%)	93 (59.6)	104 (63.0)	0.75 [0.47; 1.20] 0.237	0.95 [0.79; 1.13] 0.531	-0.03 [-0.14; 0.07] 0.532

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by exposure (week 52) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N''/N'/N	172 / 212 / 212	174 / 203 / 203			
Gain in BCVA of ≥ 10 Letters, n (%)	116 (54.7)	109 (53.7)	1.21 [0.81; 1.81] 0.363	1.02 [0.85; 1.22] 0.829	0.01 [-0.09; 0.11] 0.829
Gain in BCVA of ≥ 15 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.043 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.017 *				
Non-exposed					
N''/N'/N	58 / 71 / 71	62 / 75 / 75			
Gain in BCVA of ≥ 15 Letters, n (%)	24 (33.8)	35 (46.7)	0.41 [0.20; 0.84] 0.015 *	0.72 [0.48; 1.09] 0.119	-0.13 [-0.29; 0.03] 0.110
Exposed					
N''/N'/N	96 / 118 / 118	99 / 112 / 112			
Gain in BCVA of ≥ 15 Letters, n (%)	46 (39.0)	39 (34.8)	1.24 [0.71; 2.17] 0.442	1.12 [0.80; 1.57] 0.514	0.04 [-0.08; 0.17] 0.513
KITE: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.723				
Non-exposed					
N''/N'/N	71 / 85 / 85	76 / 90 / 90			
Gain in BCVA of ≥ 15 Letters, n (%)	42 (49.4)	33 (36.7)	1.63 [0.88; 3.02] 0.120	1.35 [0.95; 1.91] 0.091	0.13 [-0.02; 0.27] 0.086
Exposed					
N''/N'/N	76 / 94 / 94	75 / 91 / 91			
Gain in BCVA of ≥ 15 Letters, n (%)	41 (43.6)	35 (38.5)	1.40 [0.76; 2.55] 0.278	1.13 [0.80; 1.60] 0.477	0.05 [-0.09; 0.19] 0.475
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 52					
Interaction Test:	p = 0.169				
Non-exposed					
N''/N'/N	129 / 156 / 156	138 / 165 / 165			
Gain in BCVA of ≥ 15 Letters, n (%)	66 (42.3)	68 (41.2)	0.89 [0.56; 1.41] 0.622	1.03 [0.79; 1.33] 0.843	0.01 [-0.10; 0.12] 0.843

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by exposure (week 52) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N"/N'/N	172 / 212 / 212	174 / 203 / 203			
Gain in BCVA of ≥ 15 Letters, n (%)	87 (41.0)	74 (36.5)	1.38 [0.91; 2.07] 0.127	1.13 [0.88; 1.44] 0.337	0.05 [-0.05; 0.14] 0.335

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 4.13 BCVA - Gain of 10 respectively 15 letters by exposure (week 100) (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.019 ***					
KESTREL: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.003 *				
Non-exposed					
N"/N'/N	0 / 12 / 12	0 / 13 / 13			
Gain in BCVA of ≥ 10 Letters, n (%)	2 (16.7)	9 (69.2)	0.04 [<0.01; 0.31] 0.002 *	0.24 [0.06; 0.90] 0.034 *	-0.53 [-0.85; -0.20] 0.002 *
Exposed					
N"/N'/N	149 / 177 / 177	147 / 174 / 174			
Gain in BCVA of ≥ 10 Letters, n (%)	103 (58.2)	104 (59.8)	0.89 [0.57; 1.39] 0.620	0.97 [0.82; 1.16] 0.764	-0.02 [-0.12; 0.09] 0.764
KITE: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.889				
Non-exposed					
N"/N'/N	0 / 17 / 17	0 / 12 / 12			
Gain in BCVA of ≥ 10 Letters, n (%)	7 (41.2)	4 (33.3)	1.43 [0.29; 7.07] 0.657	1.24 [0.46; 3.30] 0.673	0.08 [-0.28; 0.43] 0.665
Exposed					
N"/N'/N	133 / 162 / 162	146 / 169 / 169			
Gain in BCVA of ≥ 10 Letters, n (%)	103 (63.6)	94 (55.6)	1.61 [1.02; 2.56] 0.041 *	1.14 [0.96; 1.37] 0.141	0.08 [-0.03; 0.18] 0.139
Pooled Analysis: Gain in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.022 *				
Non-exposed					
N"/N'/N	0 / 29 / 29	0 / 25 / 25			
Gain in BCVA of ≥ 10 Letters, n (%)	9 (31.0)	13 (52.0)	0.29 [0.09; 0.94] 0.038 *	0.59 [0.28; 1.24] 0.134	-0.21 [-0.48; 0.07] 0.137

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N"/N'/N	282 / 339 / 339	293 / 343 / 343			
Gain in BCVA of ≥ 10 Letters, n (%)	206 (60.8)	198 (57.7)	1.20 [0.88; 1.66] 0.251	1.05 [0.93; 1.19] 0.418	0.03 [-0.04; 0.10] 0.418
Gain in BCVA of ≥ 15 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.013 ***					
KESTREL: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.456				
Non-exposed					
N"/N'/N	0 / 12 / 12	0 / 13 / 13			
Gain in BCVA of ≥ 15 Letters, n (%)	2 (16.7)	3 (23.1)	0.41 [0.05; 3.21] 0.396	0.72 [0.14; 3.61] 0.692	-0.06 [-0.38; 0.25] 0.687
Exposed					
N"/N'/N	149 / 177 / 177	147 / 174 / 174			
Gain in BCVA of ≥ 15 Letters, n (%)	75 (42.4)	75 (43.1)	0.91 [0.59; 1.42] 0.686	0.98 [0.77; 1.25] 0.890	-0.01 [-0.11; 0.10] 0.890
KITE: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.532				
Non-exposed					
N"/N'/N	0 / 17 / 17	0 / 12 / 12			
Gain in BCVA of ≥ 15 Letters, n (%)	5 (29.4)	3 (25.0)	1.12 [0.20; 6.16] 0.898	1.18 [0.35; 4.01] 0.795	0.04 [-0.28; 0.37] 0.791
Exposed					
N"/N'/N	133 / 162 / 162	146 / 169 / 169			
Gain in BCVA of ≥ 15 Letters, n (%)	84 (51.9)	64 (37.9)	1.96 [1.25; 3.09] 0.004 *	1.37 [1.07; 1.75] 0.011 *	0.14 [0.03; 0.25] 0.010 *
Pooled Analysis: Gain in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.390				
Non-exposed					
N"/N'/N	0 / 29 / 29	0 / 25 / 25			
Gain in BCVA of ≥ 15 Letters, n (%)	7 (24.1)	6 (24.0)	0.76 [0.21; 2.76] 0.682	0.97 [0.37; 2.56] 0.955	-0.01 [-0.24; 0.22] 0.954

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N"/N'/N	282 / 339 / 339	293 / 343 / 343			
Gain in BCVA of ≥ 15 Letters, n (%)	159 (46.9)	139 (40.5)	1.37 [1.00; 1.87] 0.051	1.16 [0.98; 1.37] 0.092	0.06 [-0.01; 0.14] 0.092

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

5 BCVA: Binary analysis (Loss)

Table 5.1 BCVA - Loss of 10 respectively 15 letters (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Loss in BCVA of ≥ 10 Letters, Week 52					
KESTREL, N"/N'/N	154 / 189 / 189	161 / 187 / 187			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (1.1)	3 (1.6)	0.67 [0.11; 4.08] 0.664	0.66 [0.11; 3.90] 0.646	-0.01 [-0.03; 0.02] 0.644
KITE, N"/N'/N	147 / 179 / 179	151 / 181 / 181			
Loss in BCVA of ≥ 10 Letters, n (%)	4 (2.2)	4 (2.2)	0.92 [0.22; 3.77] 0.906	1.01 [0.26; 3.98] 0.987	0.00 [-0.03; 0.03] 0.987
Pooled Analysis, N"/N'/N	301 / 368 / 368	312 / 368 / 368			
Loss in BCVA of ≥ 10 Letters, n (%)	6 (1.6)	7 (1.9)	0.80 [0.25; 2.54] 0.711	0.86 [0.29; 2.53] 0.784	-0.00 [-0.02; 0.02] 0.783
p_H=0.774					
Loss in BCVA of ≥ 10 Letters, Week 100					
KESTREL, N"/N'/N	149 / 189 / 189	147 / 187 / 187			
Loss in BCVA of ≥ 10 Letters, n (%)	6 (3.2)	3 (1.6)	2.11 [0.52; 8.58] 0.299	1.98 [0.50; 7.80] 0.329	0.02 [-0.02; 0.05] 0.318
KITE, N"/N'/N	133 / 179 / 179	146 / 181 / 181			
Loss in BCVA of ≥ 10 Letters, n (%)	4 (2.2)	11 (6.1)	0.33 [0.10; 1.05] 0.061	0.37 [0.12; 1.13] 0.081	-0.04 [-0.08; 0.00] 0.066
Pooled Analysis, N"/N'/N	282 / 368 / 368	293 / 368 / 368			
Loss in BCVA of ≥ 10 Letters, n (%)	10 (2.7)	14 (3.8)	0.85 [0.34; 2.12] 0.728	0.72 [0.32; 1.60] 0.411	-0.01 [-0.04; 0.01] 0.411
p_H=0.049 *					
Loss in BCVA of ≥ 15 Letters, Week 52					
KESTREL, N"/N'/N	154 / 189 / 189	161 / 187 / 187			
Loss in BCVA of ≥ 15 Letters, n (%)	0 (0.0)	1 (0.5)	N.E.	0.33 [0.01; 8.05] 0.496	-0.01 [-0.02; 0.01] 0.316
KITE, N"/N'/N	147 / 179 / 179	151 / 181 / 181			
Loss in BCVA of ≥ 15 Letters, n (%)	2 (1.1)	3 (1.7)	0.59 [0.10; 3.63] 0.570	0.67 [0.11; 3.99] 0.664	-0.01 [-0.03; 0.02] 0.661

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N''/N'/N	301 / 368 / 368	312 / 368 / 368			
Loss in BCVA of ≥ 15 Letters, n (%)	2 (0.5)	4 (1.1)	N.E.	0.56 [0.12; 2.60] 0.452	-0.01 [-0.02; 0.01] 0.416
p_H=N.E.					
Loss in BCVA of ≥ 15 Letters, Week 100					
KESTREL, N''/N'/N	149 / 189 / 189	147 / 187 / 187			
Loss in BCVA of ≥ 15 Letters, n (%)	3 (1.6)	2 (1.1)	1.56 [0.26; 9.45] 0.631	1.48 [0.25; 8.78] 0.663	0.01 [-0.02; 0.03] 0.661
KITE, N''/N'/N	133 / 179 / 179	146 / 181 / 181			
Loss in BCVA of ≥ 15 Letters, n (%)	4 (2.2)	6 (3.3)	0.61 [0.17; 2.23] 0.457	0.67 [0.19; 2.35] 0.536	-0.01 [-0.04; 0.02] 0.532
Pooled Analysis, N''/N'/N	282 / 368 / 368	293 / 368 / 368			
Loss in BCVA of ≥ 15 Letters, n (%)	7 (1.9)	8 (2.2)	0.98 [0.32; 2.99] 0.973	0.88 [0.32; 2.40] 0.800	-0.00 [-0.02; 0.02] 0.800
p_H=0.409					

N: Number of patients
N': Number of patients in the analysis
N'': Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 5.2 BCVA - Loss of 10 respectively 15 letters by age (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Loss in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.049 ***					
KESTREL: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.895				
< 65 years					
N"/N'/N	82 / 104 / 104	76 / 93 / 93			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (1.9)	1 (1.1)	1.84 [0.16; 20.86] 0.622	1.79 [0.16; 19.40] 0.633	0.01 [-0.03; 0.04] 0.622
≥ 65 years					
N"/N'/N	67 / 85 / 85	71 / 94 / 94			
Loss in BCVA of ≥ 10 Letters, n (%)	4 (4.7)	2 (2.1)	2.25 [0.40; 12.65] 0.357	2.21 [0.42; 11.77] 0.352	0.03 [-0.03; 0.08] 0.346
KITE: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.298				
< 65 years					
N"/N'/N	73 / 100 / 100	87 / 102 / 102			
Loss in BCVA of ≥ 10 Letters, n (%)	1 (1.0)	6 (5.9)	0.14 [0.02; 1.21] 0.075	0.17 [0.02; 1.39] 0.098	-0.05 [-0.10; 0.00] 0.054
≥ 65 years					
N"/N'/N	60 / 79 / 79	59 / 79 / 79			
Loss in BCVA of ≥ 10 Letters, n (%)	3 (3.8)	5 (6.3)	0.56 [0.13; 2.46] 0.446	0.60 [0.15; 2.43] 0.474	-0.03 [-0.09; 0.04] 0.467
Pooled Analysis: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.332				
< 65 years					
N"/N'/N	155 / 204 / 204	163 / 195 / 195			
Loss in BCVA of ≥ 10 Letters, n (%)	3 (1.5)	7 (3.6)	0.50 [0.12; 2.11] 0.349	0.41 [0.11; 1.62] 0.189	-0.02 [-0.05; 0.01] 0.189

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N"/N'/N	127 / 164 / 164	130 / 173 / 173			
Loss in BCVA of ≥ 10 Letters, n (%)	7 (4.3)	7 (4.0)	1.20 [0.38; 3.73] 0.757	1.04 [0.38; 2.89] 0.934	0.00 [-0.04; 0.04] 0.935

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + baseline category + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + baseline category + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 5.3 BCVA - Loss of 10 respectively 15 letters by gender (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Loss in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.049 ***					
KESTREL: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.518				
Male					
N"/N'/N	86 / 110 / 110	95 / 126 / 126			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (1.8)	2 (1.6)	1.22 [0.17; 8.84] 0.845	1.15 [0.16; 8.00] 0.891	0.00 [-0.03; 0.04] 0.891
Female					
N"/N'/N	63 / 79 / 79	52 / 61 / 61			
Loss in BCVA of ≥ 10 Letters, n (%)	4 (5.1)	1 (1.6)	3.26 [0.35; 30.05] 0.298	3.09 [0.35; 26.93] 0.307	0.03 [-0.02; 0.09] 0.246
KITE: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.210				
Male					
N"/N'/N	91 / 120 / 120	93 / 115 / 115			
Loss in BCVA of ≥ 10 Letters, n (%)	1 (0.8)	7 (6.1)	0.13 [0.02; 1.05] 0.055	0.14 [0.02; 1.10] 0.061	-0.05 [-0.10; -0.01] 0.027 *
Female					
N"/N'/N	42 / 59 / 59	53 / 66 / 66			
Loss in BCVA of ≥ 10 Letters, n (%)	3 (5.1)	4 (6.1)	0.68 [0.14; 3.28] 0.631	0.84 [0.20; 3.60] 0.813	-0.01 [-0.09; 0.07] 0.812
Pooled Analysis: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.172				
Male					
N"/N'/N	177 / 230 / 230	188 / 241 / 241			
Loss in BCVA of ≥ 10 Letters, n (%)	3 (1.3)	9 (3.7)	0.43 [0.11; 1.69] 0.224	0.35 [0.10; 1.23] 0.084	-0.03 [-0.05; 0.00] 0.084

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N"/N'/N	105 / 138 / 138	105 / 127 / 127			
Loss in BCVA of ≥ 10 Letters, n (%)	7 (5.1)	5 (3.9)	1.48 [0.42; 5.21] 0.543	1.36 [0.43; 4.32] 0.605	0.01 [-0.04; 0.06] 0.597

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 5.4 BCVA - Loss of 10 respectively 15 letters by BCVA (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Loss in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.049 ***					
KESTREL: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.993				
≤ 65 letters					
N"/N'/N	55 / 74 / 74	51 / 64 / 64			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (2.7)	1 (1.6)	2.09 [0.18; 24.04] 0.555	1.73 [0.16; 18.63] 0.651	0.01 [-0.04; 0.06] 0.640
> 65 letters					
N"/N'/N	94 / 115 / 115	96 / 123 / 123			
Loss in BCVA of ≥ 10 Letters, n (%)	4 (3.5)	2 (1.6)	2.12 [0.38; 11.82] 0.393	2.14 [0.40; 11.46] 0.375	0.02 [-0.02; 0.06] 0.367
KITE: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.990				
≤ 65 letters					
N"/N'/N	49 / 65 / 65	68 / 91 / 91			
Loss in BCVA of ≥ 10 Letters, n (%)	1 (1.5)	4 (4.4)	0.32 [0.03; 2.96] 0.317	0.35 [0.04; 3.06] 0.343	-0.03 [-0.08; 0.02] 0.278
> 65 letters					
N"/N'/N	84 / 114 / 114	78 / 90 / 90			
Loss in BCVA of ≥ 10 Letters, n (%)	3 (2.6)	7 (7.8)	0.33 [0.08; 1.31] 0.114	0.34 [0.09; 1.27] 0.109	-0.05 [-0.11; 0.01] 0.107
Pooled Analysis: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.864				
≤ 65 letters					
N"/N'/N	104 / 139 / 139	119 / 155 / 155			
Loss in BCVA of ≥ 10 Letters, n (%)	3 (2.2)	5 (3.2)	0.95 [0.20; 4.37] 0.944	0.69 [0.15; 3.04] 0.617	-0.01 [-0.05; 0.03] 0.606

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N"/N'/N	178 / 229 / 229	174 / 213 / 213			
Loss in BCVA of ≥ 10 Letters, n (%)	7 (3.1)	9 (4.2)	0.81 [0.28; 2.36] 0.699	0.70 [0.27; 1.78] 0.447	-0.01 [-0.05; 0.02] 0.458
Loss in BCVA of ≥ 15 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.409**					
KESTREL: Loss in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	N.E.				
≤ 65 letters					
N"/N'/N	55 / 74 / 74	51 / 64 / 64			
Loss in BCVA of ≥ 15 Letters, n (%)	0 (0.0)	1 (1.6)	N.E.	0.29 [0.01; 6.97] 0.445	-0.02 [-0.05; 0.01] 0.313
> 65 letters					
N"/N'/N	94 / 115 / 115	96 / 123 / 123			
Loss in BCVA of ≥ 15 Letters, n (%)	3 (2.6)	1 (0.8)	3.27 [0.34; 31.86] 0.308	3.21 [0.34; 30.41] 0.310	0.02 [-0.02; 0.05] 0.289
KITE: Loss in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.931				
≤ 65 letters					
N"/N'/N	49 / 65 / 65	68 / 91 / 91			
Loss in BCVA of ≥ 15 Letters, n (%)	1 (1.5)	2 (2.2)	0.67 [0.06; 7.59] 0.747	0.70 [0.06; 7.56] 0.769	-0.01 [-0.05; 0.04] 0.761
> 65 letters					
N"/N'/N	84 / 114 / 114	78 / 90 / 90			
Loss in BCVA of ≥ 15 Letters, n (%)	3 (2.6)	4 (4.4)	0.59 [0.13; 2.72] 0.499	0.59 [0.14; 2.58] 0.485	-0.02 [-0.07; 0.03] 0.492
Pooled Analysis: Loss in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.482				
≤ 65 letters					
N"/N'/N	104 / 139 / 139	119 / 155 / 155			
Loss in BCVA of ≥ 15 Letters, n (%)	1 (0.7)	3 (1.9)	0.48 [0.05; 5.00] 0.540	0.50 [0.08; 3.22] 0.456	-0.01 [-0.04; 0.02] 0.417

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N"/N'/N	178 / 229 / 229	174 / 213 / 213			
Loss in BCVA of ≥ 15 Letters, n (%)	6 (2.6)	5 (2.3)	1.21 [0.34; 4.28] 0.763	1.06 [0.34; 3.31] 0.924	0.00 [-0.03; 0.03] 0.925

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Loss in BCVA of ≥ 15 Letters / KESTREL / Week 100: logit(proportion) = treatment [by BCVA].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 5.5 BCVA - Loss of 10 respectively 15 letters by region (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Loss in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.049 ***					
KESTREL: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	N.E.				
Region of the Americas					
N"/N'/N	67 / 90 / 90	66 / 83 / 83			
Loss in BCVA of ≥ 10 Letters, n (%)	3 (3.3)	1 (1.2)	2.83 [0.29; 27.73] 0.372	2.77 [0.29; 26.08] 0.374	0.02 [-0.02; 0.07] 0.342
European Region					
N"/N'/N	56 / 69 / 69	57 / 75 / 75			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (2.9)	2 (2.7)	1.09 [0.15; 7.95] 0.933	1.09 [0.16; 7.51] 0.933	0.00 [-0.05; 0.06] 0.933
Western Pacific Region					
N"/N'/N	26 / 30 / 30	24 / 29 / 29			
Loss in BCVA of ≥ 10 Letters, n (%)	1 (3.3)	0 (0.0)	N.E.	2.90 [0.12; 68.50] 0.509	0.03 [-0.03; 0.10] 0.309
KITE: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	N.E.				
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	13 / 26 / 26	15 / 21 / 21			
Loss in BCVA of ≥ 10 Letters, n (%)	1 (3.8)	0 (0.0)	N.E.	2.44 [0.10; 57.08] 0.578	0.04 [-0.04; 0.11] 0.308
European Region					
N"/N'/N	108 / 135 / 135	108 / 132 / 132			
Loss in BCVA of ≥ 10 Letters, n (%)	1 (0.7)	7 (5.3)	0.13 [0.02; 1.10] 0.061	0.14 [0.02; 1.12] 0.064	-0.05 [-0.09; -0.00] 0.029 *
Western Pacific Region					
N"/N'/N	12 / 18 / 18	23 / 28 / 28			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (11.1)	4 (14.3)	0.75 [0.12; 4.59] 0.756	0.78 [0.16; 3.82] 0.757	-0.03 [-0.23; 0.16] 0.749

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	N.E.				
Region of the Americas					
N"/N'/N	67 / 90 / 90	66 / 83 / 83			
Loss in BCVA of ≥ 10 Letters, n (%)	3 (3.3)	1 (1.2)	N.E.	2.77 [0.29; 26.08] 0.353	0.02 [-0.02; 0.07] 0.342
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	13 / 26 / 26	15 / 21 / 21			
Loss in BCVA of ≥ 10 Letters, n (%)	1 (3.8)	0 (0.0)	N.E.	2.44 [0.10; 57.08] 0.567	0.04 [-0.04; 0.11] 0.308
European Region					
N"/N'/N	164 / 204 / 204	165 / 207 / 207			
Loss in BCVA of ≥ 10 Letters, n (%)	3 (1.5)	9 (4.3)	0.39 [0.09; 1.66] 0.201	0.34 [0.10; 1.23] 0.083	-0.03 [-0.06; 0.00] 0.083
Western Pacific Region					
N"/N'/N	38 / 48 / 48	47 / 57 / 57			
Loss in BCVA of ≥ 10 Letters, n (%)	3 (6.3)	4 (7.0)	N.E.	1.07 [0.27; 4.24] 0.919	0.01 [-0.09; 0.10] 0.906

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Loss in BCVA of ≥ 10 Letters / KESTREL / Week 100, Loss in BCVA of ≥ 10 Letters / KITE / Week 100: logit(proportion) = treatment [by region].
Loss in BCVA of ≥ 10 Letters / Pooled Analysis / Week 100: logit(proportion) = treatment + study + treatment * study [by region].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 5.6 BCVA - Loss of 10 respectively 15 letters by diabetes type (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Loss in BCVA of ≥ 10 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.774**					
KESTREL: Loss in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	9 / 12 / 12	6 / 6 / 6			
Loss in BCVA of ≥ 10 Letters, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N"/N'/N	145 / 177 / 177	155 / 181 / 181			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (1.1)	3 (1.7)	0.68 [0.11; 4.11] 0.673	0.68 [0.12; 4.03] 0.673	-0.01 [-0.03; 0.02] 0.670
KITE: Loss in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	18 / 19 / 19	7 / 7 / 7			
Loss in BCVA of ≥ 10 Letters, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N"/N'/N	129 / 160 / 160	144 / 174 / 174			
Loss in BCVA of ≥ 10 Letters, n (%)	4 (2.5)	4 (2.3)	1.09 [0.27; 4.43] 0.904	1.09 [0.28; 4.28] 0.904	0.00 [-0.03; 0.03] 0.905
Pooled Analysis: Loss in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	27 / 31 / 31	13 / 13 / 13			
Loss in BCVA of ≥ 10 Letters, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N"/N'/N	274 / 337 / 337	299 / 355 / 355			
Loss in BCVA of ≥ 10 Letters, n (%)	6 (1.8)	7 (2.0)	0.86 [0.27; 2.69] 0.790	0.91 [0.31; 2.68] 0.865	-0.00 [-0.02; 0.02] 0.864

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Loss in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.049 ***					
KESTREL: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	10 / 12 / 12	4 / 6 / 6			
Loss in BCVA of ≥ 10 Letters, n (%)	0 (0.0)	1 (16.7)	N.E.	0.18 [0.01; 3.85] 0.272	-0.17 [-0.46; 0.13] 0.273
Type 2					
N"/N'/N	139 / 177 / 177	143 / 181 / 181			
Loss in BCVA of ≥ 10 Letters, n (%)	6 (3.4)	2 (1.1)	3.14 [0.63; 15.77] 0.165	3.07 [0.63; 15.00] 0.166	0.02 [-0.01; 0.05] 0.145
KITE: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	17 / 19 / 19	5 / 7 / 7			
Loss in BCVA of ≥ 10 Letters, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N"/N'/N	116 / 160 / 160	141 / 174 / 174			
Loss in BCVA of ≥ 10 Letters, n (%)	4 (2.5)	11 (6.3)	0.38 [0.12; 1.22] 0.104	0.40 [0.13; 1.22] 0.106	-0.04 [-0.08; 0.01] 0.085
Pooled Analysis: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	27 / 31 / 31	9 / 13 / 13			
Loss in BCVA of ≥ 10 Letters, n (%)	0 (0.0)	1 (7.7)	N.E.	0.18 [0.01; 3.85] 0.223	-0.07 [-0.22; 0.07] 0.313
Type 2					
N"/N'/N	255 / 337 / 337	284 / 355 / 355			
Loss in BCVA of ≥ 10 Letters, n (%)	10 (3.0)	13 (3.7)	1.12 [0.41; 3.04] 0.830	0.82 [0.36; 1.85] 0.628	-0.01 [-0.03; 0.02] 0.627
Loss in BCVA of ≥ 15 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.409**					

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL: Loss in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	10 / 12 / 12	4 / 6 / 6			
Loss in BCVA of ≥ 15 Letters, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N"/N'/N	139 / 177 / 177	143 / 181 / 181			
Loss in BCVA of ≥ 15 Letters, n (%)	3 (1.7)	2 (1.1)	1.54 [0.25; 9.35] 0.637	1.53 [0.26; 9.07] 0.637	0.01 [-0.02; 0.03] 0.635
KITE: Loss in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	17 / 19 / 19	5 / 7 / 7			
Loss in BCVA of ≥ 15 Letters, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N"/N'/N	116 / 160 / 160	141 / 174 / 174			
Loss in BCVA of ≥ 15 Letters, n (%)	4 (2.5)	6 (3.4)	0.72 [0.20; 2.59] 0.613	0.73 [0.21; 2.52] 0.613	-0.01 [-0.05; 0.03] 0.609
Pooled Analysis: Loss in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	27 / 31 / 31	9 / 13 / 13			
Loss in BCVA of ≥ 15 Letters, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N"/N'/N	255 / 337 / 337	284 / 355 / 355			
Loss in BCVA of ≥ 15 Letters, n (%)	7 (2.1)	8 (2.3)	1.06 [0.35; 3.23] 0.918	0.93 [0.34; 2.55] 0.891	-0.00 [-0.02; 0.02] 0.891

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Loss in BCVA of ≥ 10 Letters / KESTREL / Week 52, Loss in BCVA of ≥ 10 Letters / KITE / Week 52, Loss in BCVA of ≥ 10 Letters / KESTREL / Week 100, Loss in BCVA of ≥ 10 Letters / KITE / Week 100, Loss in BCVA of ≥ 15 Letters / KESTREL / Week 100, Loss in BCVA of ≥ 15 Letters / KITE / Week 100: logit(proportion) = treatment [by diabetes type].
Loss in BCVA of ≥ 10 Letters / Pooled Analysis / Week 52, Loss in BCVA of ≥ 10 Letters / Pooled Analysis / Week 100, Loss in BCVA of ≥ 15 Letters / Pooled Analysis / Week 100: logit(proportion) = treatment + study + treatment * study [by diabetes type].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 5.7 BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Loss in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.049 ***					
KESTREL: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.834				
< 7.5 %					
N"/N'/N	59 / 76 / 76	91 / 107 / 107			
Loss in BCVA of ≥ 10 Letters, n (%)	1 (1.3)	1 (0.9)	1.42 [0.09; 23.15] 0.806	1.41 [0.09; 22.16] 0.808	0.00 [-0.03; 0.04] 0.812
≥ 7.5 %					
N"/N'/N	89 / 112 / 112	56 / 80 / 80			
Loss in BCVA of ≥ 10 Letters, n (%)	5 (4.5)	2 (2.5)	2.01 [0.37; 10.77] 0.416	1.79 [0.36; 8.97] 0.482	0.02 [-0.03; 0.07] 0.453
KITE: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.309				
< 7.5 %					
N"/N'/N	61 / 82 / 82	75 / 96 / 96			
Loss in BCVA of ≥ 10 Letters, n (%)	1 (1.2)	7 (7.3)	0.15 [0.02; 1.25] 0.079	0.17 [0.02; 1.33] 0.091	-0.06 [-0.12; -0.00] 0.037 *
≥ 7.5 %					
N"/N'/N	72 / 97 / 97	71 / 85 / 85			
Loss in BCVA of ≥ 10 Letters, n (%)	3 (3.1)	4 (4.7)	0.58 [0.12; 2.71] 0.490	0.66 [0.15; 2.85] 0.575	-0.02 [-0.07; 0.04] 0.577
Pooled Analysis: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.208				
< 7.5 %					
N"/N'/N	120 / 158 / 158	166 / 203 / 203			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (1.3)	8 (3.9)	0.38 [0.08; 1.89] 0.236	0.31 [0.07; 1.40] 0.104	-0.03 [-0.06; 0.00] 0.086

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N"/N'/N	161 / 209 / 209	127 / 165 / 165			
Loss in BCVA of ≥ 10 Letters, n (%)	8 (3.8)	6 (3.6)	1.29 [0.40; 4.12] 0.668	1.06 [0.37; 3.03] 0.919	0.00 [-0.04; 0.04] 0.918

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 5.8 BCVA - Loss of 10 respectively 15 letters by duration of DME (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Loss in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.049 ***					
KESTREL: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	N.E.				
≤ 3 months					
N"/N'/N	99 / 120 / 120	86 / 110 / 110			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (1.7)	1 (0.9)	1.85 [0.17; 20.66] 0.618	1.83 [0.17; 19.94] 0.619	0.01 [-0.02; 0.04] 0.608
> 3 - < 12 months					
N"/N'/N	22 / 30 / 30	27 / 39 / 39			
Loss in BCVA of ≥ 10 Letters, n (%)	1 (3.3)	2 (5.1)	0.64 [0.06; 7.39] 0.719	0.65 [0.06; 6.83] 0.720	-0.02 [-0.11; 0.08] 0.710
≥ 12 months					
N"/N'/N	28 / 39 / 39	34 / 38 / 38			
Loss in BCVA of ≥ 10 Letters, n (%)	3 (7.7)	0 (0.0)	N.E.	6.83 [0.36; 127.84] 0.199	0.08 [-0.01; 0.16] 0.071
KITE: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	N.E.				
≤ 3 months					
N"/N'/N	58 / 85 / 85	73 / 92 / 92			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (2.4)	6 (6.5)	0.35 [0.07; 1.76] 0.201	0.36 [0.07; 1.74] 0.204	-0.04 [-0.10; 0.02] 0.172
> 3 - < 12 months					
N"/N'/N	43 / 51 / 51	38 / 49 / 49			
Loss in BCVA of ≥ 10 Letters, n (%)	0 (0.0)	3 (6.1)	N.E.	0.14 [0.01; 2.59] 0.185	-0.06 [-0.13; 0.01] 0.074
≥ 12 months					
N"/N'/N	32 / 43 / 43	35 / 40 / 40			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (4.7)	2 (5.0)	0.93 [0.12; 6.91] 0.941	0.93 [0.14; 6.30] 0.941	-0.00 [-0.10; 0.09] 0.941

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.150				
≤ 3 months					
N"/N'/N	157 / 205 / 205	159 / 202 / 202			
Loss in BCVA of ≥ 10 Letters, n (%)	4 (2.0)	7 (3.5)	0.60 [0.16; 2.23] 0.446	0.59 [0.17; 2.00] 0.388	-0.01 [-0.05; 0.02] 0.385
> 3 - < 12 months					
N"/N'/N	65 / 81 / 81	65 / 88 / 88			
Loss in BCVA of ≥ 10 Letters, n (%)	1 (1.2)	5 (5.7)	0.28 [0.03; 2.55] 0.257	0.31 [0.05; 1.74] 0.156	-0.04 [-0.10; 0.01] 0.118
≥ 12 months					
N"/N'/N	60 / 82 / 82	69 / 78 / 78			
Loss in BCVA of ≥ 10 Letters, n (%)	5 (6.1)	2 (2.6)	3.29 [0.58; 18.51] 0.177	2.09 [0.48; 9.00] 0.312	0.04 [-0.03; 0.10] 0.273

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Loss in BCVA of ≥ 10 Letters / KESTREL / Week 100, Loss in BCVA of ≥ 10 Letters / KITE / Week 100: logit(proportion) = treatment [by duration of DME].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 5.9 BCVA - Loss of 10 respectively 15 letters by DME type (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Loss in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.049 ***					
KESTREL: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.093				
focal					
N"/N'/N	51 / 59 / 59	35 / 48 / 48			
Loss in BCVA of ≥ 10 Letters, n (%)	1 (1.7)	2 (4.2)	0.37 [0.03; 4.21] 0.419	0.41 [0.04; 4.35] 0.457	-0.02 [-0.09; 0.04] 0.459
diffuse					
N"/N'/N	96 / 127 / 127	108 / 134 / 134			
Loss in BCVA of ≥ 10 Letters, n (%)	5 (3.9)	1 (0.7)	6.06 [0.69; 53.00] 0.104	5.28 [0.62; 44.54] 0.127	0.03 [-0.00; 0.07] 0.089
KITE: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.564				
focal					
N"/N'/N	46 / 63 / 63	54 / 66 / 66			
Loss in BCVA of ≥ 10 Letters, n (%)	1 (1.6)	5 (7.6)	0.19 [0.02; 1.68] 0.135	0.21 [0.03; 1.74] 0.148	-0.06 [-0.13; 0.01] 0.098
diffuse					
N"/N'/N	86 / 115 / 115	88 / 109 / 109			
Loss in BCVA of ≥ 10 Letters, n (%)	3 (2.6)	6 (5.5)	0.41 [0.10; 1.70] 0.219	0.47 [0.12; 1.85] 0.282	-0.03 [-0.08; 0.02] 0.273
Pooled Analysis: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.169				
focal					
N"/N'/N	97 / 122 / 122	89 / 114 / 114			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (1.6)	7 (6.1)	0.34 [0.06; 1.76] 0.197	0.27 [0.06; 1.30] 0.079	-0.04 [-0.09; 0.01] 0.080

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N"/N'/N	182 / 242 / 242	196 / 243 / 243			
Loss in BCVA of ≥ 10 Letters, n (%)	8 (3.3)	7 (2.9)	1.28 [0.43; 3.81] 0.656	1.13 [0.42; 3.03] 0.809	0.00 [-0.03; 0.03] 0.811

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 5.10 BCVA - Loss of 10 respectively 15 letters by CSFT (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Loss in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.049 ***					
KESTREL: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	N.E.				
< 450 µm					
N"/N'/N	86 / 107 / 107	76 / 96 / 96			
Loss in BCVA of ≥ 10 Letters, n (%)	3 (2.8)	3 (3.1)	0.89 [0.18; 4.54] 0.893	0.90 [0.19; 4.34] 0.893	-0.00 [-0.05; 0.04] 0.893
≥ 450 - < 650 µm					
N"/N'/N	55 / 70 / 70	55 / 71 / 71			
Loss in BCVA of ≥ 10 Letters, n (%)	3 (4.3)	0 (0.0)	N.E.	7.10 [0.37; 134.95] 0.192	0.04 [-0.00; 0.09] 0.077
≥ 650 µm					
N"/N'/N	8 / 12 / 12	16 / 20 / 20			
Loss in BCVA of ≥ 10 Letters, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	N.E.				
< 450 µm					
N"/N'/N	62 / 85 / 85	63 / 82 / 82			
Loss in BCVA of ≥ 10 Letters, n (%)	3 (3.5)	6 (7.3)	0.46 [0.11; 1.92] 0.289	0.48 [0.12; 1.86] 0.291	-0.04 [-0.11; 0.03] 0.280
≥ 450 - < 650 µm					
N"/N'/N	56 / 74 / 74	67 / 79 / 79			
Loss in BCVA of ≥ 10 Letters, n (%)	1 (1.4)	5 (6.3)	0.20 [0.02; 1.78] 0.150	0.21 [0.03; 1.79] 0.154	-0.05 [-0.11; 0.01] 0.103
≥ 650 µm					
N"/N'/N	15 / 20 / 20	15 / 19 / 19			
Loss in BCVA of ≥ 10 Letters, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	N.E.				
< 450 µm					
N"/N'/N	148 / 192 / 192	139 / 178 / 178			
Loss in BCVA of ≥ 10 Letters, n (%)	6 (3.1)	9 (5.1)	0.65 [0.22; 1.91] 0.432	0.62 [0.23; 1.72] 0.358	-0.02 [-0.06; 0.02] 0.360
≥ 450 - < 650 µm					
N"/N'/N	111 / 144 / 144	122 / 150 / 150			
Loss in BCVA of ≥ 10 Letters, n (%)	4 (2.8)	5 (3.3)	N.E.	0.85 [0.25; 2.97] 0.803	-0.01 [-0.04; 0.03] 0.791
≥ 650 µm					
N"/N'/N	23 / 32 / 32	31 / 39 / 39			
Loss in BCVA of ≥ 10 Letters, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Loss in BCVA of ≥ 15 Letters, Week 100					
Test of heterogeneity in main analysis: $\mathbf{p_H=0.409}$					
KESTREL: Loss in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	N.E.				
< 450 µm					
N"/N'/N	86 / 107 / 107	76 / 96 / 96			
Loss in BCVA of ≥ 15 Letters, n (%)	2 (1.9)	2 (2.1)	0.90 [0.12; 6.48] 0.913	0.90 [0.13; 6.25] 0.913	-0.00 [-0.04; 0.04] 0.913
≥ 450 - < 650 µm					
N"/N'/N	55 / 70 / 70	55 / 71 / 71			
Loss in BCVA of ≥ 15 Letters, n (%)	1 (1.4)	0 (0.0)	N.E.	3.04 [0.13; 73.43] 0.493	0.01 [-0.01; 0.04] 0.314
≥ 650 µm					
N"/N'/N	8 / 12 / 12	16 / 20 / 20			
Loss in BCVA of ≥ 15 Letters, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE: Loss in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	N.E.				
< 450 µm					
N"/N'/N	62 / 85 / 85	63 / 82 / 82			
Loss in BCVA of ≥ 15 Letters, n (%)	3 (3.5)	3 (3.7)	0.96 [0.19; 4.92] 0.964	0.96 [0.20; 4.64] 0.964	-0.00 [-0.06; 0.06] 0.964

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 450 - < 650 µm					
N"/N'/N	56 / 74 / 74	67 / 79 / 79			
Loss in BCVA of ≥ 15 Letters, n (%)	1 (1.4)	3 (3.8)	0.35 [0.04; 3.41] 0.364	0.36 [0.04; 3.35] 0.366	-0.02 [-0.07; 0.03] 0.335
≥ 650 µm					
N"/N'/N	15 / 20 / 20	15 / 19 / 19			
Loss in BCVA of ≥ 15 Letters, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Pooled Analysis: Loss in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	N.E.				
< 450 µm					
N"/N'/N	148 / 192 / 192	139 / 178 / 178			
Loss in BCVA of ≥ 15 Letters, n (%)	5 (2.6)	5 (2.8)	0.93 [0.26; 3.36] 0.909	0.94 [0.28; 3.18] 0.917	-0.00 [-0.03; 0.03] 0.917
≥ 450 - < 650 µm					
N"/N'/N	111 / 144 / 144	122 / 150 / 150			
Loss in BCVA of ≥ 15 Letters, n (%)	2 (1.4)	3 (2.0)	N.E.	0.75 [0.15; 3.78] 0.725	-0.01 [-0.04; 0.02] 0.695

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm					
N"/N'/N	23 / 32 / 32	31 / 39 / 39			
Loss in BCVA of ≥ 15 Letters, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Loss in BCVA of ≥ 10 Letters / KESTREL / Week 100, Loss in BCVA of ≥ 10 Letters / KITE / Week 100, Loss in BCVA of ≥ 15 Letters / KESTREL / Week 100, Loss in BCVA of ≥ 15 Letters / KITE / Week 100: logit(proportion) = treatment [by CSFT].
Loss in BCVA of ≥ 10 Letters / Pooled Analysis / Week 100, Loss in BCVA of ≥ 15 Letters / Pooled Analysis / Week 100: logit(proportion) = treatment + study + treatment * study [by CSFT].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 5.11 BCVA - Loss of 10 respectively 15 letters by status of SRF (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Loss in BCVA of ≥ 10 Letters, Week 52					
Test of heterogeneity in main analysis: **p_H=0.774**					
KESTREL: Loss in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	N.E.				
presence					
N"/N'/N	49 / 62 / 62	53 / 61 / 61			
Loss in BCVA of ≥ 10 Letters, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
absence					
N"/N'/N	105 / 127 / 127	108 / 126 / 126			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (1.6)	3 (2.4)	0.66 [0.11; 3.99] 0.647	0.66 [0.11; 3.89] 0.648	-0.01 [-0.04; 0.03] 0.645
KITE: Loss in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.867				
presence					
N"/N'/N	45 / 56 / 56	58 / 67 / 67			
Loss in BCVA of ≥ 10 Letters, n (%)	1 (1.8)	1 (1.5)	1.12 [0.07; 18.49] 0.936	1.20 [0.08; 18.70] 0.898	0.00 [-0.04; 0.05] 0.899
absence					
N"/N'/N	102 / 123 / 123	93 / 114 / 114			
Loss in BCVA of ≥ 10 Letters, n (%)	3 (2.4)	3 (2.6)	0.85 [0.17; 4.36] 0.846	0.93 [0.19; 4.50] 0.925	-0.00 [-0.04; 0.04] 0.925
Pooled Analysis: Loss in BCVA of ≥ 10 Letters, Week 52					
Interaction Test:	p = 0.842				
presence					
N"/N'/N	94 / 118 / 118	111 / 128 / 128			
Loss in BCVA of ≥ 10 Letters, n (%)	1 (0.8)	1 (0.8)	1.03 [0.06; 17.15] 0.981	1.20 [0.08; 18.70] 0.899	0.00 [-0.02; 0.02] 0.899
absence					
N"/N'/N	207 / 250 / 250	201 / 240 / 240			
Loss in BCVA of ≥ 10 Letters, n (%)	5 (2.0)	6 (2.5)	0.76 [0.22; 2.64] 0.665	0.80 [0.25; 2.58] 0.704	-0.01 [-0.03; 0.02] 0.704

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Loss in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.049 ***					
KESTREL: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	N.E.				
presence					
N"/N'/N	52 / 62 / 62	48 / 61 / 61			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (3.2)	0 (0.0)	N.E.	4.92 [0.24; 100.43] 0.300	0.03 [-0.01; 0.08] 0.151
absence					
N"/N'/N	97 / 127 / 127	99 / 126 / 126			
Loss in BCVA of ≥ 10 Letters, n (%)	4 (3.1)	3 (2.4)	1.33 [0.29; 6.08] 0.710	1.32 [0.30; 5.79] 0.710	0.01 [-0.03; 0.05] 0.709
KITE: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.708				
presence					
N"/N'/N	39 / 56 / 56	54 / 67 / 67			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (3.6)	5 (7.5)	0.43 [0.08; 2.31] 0.323	0.48 [0.10; 2.37] 0.367	-0.04 [-0.12; 0.04] 0.337
absence					
N"/N'/N	94 / 123 / 123	92 / 114 / 114			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (1.6)	6 (5.3)	0.27 [0.05; 1.39] 0.119	0.31 [0.06; 1.50] 0.145	-0.04 [-0.08; 0.01] 0.127
Pooled Analysis: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.683				
presence					
N"/N'/N	91 / 118 / 118	102 / 128 / 128			
Loss in BCVA of ≥ 10 Letters, n (%)	4 (3.4)	5 (3.9)	1.07 [0.26; 4.40] 0.925	0.92 [0.26; 3.21] 0.898	-0.00 [-0.05; 0.04] 0.893

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N"/N'/N	191 / 250 / 250	191 / 240 / 240			
Loss in BCVA of ≥ 10 Letters, n (%)	6 (2.4)	9 (3.8)	0.75 [0.25; 2.29] 0.613	0.64 [0.23; 1.76] 0.383	-0.01 [-0.04; 0.02] 0.386

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Loss in BCVA of ≥ 10 Letters / KESTREL / Week 52, Loss in BCVA of ≥ 10 Letters / KESTREL / Week 100: logit(proportion) = treatment [by status of SRF].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 5.12 BCVA - Loss of 10 respectively 15 letters by exposure (week 52) (FAS), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 5.13 BCVA - Loss of 10 respectively 15 letters by exposure (week 100) (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Loss in BCVA of ≥ 10 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.049 ***					
KESTREL: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	N.E.				
Non-exposed					
N"/N'/N	0 / 12 / 12	0 / 13 / 13			
Loss in BCVA of ≥ 10 Letters, n (%)	0 (0.0)	1 (7.7)	N.E.	0.36 [0.02; 8.05] 0.519	-0.08 [-0.22; 0.07] 0.298
Exposed					
N"/N'/N	149 / 177 / 177	147 / 174 / 174			
Loss in BCVA of ≥ 10 Letters, n (%)	6 (3.4)	2 (1.1)	3.02 [0.60; 15.16] 0.180	2.95 [0.60; 14.41] 0.182	0.02 [-0.01; 0.05] 0.157
KITE: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	N.E.				
Non-exposed					
N"/N'/N	0 / 17 / 17	0 / 12 / 12			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (11.8)	0 (0.0)	N.E.	3.61 [0.19; 69.09] 0.394	0.12 [-0.04; 0.27] 0.132
Exposed					
N"/N'/N	133 / 162 / 162	146 / 169 / 169			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (1.2)	11 (6.5)	0.18 [0.04; 0.82] 0.027 *	0.19 [0.04; 0.84] 0.029 *	-0.05 [-0.09; -0.01] 0.011 *
Pooled Analysis: Loss in BCVA of ≥ 10 Letters, Week 100					
Interaction Test:	p = 0.309				
Non-exposed					
N"/N'/N	0 / 29 / 29	0 / 25 / 25			
Loss in BCVA of ≥ 10 Letters, n (%)	2 (6.9)	1 (4.0)	2.87 [0.23; 36.19] 0.414	1.29 [0.21; 8.10] 0.784	0.03 [-0.09; 0.14] 0.664

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N"/N'/N	282 / 339 / 339	293 / 343 / 343			
Loss in BCVA of ≥ 10 Letters, n (%)	8 (2.4)	13 (3.8)	0.72 [0.27; 1.92] 0.505	0.63 [0.26; 1.51] 0.288	-0.01 [-0.04; 0.01] 0.287
Loss in BCVA of ≥ 15 Letters, Week 100					
Test of heterogeneity in main analysis: **p_H=0.409**					
KESTREL: Loss in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	N.E.				
Non-exposed					
N"/N'/N	0 / 12 / 12	0 / 13 / 13			
Loss in BCVA of ≥ 15 Letters, n (%)	0 (0.0)	1 (7.7)	N.E.	0.36 [0.02; 8.05] 0.519	-0.08 [-0.22; 0.07] 0.298
Exposed					
N"/N'/N	149 / 177 / 177	147 / 174 / 174			
Loss in BCVA of ≥ 15 Letters, n (%)	3 (1.7)	1 (0.6)	2.98 [0.31; 28.95] 0.346	2.95 [0.31; 28.08] 0.347	0.01 [-0.01; 0.03] 0.320
KITE: Loss in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	N.E.				
Non-exposed					
N"/N'/N	0 / 17 / 17	0 / 12 / 12			
Loss in BCVA of ≥ 15 Letters, n (%)	2 (11.8)	0 (0.0)	N.E.	3.61 [0.19; 69.09] 0.394	0.12 [-0.04; 0.27] 0.132
Exposed					
N"/N'/N	133 / 162 / 162	146 / 169 / 169			
Loss in BCVA of ≥ 15 Letters, n (%)	2 (1.2)	6 (3.6)	0.34 [0.07; 1.71] 0.190	0.35 [0.07; 1.70] 0.192	-0.02 [-0.06; 0.01] 0.165
Pooled Analysis: Loss in BCVA of ≥ 15 Letters, Week 100					
Interaction Test:	p = 0.459				
Non-exposed					
N"/N'/N	0 / 29 / 29	0 / 25 / 25			
Loss in BCVA of ≥ 15 Letters, n (%)	2 (6.9)	1 (4.0)	2.33 [0.18; 30.48] 0.519	1.29 [0.21; 8.10] 0.784	0.03 [-0.09; 0.14] 0.664

	Treatment Groups		Comparison		
BCVA - Loss of 10 respectively 15 letters by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N"/N'/N	282 / 339 / 339	293 / 343 / 343			
Loss in BCVA of ≥ 15 Letters, n (%)	5 (1.5)	7 (2.0)	0.81 [0.23; 2.79] 0.737	0.73 [0.23; 2.29] 0.587	-0.01 [-0.03; 0.01] 0.586

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Loss in BCVA of ≥ 10 Letters / KESTREL / Week 100, Loss in BCVA of ≥ 10 Letters / KITE / Week 100, Loss in BCVA of ≥ 15 Letters / KESTREL / Week 100, Loss in BCVA of ≥ 15 Letters / KITE / Week 100: logit(proportion) = treatment [by exposure (week 100)].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

6 BCVA: Time-to-event analysis (Gain)

Table 6.1 BCVA - Gain of 10 respectively 15 letters (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥10 letters, Week 52				
KESTREL, N'/ N	189 / 189	187 / 187		
Number of patients with at least one event, n (%)	140 (74.1)	146 (78.1)		
Median (in weeks)	15.1 [12.0; 18.9]	12.9 [11.4; 18.0]		
% of outcome-free patients[1]	20.60 [12.33; 28.87]	18.32 [11.58; 25.06]	0.87 [0.69; 1.10] 0.235	0.472
KITE, N'/ N	179 / 179	181 / 181		
Number of patients with at least one event, n (%)	139 (77.7)	145 (80.1)		
Median (in weeks)	11.9 [8.1; 17.6]	12.1 [9.0; 15.1]		
% of outcome-free patients[1]	19.66 [13.55; 25.78]	17.68 [11.95; 23.41]	1.01 [0.80; 1.28] 0.934	0.524
Pooled Analysis, N'/ N	368 / 368	368 / 368		
Number of patients with at least one event, n (%)	279 (75.8)	291 (79.1)		
Median (in weeks)	12.4 [10.1; 17.1]	12.4 [11.6; 16.0]		
% of outcome-free patients[1] p_H=0.347	19.46 [13.48; 25.43]	17.49 [12.79; 22.19]	0.95 [0.80; 1.12] 0.510	0.337
Time to first gain in BCVA of ≥10 letters, Week 100				
KESTREL, N'/ N	189 / 189	187 / 187		
Number of patients with at least one event, n (%)	152 (80.4)	156 (83.4)		
Median (in weeks)	15.1 [12.0; 18.9]	12.9 [11.4; 18.0]		
% of outcome-free patients[1]	15.44 [9.86; 21.02]	10.56 [1.39; 19.72]	0.90 [0.72; 1.12] 0.349	0.590
KITE, N'/ N	179 / 179	181 / 181		
Number of patients with at least one event, n (%)	145 (81.0)	156 (86.2)		
Median (in weeks)	11.9 [8.1; 17.6]	12.1 [9.0; 15.1]		
% of outcome-free patients[1]	16.24 [10.62; 21.86]	9.18 [3.96; 14.40]	0.98 [0.78; 1.23] 0.833	0.328

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis, N'/ N	368 / 368	368 / 368		
Number of patients with at least one event, n (%)	297 (80.7)	312 (84.8)		
Median (in weeks)	12.4 [10.1; 17.1]	12.4 [11.6; 16.0]		
% of outcome-free patients[1] p_H=0.583	15.90 [11.93; 19.87]	9.84 [4.46; 15.22]	0.94 [0.80; 1.10] 0.440	0.285
Time to first gain in BCVA of ≥15 letters, Week 52				
KESTREL, N'/ N	189 / 189	187 / 187		
Number of patients with at least one event, n (%)	114 (60.3)	108 (57.8)		
Median (in weeks)	29.3 [23.7; 40.1]	29.3 [20.6; 48.1]		
% of outcome-free patients[1]	33.92 [24.39; 43.45]	26.35 [4.60; 48.10]	1.01 [0.78; 1.32] 0.935	0.741
KITE, N'/ N	179 / 179	181 / 181		
Number of patients with at least one event, n (%)	119 (66.5)	117 (64.6)		
Median (in weeks)	24.1 [18.1; 31.4]	20.1 [18.1; 25.1]		
% of outcome-free patients[1]	23.87 [11.60; 36.14]	31.49 [23.31; 39.66]	1.08 [0.83; 1.39] 0.581	0.767
Pooled Analysis, N'/ N	368 / 368	368 / 368		
Number of patients with at least one event, n (%)	233 (63.3)	225 (61.1)		
Median (in weeks)	27.3 [21.7; 32.1]	24.1 [19.7; 28.9]		
% of outcome-free patients[1] p_H=0.696	29.41 [21.95; 36.88]	23.75 [4.37; 43.13]	1.06 [0.88; 1.28] 0.518	0.658
Time to first gain in BCVA of ≥15 letters, Week 100				
KESTREL, N'/ N	189 / 189	187 / 187		
Number of patients with at least one event, n (%)	133 (70.4)	124 (66.3)		
Median (in weeks)	29.3 [23.7; 41.1]	29.3 [20.6; 48.1]		
% of outcome-free patients[1]	24.39 [17.73; 31.05]	29.16 [21.57; 36.74]	1.07 [0.84; 1.37] 0.570	0.436

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE, N'/ N	179 / 179	181 / 181		
Number of patients with at least one event, n (%)	128 (71.5)	128 (70.7)		
Median (in weeks)	24.1 [18.1; 31.4]	20.1 [18.1; 25.1]		
% of outcome-free patients[1]	23.43 [15.93; 30.93]	25.78 [19.01; 32.55]	1.07 [0.83; 1.37] 0.610	0.832
Pooled Analysis, N'/ N	368 / 368	368 / 368		
Number of patients with at least one event, n (%)	261 (70.9)	252 (68.5)		
Median (in weeks)	27.3 [21.7; 32.1]	24.1 [19.7; 28.9]		
% of outcome-free patients[1] p_H=0.933	23.60 [18.26; 28.94]	27.46 [22.32; 32.59]	1.08 [0.91; 1.29] 0.368	0.483

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study.

Table 6.2 BCVA - Gain of 10 respectively 15 letters by age (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.347**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.040 *			
< 65 years				
KESTREL, N'/ N	104 / 104	93 / 93		
Number of patients with at least one event, n (%)	91 (87.5)	78 (83.9)		
Median (in weeks)	8.1 [6.1; 12.1]	12.1 [9.1; 16.1]		
% of outcome-free patients[1]	5.58 [0.00; 13.92]	15.29 [7.61; 22.97]	1.07 [0.79; 1.45] 0.670	0.202
≥ 65 years				
KESTREL, N'/ N	85 / 85	94 / 94		
Number of patients with at least one event, n (%)	49 (57.6)	68 (72.3)		
Median (in weeks)	31.1 [20.3; N.E.]	18.1 [8.1; 28.0]		
% of outcome-free patients[1]	39.74 [28.87; 50.61]	20.09 [8.29; 31.89]	0.65 [0.45; 0.93] 0.020 *	0.020 *
KITE: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.439			
< 65 years				
KITE, N'/ N	100 / 100	102 / 102		
Number of patients with at least one event, n (%)	82 (82.0)	85 (83.3)		
Median (in weeks)	8.1 [6.6; 12.4]	11.1 [8.1; 12.4]		
% of outcome-free patients[1]	14.83 [7.52; 22.15]	14.15 [7.19; 21.12]	1.09 [0.80; 1.48] 0.576	0.960
≥ 65 years				
KITE, N'/ N	79 / 79	79 / 79		
Number of patients with at least one event, n (%)	57 (72.2)	60 (75.9)		
Median (in weeks)	18.1 [9.1; 28.1]	13.3 [8.6; 19.1]		
% of outcome-free patients[1]	25.30 [15.02; 35.58]	22.12 [12.69; 31.55]	0.91 [0.63; 1.30] 0.592	0.363

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.040 *			
< 65 years				
Pooled Analysis, N'/ N	204 / 204	195 / 195		
Number of patients with at least one event, n (%)	173 (84.8)	163 (83.6)		
Median (in weeks)	8.1 [6.7; 12.0]	12.1 [9.1; 12.6]		
% of outcome-free patients[1]	6.47 [0.00; 15.76]	14.34 [9.01; 19.67]	1.09 [0.88; 1.35] 0.415	0.348
≥ 65 years				
Pooled Analysis, N'/ N	164 / 164	173 / 173		
Number of patients with at least one event, n (%)	106 (64.6)	128 (74.0)		
Median (in weeks)	24.9 [17.1; 32.1]	16.1 [11.9; 20.0]		
% of outcome-free patients[1]	32.75 [25.15; 40.34]	20.02 [11.41; 28.63]	0.77 [0.59; 0.99] 0.046 *	0.022 *
Time to first gain in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.583**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.082			
< 65 years				
KESTREL, N'/ N	104 / 104	93 / 93		
Number of patients with at least one event, n (%)	93 (89.4)	82 (88.2)		
Median (in weeks)	8.1 [6.1; 12.1]	12.1 [9.1; 16.1]		
% of outcome-free patients[1]	7.65 [2.21; 13.08]	11.73 [5.16; 18.30]	1.07 [0.79; 1.45] 0.652	0.233
≥ 65 years				
KESTREL, N'/ N	85 / 85	94 / 94		
Number of patients with at least one event, n (%)	59 (69.4)	74 (78.7)		
Median (in weeks)	31.1 [20.3; 55.9]	18.1 [8.1; 28.0]		
% of outcome-free patients[1]	24.82 [14.75; 34.89]	13.32 [1.30; 25.33]	0.72 [0.51; 1.01] 0.055	0.058

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.618			
< 65 years				
KITE, N'/ N	100 / 100	102 / 102		
Number of patients with at least one event, n (%)	84 (84.0)	92 (90.2)		
Median (in weeks)	8.1 [6.6; 12.4]	11.1 [8.1; 12.4]		
% of outcome-free patients[1]	12.59 [5.73; 19.44]	5.72 [0.55; 10.88]	1.02 [0.76; 1.38] 0.874	0.735
≥ 65 years				
KITE, N'/ N	79 / 79	79 / 79		
Number of patients with at least one event, n (%)	61 (77.2)	64 (81.0)		
Median (in weeks)	18.1 [9.1; 28.1]	13.3 [8.6; 19.1]		
% of outcome-free patients[1]	20.89 [11.68; 30.10]	15.66 [7.04; 24.28]	0.91 [0.64; 1.30] 0.606	0.351
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.112			
< 65 years				
Pooled Analysis, N'/ N	204 / 204	195 / 195		
Number of patients with at least one event, n (%)	177 (86.8)	174 (89.2)		
Median (in weeks)	8.1 [6.7; 12.0]	12.1 [9.1; 12.6]		
% of outcome-free patients[1]	10.10 [5.73; 14.47]	7.17 [2.01; 12.32]	1.05 [0.85; 1.29] 0.652	0.548
≥ 65 years				
Pooled Analysis, N'/ N	164 / 164	173 / 173		
Number of patients with at least one event, n (%)	120 (73.2)	138 (79.8)		
Median (in weeks)	24.9 [17.1; 32.1]	16.1 [11.9; 20.0]		
% of outcome-free patients[1]	22.94 [16.07; 29.80]	13.62 [4.70; 22.54]	0.81 [0.63; 1.03] 0.088	0.044 *
Time to first gain in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.696**				

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.115			
< 65 years				
KESTREL, N'/ N	104 / 104	93 / 93		
Number of patients with at least one event, n (%)	75 (72.1)	59 (63.4)		
Median (in weeks)	18.1 [12.1; 24.1]	21.0 [16.3; 36.9]		
% of outcome-free patients[1]	19.83 [6.82; 32.84]	18.42 [0.00; 44.42]	1.21 [0.85; 1.71] 0.286	0.134
≥ 65 years				
KESTREL, N'/ N	85 / 85	94 / 94		
Number of patients with at least one event, n (%)	39 (45.9)	49 (52.1)		
Median (in weeks)	N.E.	43.1 [24.1; N.E.]		
% of outcome-free patients[1]	51.35 [40.25; 62.46]	41.43 [28.10; 54.76]	0.78 [0.51; 1.19] 0.243	0.216
KITE: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.398			
< 65 years				
KITE, N'/ N	100 / 100	102 / 102		
Number of patients with at least one event, n (%)	74 (74.0)	71 (69.6)		
Median (in weeks)	20.1 [12.6; 25.1]	18.4 [16.4; 25.0]		
% of outcome-free patients[1]	0.00 [0.00; 0.00]	28.18 [19.25; 37.11]	1.18 [0.84; 1.64] 0.338	0.408
≥ 65 years				
KITE, N'/ N	79 / 79	79 / 79		
Number of patients with at least one event, n (%)	45 (57.0)	46 (58.2)		
Median (in weeks)	32.1 [19.9; N.E.]	24.1 [18.1; N.E.]		
% of outcome-free patients[1]	37.86 [24.01; 51.72]	36.53 [22.92; 50.15]	0.94 [0.62; 1.41] 0.755	0.737

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.063			
< 65 years				
Pooled Analysis, N'/ N	204 / 204	195 / 195		
Number of patients with at least one event, n (%)	149 (73.0)	130 (66.7)		
Median (in weeks)	18.1 [15.4; 24.1]	19.7 [17.1; 25.0]		
% of outcome-free patients[1]	14.89 [3.61; 26.18]	16.18 [0.00; 38.85]	1.22 [0.97; 1.55] 0.096	0.102
≥ 65 years				
Pooled Analysis, N'/ N	164 / 164	173 / 173		
Number of patients with at least one event, n (%)	84 (51.2)	95 (54.9)		
Median (in weeks)	44.1 [35.1; N.E.]	32.3 [21.0; 52.9]		
% of outcome-free patients[1]	44.98 [36.01; 53.94]	39.21 [29.66; 48.76]	0.86 [0.64; 1.15] 0.296	0.268
Time to first gain in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.933**				
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.094			
< 65 years				
KESTREL, N'/ N	104 / 104	93 / 93		
Number of patients with at least one event, n (%)	83 (79.8)	65 (69.9)		
Median (in weeks)	18.1 [12.1; 24.1]	21.0 [16.3; 36.9]		
% of outcome-free patients[1]	15.24 [7.65; 22.83]	28.54 [19.13; 37.95]	1.29 [0.93; 1.80] 0.126	0.070
≥ 65 years				
KESTREL, N'/ N	85 / 85	94 / 94		
Number of patients with at least one event, n (%)	50 (58.8)	59 (62.8)		
Median (in weeks)	60.1 [40.1; 87.6]	43.1 [24.1; 72.1]		
% of outcome-free patients[1]	35.44 [24.39; 46.48]	30.88 [19.98; 41.79]	0.84 [0.58; 1.23] 0.373	0.373

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.467			
< 65 years				
KITE, N'/ N	100 / 100	102 / 102		
Number of patients with at least one event, n (%)	78 (78.0)	78 (76.5)		
Median (in weeks)	20.1 [12.6; 25.1]	18.4 [16.4; 25.0]		
% of outcome-free patients[1]	13.78 [3.92; 23.64]	19.41 [11.19; 27.63]	1.15 [0.84; 1.58] 0.394	0.495
≥ 65 years				
KITE, N'/ N	79 / 79	79 / 79		
Number of patients with at least one event, n (%)	50 (63.3)	50 (63.3)		
Median (in weeks)	32.1 [19.9; 68.7]	24.1 [18.1; 56.6]		
% of outcome-free patients[1]	34.64 [23.81; 45.46]	34.23 [23.29; 45.17]	0.95 [0.64; 1.41] 0.809	0.777
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.069			
< 65 years				
Pooled Analysis, N'/ N	204 / 204	195 / 195		
Number of patients with at least one event, n (%)	161 (78.9)	143 (73.3)		
Median (in weeks)	18.1 [15.4; 24.1]	19.7 [17.1; 25.0]		
% of outcome-free patients[1]	14.07 [7.25; 20.90]	23.82 [17.55; 30.08]	1.24 [0.99; 1.55] 0.064	0.080

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
≥ 65 years				
Pooled Analysis, N'/ N	164 / 164	173 / 173		
Number of patients with at least one event, n (%)	100 (61.0)	109 (63.0)		
Median (in weeks)	44.1 [35.1; 64.0]	32.3 [21.0; 56.6]		
% of outcome-free patients[1]	35.25 [27.50; 42.99]	31.76 [23.57; 39.95]	0.89 [0.68; 1.17] 0.409	0.401

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
*: $p < 0.05$
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + baseline category + age + treatment * age.
Pooled analysis: log(hazard ratio) = treatment + baseline category + study + treatment * study + age + treatment * age.

Table 6.3 BCVA - Gain of 10 respectively 15 letters by gender (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.347**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.191			
Male				
KESTREL, N'/ N	110 / 110	126 / 126		
Number of patients with at least one event, n (%)	82 (74.5)	96 (76.2)		
Median (in weeks)	15.1 [8.1; 18.9]	12.4 [8.7; 18.1]		
% of outcome-free patients[1]	17.20 [5.63; 28.76]	20.39 [12.39; 28.38]	0.99 [0.73; 1.33] 0.935	0.962
Female				
KESTREL, N'/ N	79 / 79	61 / 61		
Number of patients with at least one event, n (%)	58 (73.4)	50 (82.0)		
Median (in weeks)	16.1 [12.0; 24.1]	13.1 [9.1; 19.7]		
% of outcome-free patients[1]	25.63 [15.82; 35.44]	13.11 [0.69; 25.54]	0.72 [0.49; 1.05] 0.086	0.291
KITE: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.190			
Male				
KITE, N'/ N	120 / 120	115 / 115		
Number of patients with at least one event, n (%)	94 (78.3)	96 (83.5)		
Median (in weeks)	11.9 [8.1; 17.1]	12.1 [8.4; 15.4]		
% of outcome-free patients[1]	20.16 [12.84; 27.47]	15.06 [8.37; 21.75]	0.90 [0.68; 1.19] 0.461	0.342
Female				
KITE, N'/ N	59 / 59	66 / 66		
Number of patients with at least one event, n (%)	45 (76.3)	49 (74.2)		
Median (in weeks)	11.9 [6.6; 23.6]	12.4 [9.0; 18.7]		
% of outcome-free patients[1]	17.30 [5.65; 28.95]	22.50 [12.01; 32.98]	1.25 [0.83; 1.89] 0.282	0.866

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.886			
Male				
Pooled Analysis, N'/ N	230 / 230	241 / 241		
Number of patients with at least one event, n (%)	176 (76.5)	192 (79.7)		
Median (in weeks)	12.0 [8.1; 16.7]	12.1 [9.1; 16.1]		
% of outcome-free patients[1]	17.91 [10.03; 25.80]	17.60 [12.21; 22.99]	0.94 [0.77; 1.15] 0.552	0.475
Female				
Pooled Analysis, N'/ N	138 / 138	127 / 127		
Number of patients with at least one event, n (%)	103 (74.6)	99 (78.0)		
Median (in weeks)	13.1 [11.1; 20.4]	12.9 [11.4; 18.1]		
% of outcome-free patients[1]	22.29 [14.73; 29.84]	15.73 [5.30; 26.16]	0.96 [0.73; 1.27] 0.794	0.514
Time to first gain in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.583**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.146			
Male				
KESTREL, N'/ N	110 / 110	126 / 126		
Number of patients with at least one event, n (%)	91 (82.7)	105 (83.3)		
Median (in weeks)	15.1 [8.1; 18.9]	12.4 [8.7; 18.1]		
% of outcome-free patients[1]	9.49 [3.02; 15.96]	10.44 [1.03; 19.85]	1.04 [0.78; 1.38] 0.783	0.736
Female				
KESTREL, N'/ N	79 / 79	61 / 61		
Number of patients with at least one event, n (%)	61 (77.2)	51 (83.6)		
Median (in weeks)	16.1 [12.0; 24.1]	13.1 [9.1; 19.7]		
% of outcome-free patients[1]	21.97 [12.68; 31.26]	16.23 [6.92; 25.54]	0.73 [0.50; 1.07] 0.107	0.329

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.207			
Male				
KITE, N'/ N	120 / 120	115 / 115		
Number of patients with at least one event, n (%)	99 (82.5)	103 (89.6)		
Median (in weeks)	11.9 [8.1; 17.1]	12.1 [8.4; 15.4]		
% of outcome-free patients[1]	15.67 [9.00; 22.35]	8.21 [2.97; 13.46]	0.87 [0.66; 1.15] 0.335	0.222
Female				
KITE, N'/ N	59 / 59	66 / 66		
Number of patients with at least one event, n (%)	46 (78.0)	53 (80.3)		
Median (in weeks)	11.9 [6.6; 23.6]	12.4 [9.0; 18.7]		
% of outcome-free patients[1]	17.47 [7.14; 27.81]	0.00 [0.00; 0.00]	1.19 [0.80; 1.78] 0.389	0.890
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.981			
Male				
Pooled Analysis, N'/ N	230 / 230	241 / 241		
Number of patients with at least one event, n (%)	190 (82.6)	208 (86.3)		
Median (in weeks)	12.0 [8.1; 16.7]	12.1 [9.1; 16.1]		
% of outcome-free patients[1]	13.29 [8.55; 18.03]	9.62 [4.20; 15.04]	0.94 [0.77; 1.15] 0.567	0.527
Female				
Pooled Analysis, N'/ N	138 / 138	127 / 127		
Number of patients with at least one event, n (%)	107 (77.5)	104 (81.9)		
Median (in weeks)	13.1 [11.1; 20.4]	12.9 [11.4; 18.1]		
% of outcome-free patients[1]	20.08 [13.14; 27.02]	0.00 [0.00; 0.00]	0.94 [0.72; 1.23] 0.656	0.421
Time to first gain in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.696**				

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.272			
Male				
KESTREL, N'/ N	110 / 110	126 / 126		
Number of patients with at least one event, n (%)	70 (63.6)	73 (57.9)		
Median (in weeks)	24.1 [18.4; 36.1]	29.3 [20.3; 52.9]		
% of outcome-free patients[1]	29.27 [17.39; 41.16]	26.07 [4.21; 47.92]	1.16 [0.83; 1.61] 0.388	0.346
Female				
KESTREL, N'/ N	79 / 79	61 / 61		
Number of patients with at least one event, n (%)	44 (55.7)	35 (57.4)		
Median (in weeks)	40.1 [24.3; N.E.]	35.4 [17.9; N.E.]		
% of outcome-free patients[1]	42.48 [31.22; 53.75]	41.50 [28.94; 54.05]	0.85 [0.54; 1.32] 0.468	0.652
KITE: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.598			
Male				
KITE, N'/ N	120 / 120	115 / 115		
Number of patients with at least one event, n (%)	84 (70.0)	79 (68.7)		
Median (in weeks)	24.1 [16.6; 32.0]	19.1 [16.4; 24.4]		
% of outcome-free patients[1]	16.95 [1.68; 32.22]	27.13 [16.80; 37.47]	1.02 [0.75; 1.38] 0.917	0.923
Female				
KITE, N'/ N	59 / 59	66 / 66		
Number of patients with at least one event, n (%)	35 (59.3)	38 (57.6)		
Median (in weeks)	23.6 [16.7; N.E.]	25.0 [18.1; N.E.]		
% of outcome-free patients[1]	37.87 [25.05; 50.70]	39.49 [27.24; 51.73]	1.18 [0.74; 1.89] 0.485	0.811

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.774			
Male				
Pooled Analysis, N'/ N	230 / 230	241 / 241		
Number of patients with at least one event, n (%)	154 (67.0)	152 (63.1)		
Median (in weeks)	24.1 [19.0; 29.3]	20.9 [18.9; 28.9]		
% of outcome-free patients[1]	23.82 [14.58; 33.06]	22.37 [3.86; 40.88]	1.09 [0.87; 1.36] 0.455	0.475
Female				
Pooled Analysis, N'/ N	138 / 138	127 / 127		
Number of patients with at least one event, n (%)	79 (57.2)	73 (57.5)		
Median (in weeks)	33.3 [23.6; 49.1]	27.9 [18.9; 48.1]		
% of outcome-free patients[1]	40.66 [32.21; 49.11]	40.49 [31.72; 49.25]	1.03 [0.75; 1.42] 0.862	0.875
Time to first gain in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.933**				
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.197			
Male				
KESTREL, N'/ N	110 / 110	126 / 126		
Number of patients with at least one event, n (%)	81 (73.6)	83 (65.9)		
Median (in weeks)	24.1 [18.4; 36.1]	29.3 [20.3; 52.9]		
% of outcome-free patients[1]	19.31 [11.06; 27.57]	28.73 [19.30; 38.16]	1.25 [0.92; 1.70] 0.161	0.142
Female				
KESTREL, N'/ N	79 / 79	61 / 61		
Number of patients with at least one event, n (%)	52 (65.8)	41 (67.2)		
Median (in weeks)	41.1 [24.3; 60.1]	35.4 [17.9; 63.9]		
% of outcome-free patients[1]	30.87 [20.07; 41.66]	30.86 [18.98; 42.75]	0.89 [0.59; 1.34] 0.578	0.723

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.395			
Male				
KITE, N'/ N	120 / 120	115 / 115		
Number of patients with at least one event, n (%)	89 (74.2)	87 (75.7)		
Median (in weeks)	24.1 [16.6; 32.0]	19.1 [16.4; 24.4]		
% of outcome-free patients[1]	20.62 [11.40; 29.83]	21.31 [13.35; 29.27]	0.98 [0.73; 1.32] 0.909	0.893
Female				
KITE, N'/ N	59 / 59	66 / 66		
Number of patients with at least one event, n (%)	39 (66.1)	41 (62.1)		
Median (in weeks)	23.6 [16.7; 60.0]	25.0 [18.1; 71.3]		
% of outcome-free patients[1]	29.50 [17.14; 41.86]	33.95 [21.84; 46.06]	1.24 [0.79; 1.94] 0.347	0.667
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.816			
Male				
Pooled Analysis, N'/ N	230 / 230	241 / 241		
Number of patients with at least one event, n (%)	170 (73.9)	170 (70.5)		
Median (in weeks)	24.1 [19.0; 29.3]	20.9 [18.9; 28.9]		
% of outcome-free patients[1]	19.58 [12.76; 26.39]	25.25 [19.08; 31.42]	1.11 [0.89; 1.37] 0.351	0.358

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Female				
Pooled Analysis, N'/ N	138 / 138	127 / 127		
Number of patients with at least one event, n (%)	91 (65.9)	82 (64.6)		
Median (in weeks)	33.3 [23.6; 49.1]	27.9 [18.9; 48.1]		
% of outcome-free patients[1]	30.35 [22.22; 38.48]	32.34 [23.85; 40.83]	1.06 [0.78; 1.43] 0.707	0.972

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + gender + treatment * gender.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + gender + treatment * gender.

Table 6.4 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.347**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.044 *			
≤ 65 letters				
KESTREL, N'/ N	74 / 74	64 / 64		
Number of patients with at least one event, n (%)	61 (82.4)	61 (95.3)		
Median (in weeks)	9.8 [6.1; 15.7]	7.4 [6.0; 9.1]		
% of outcome-free patients[1]	14.43 [5.87; 23.00]	2.93 [0.00; 7.96]	0.66 [0.46; 0.94] 0.021 *	0.081
> 65 letters				
KESTREL, N'/ N	115 / 115	123 / 123		
Number of patients with at least one event, n (%)	79 (68.7)	85 (69.1)		
Median (in weeks)	18.1 [12.4; 25.1]	19.0 [13.1; 24.1]		
% of outcome-free patients[1]	23.94 [11.37; 36.52]	26.75 [17.37; 36.13]	1.07 [0.78; 1.45] 0.677	0.979
KITE: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.615			
≤ 65 letters				
KITE, N'/ N	65 / 65	91 / 91		
Number of patients with at least one event, n (%)	57 (87.7)	77 (84.6)		
Median (in weeks)	6.6 [6.0; 12.0]	8.4 [6.4; 12.3]		
% of outcome-free patients[1]	11.18 [3.40; 18.97]	13.02 [5.85; 20.19]	1.08 [0.76; 1.52] 0.671	0.809
> 65 letters				
KITE, N'/ N	114 / 114	90 / 90		
Number of patients with at least one event, n (%)	82 (71.9)	68 (75.6)		
Median (in weeks)	16.4 [8.4; 21.9]	16.1 [12.1; 19.1]		
% of outcome-free patients[1]	24.48 [16.01; 32.95]	22.33 [13.49; 31.17]	0.95 [0.69; 1.32] 0.778	0.759

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.349			
≤ 65 letters				
Pooled Analysis, N'/ N	139 / 139	155 / 155		
Number of patients with at least one event, n (%)	118 (84.9)	138 (89.0)		
Median (in weeks)	8.1 [6.3; 12.0]	8.1 [6.4; 11.1]		
% of outcome-free patients[1]	12.97 [7.14; 18.80]	8.01 [2.77; 13.25]	0.87 [0.68; 1.11] 0.256	0.299
> 65 letters				
Pooled Analysis, N'/ N	229 / 229	213 / 213		
Number of patients with at least one event, n (%)	161 (70.3)	153 (71.8)		
Median (in weeks)	17.6 [12.4; 21.6]	17.1 [13.1; 19.4]		
% of outcome-free patients[1]	22.73 [13.15; 32.30]	24.39 [17.46; 31.31]	1.02 [0.81; 1.27] 0.884	0.818
Time to first gain in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.583**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.048 *			
≤ 65 letters				
KESTREL, N'/ N	74 / 74	64 / 64		
Number of patients with at least one event, n (%)	63 (85.1)	61 (95.3)		
Median (in weeks)	9.8 [6.1; 15.7]	7.4 [6.0; 9.1]		
% of outcome-free patients[1]	10.02 [2.10; 17.94]	4.69 [0.00; 9.87]	0.68 [0.48; 0.97] 0.033 *	0.105
> 65 letters				
KESTREL, N'/ N	115 / 115	123 / 123		
Number of patients with at least one event, n (%)	89 (77.4)	95 (77.2)		
Median (in weeks)	18.1 [12.4; 25.1]	19.0 [13.1; 24.1]		
% of outcome-free patients[1]	18.80 [11.20; 26.39]	10.85 [0.00; 26.34]	1.08 [0.81; 1.45] 0.597	0.907

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.581			
≤ 65 letters				
KITE, N'/ N	65 / 65	91 / 91		
Number of patients with at least one event, n (%)	59 (90.8)	82 (90.1)		
Median (in weeks)	6.6 [6.0; 12.0]	8.4 [6.4; 12.3]		
% of outcome-free patients[1]	7.67 [0.95; 14.39]	5.97 [0.41; 11.52]	1.05 [0.75; 1.46] 0.795	0.901
> 65 letters				
KITE, N'/ N	114 / 114	90 / 90		
Number of patients with at least one event, n (%)	86 (75.4)	74 (82.2)		
Median (in weeks)	16.4 [8.4; 21.9]	16.1 [12.1; 19.1]		
% of outcome-free patients[1]	21.28 [13.45; 29.12]	13.18 [5.08; 21.28]	0.92 [0.67; 1.25] 0.596	0.562
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.367			
≤ 65 letters				
Pooled Analysis, N'/ N	139 / 139	155 / 155		
Number of patients with at least one event, n (%)	122 (87.8)	143 (92.3)		
Median (in weeks)	8.1 [6.3; 12.0]	8.1 [6.4; 11.1]		
% of outcome-free patients[1]	8.82 [3.57; 14.06]	5.67 [1.80; 9.54]	0.86 [0.68; 1.10] 0.236	0.306
> 65 letters				
Pooled Analysis, N'/ N	229 / 229	213 / 213		
Number of patients with at least one event, n (%)	175 (76.4)	169 (79.3)		
Median (in weeks)	17.6 [12.4; 21.6]	17.1 [13.1; 19.4]		
% of outcome-free patients[1]	20.11 [14.65; 25.57]	12.95 [4.32; 21.59]	1.00 [0.81; 1.24] 0.983	0.759
Time to first gain in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.696**				

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.111			
≤ 65 letters				
KESTREL, N'/ N	74 / 74	64 / 64		
Number of patients with at least one event, n (%)	50 (67.6)	47 (73.4)		
Median (in weeks)	24.3 [18.1; 35.1]	17.9 [13.0; 32.9]		
% of outcome-free patients[1]	29.05 [18.13; 39.97]	11.24 [0.00; 28.20]	0.79 [0.53; 1.18] 0.249	0.513
> 65 letters				
KESTREL, N'/ N	115 / 115	123 / 123		
Number of patients with at least one event, n (%)	64 (55.7)	61 (49.6)		
Median (in weeks)	40.1 [23.4; N.E.]	40.9 [25.0; N.E.]		
% of outcome-free patients[1]	36.90 [23.16; 50.64]	48.91 [39.90; 57.93]	1.22 [0.86; 1.74] 0.265	0.435
KITE: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.910			
≤ 65 letters				
KITE, N'/ N	65 / 65	91 / 91		
Number of patients with at least one event, n (%)	44 (67.7)	61 (67.0)		
Median (in weeks)	21.7 [16.1; 32.6]	19.1 [16.3; 28.1]		
% of outcome-free patients[1]	27.59 [14.63; 40.54]	30.83 [21.09; 40.57]	1.06 [0.72; 1.56] 0.778	0.996
> 65 letters				
KITE, N'/ N	114 / 114	90 / 90		
Number of patients with at least one event, n (%)	75 (65.8)	56 (62.2)		
Median (in weeks)	24.1 [18.1; 32.1]	24.0 [18.1; 28.6]		
% of outcome-free patients[1]	21.60 [3.33; 39.87]	31.97 [18.95; 44.99]	1.09 [0.77; 1.54] 0.627	0.586

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.282			
≤ 65 letters				
Pooled Analysis, N'/ N	139 / 139	155 / 155		
Number of patients with at least one event, n (%)	94 (67.6)	108 (69.7)		
Median (in weeks)	24.3 [18.1; 32.0]	18.9 [16.3; 25.0]		
% of outcome-free patients[1]	28.29 [19.73; 36.86]	13.51 [0.00; 32.71]	0.95 [0.72; 1.25] 0.701	0.648
> 65 letters				
Pooled Analysis, N'/ N	229 / 229	213 / 213		
Number of patients with at least one event, n (%)	139 (60.7)	117 (54.9)		
Median (in weeks)	28.1 [21.6; 36.3]	28.9 [21.0; 52.9]		
% of outcome-free patients[1]	30.27 [19.55; 40.99]	41.93 [34.31; 49.54]	1.16 [0.91; 1.49] 0.231	0.350
Time to first gain in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.933**				
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.041 *			
≤ 65 letters				
KESTREL, N'/ N	74 / 74	64 / 64		
Number of patients with at least one event, n (%)	54 (73.0)	51 (79.7)		
Median (in weeks)	24.3 [18.1; 35.1]	17.9 [13.0; 32.9]		
% of outcome-free patients[1]	21.98 [11.67; 32.28]	17.51 [7.74; 27.28]	0.79 [0.54; 1.16] 0.224	0.413
> 65 letters				
KESTREL, N'/ N	115 / 115	123 / 123		
Number of patients with at least one event, n (%)	79 (68.7)	73 (59.3)		
Median (in weeks)	40.1 [23.4; 60.1]	40.9 [25.0; 80.9]		
% of outcome-free patients[1]	25.88 [17.19; 34.57]	35.53 [25.54; 45.51]	1.33 [0.97; 1.83] 0.081	0.153

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.917			
≤ 65 letters				
KITE, N'/ N	65 / 65	91 / 91		
Number of patients with at least one event, n (%)	47 (72.3)	66 (72.5)		
Median (in weeks)	21.7 [16.1; 32.6]	19.1 [16.3; 28.1]		
% of outcome-free patients[1]	23.84 [12.66; 35.02]	23.11 [13.57; 32.64]	1.05 [0.72; 1.53] 0.796	0.962
> 65 letters				
KITE, N'/ N	114 / 114	90 / 90		
Number of patients with at least one event, n (%)	81 (71.1)	62 (68.9)		
Median (in weeks)	24.1 [18.1; 32.1]	24.0 [18.1; 28.6]		
% of outcome-free patients[1]	23.32 [13.75; 32.88]	28.20 [18.49; 37.90]	1.08 [0.78; 1.50] 0.652	0.637
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.154			
≤ 65 letters				
Pooled Analysis, N'/ N	139 / 139	155 / 155		
Number of patients with at least one event, n (%)	101 (72.7)	117 (75.5)		
Median (in weeks)	24.3 [18.1; 32.0]	18.9 [16.3; 25.0]		
% of outcome-free patients[1]	22.84 [15.25; 30.43]	20.82 [13.92; 27.71]	0.93 [0.71; 1.22] 0.613	0.545

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
> 65 letters				
Pooled Analysis, N'/ N	229 / 229	213 / 213		
Number of patients with at least one event, n (%)	160 (69.9)	135 (63.4)		
Median (in weeks)	28.1 [21.6; 36.3]	28.9 [21.0; 56.1]		
% of outcome-free patients[1]	23.92 [16.57; 31.27]	32.51 [25.49; 39.53]	1.21 [0.96; 1.52] 0.107	0.176

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
*: $p < 0.05$
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + BCVA + treatment * BCVA.
Pooled analysis: log(hazard ratio) = treatment + age category + study + treatment * study + BCVA + treatment * BCVA.

Table 6.5 BCVA - Gain of 10 respectively 15 letters by region (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.347**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.717			
Region of the Americas				
KESTREL, N'/ N	90 / 90	83 / 83		
Number of patients with at least one event, n (%)	66 (73.3)	66 (79.5)		
Median (in weeks)	13.0 [8.3; 20.1]	12.1 [8.0; 17.1]		
% of outcome-free patients[1]	25.12 [15.87; 34.37]	17.94 [8.49; 27.39]	0.86 [0.61; 1.22] 0.408	0.517
European Region				
KESTREL, N'/ N	69 / 69	75 / 75		
Number of patients with at least one event, n (%)	56 (81.2)	58 (77.3)		
Median (in weeks)	12.4 [8.1; 20.3]	14.6 [8.1; 19.7]		
% of outcome-free patients[1]	10.41 [0.00; 20.81]	18.92 [8.44; 29.40]	0.95 [0.65; 1.37] 0.766	0.812
Western Pacific Region				
KESTREL, N'/ N	30 / 30	29 / 29		
Number of patients with at least one event, n (%)	18 (60.0)	22 (75.9)		
Median (in weeks)	23.7 [5.9; N.E.]	18.1 [6.1; 28.1]		
% of outcome-free patients[1]	37.93 [20.27; 55.59]	21.67 [6.36; 36.99]	0.70 [0.37; 1.31] 0.262	0.343
KITE: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.679			
South-East Asia Region and Eastern Mediterranean Region				
KITE, N'/ N	26 / 26	21 / 21		
Number of patients with at least one event, n (%)	21 (80.8)	19 (90.5)		
Median (in weeks)	14.4 [6.1; 24.1]	12.3 [6.3; 18.1]		
% of outcome-free patients[1]	18.46 [3.19; 33.74]	5.56 [0.00; 16.05]	0.79 [0.42; 1.46] 0.447	0.281

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
European Region				
KITE, N'/ N	135 / 135	132 / 132		
Number of patients with at least one event, n (%)	105 (77.8)	104 (78.8)		
Median (in weeks)	9.1 [8.1; 17.1]	12.1 [8.4; 16.1]		
% of outcome-free patients[1]	19.41 [12.43; 26.40]	19.80 [12.86; 26.74]	1.06 [0.81; 1.40] 0.668	0.849
Western Pacific Region				
KITE, N'/ N	18 / 18	28 / 28		
Number of patients with at least one event, n (%)	13 (72.2)	22 (78.6)		
Median (in weeks)	15.6 [6.7; 35.1]	12.1 [8.7; 18.1]		
% of outcome-free patients[1]	23.33 [1.85; 44.81]	15.96 [1.70; 30.23]	0.97 [0.49; 1.92] 0.922	0.537
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.745			
Region of the Americas				
Pooled Analysis, N'/ N	90 / 90	83 / 83		
Number of patients with at least one event, n (%)	66 (73.3)	66 (79.5)		
Median (in weeks)	13.0 [8.3; 20.1]	12.1 [8.0; 17.1]		
% of outcome-free patients[1]	25.12 [15.87; 34.37]	17.94 [8.49; 27.39]	0.93 [0.63; 1.39] 0.736	0.517
South-East Asia Region and Eastern Mediterranean Region				
Pooled Analysis, N'/ N	26 / 26	21 / 21		
Number of patients with at least one event, n (%)	21 (80.8)	19 (90.5)		
Median (in weeks)	14.4 [6.1; 24.1]	12.3 [6.3; 18.1]		
% of outcome-free patients[1]	18.46 [3.19; 33.74]	5.56 [0.00; 16.05]	0.72 [0.38; 1.39] 0.331	0.281
European Region				
Pooled Analysis, N'/ N	204 / 204	207 / 207		
Number of patients with at least one event, n (%)	161 (78.9)	162 (78.3)		
Median (in weeks)	12.0 [8.1; 16.4]	12.4 [9.0; 16.1]		
% of outcome-free patients[1]	14.72 [6.86; 22.58]	18.92 [12.69; 25.14]	1.01 [0.80; 1.27] 0.936	0.991

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Western Pacific Region				
Pooled Analysis, N'/ N	48 / 48	57 / 57		
Number of patients with at least one event, n (%)	31 (64.6)	44 (77.2)		
Median (in weeks)	19.1 [8.4; 36.1]	16.1 [11.1; 20.0]		
% of outcome-free patients[1]	32.85 [19.14; 46.56]	18.94 [8.41; 29.47]	0.86 [0.54; 1.36] 0.512	0.265
Time to first gain in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.583**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.610			
Region of the Americas				
KESTREL, N'/ N	90 / 90	83 / 83		
Number of patients with at least one event, n (%)	73 (81.1)	72 (86.7)		
Median (in weeks)	13.0 [8.3; 20.1]	12.1 [8.0; 17.1]		
% of outcome-free patients[1]	15.55 [7.44; 23.65]	7.14 [0.00; 17.73]	0.87 [0.63; 1.22] 0.423	0.544
European Region				
KESTREL, N'/ N	69 / 69	75 / 75		
Number of patients with at least one event, n (%)	58 (84.1)	60 (80.0)		
Median (in weeks)	12.4 [8.1; 20.3]	14.6 [8.1; 19.7]		
% of outcome-free patients[1]	9.76 [1.91; 17.60]	18.67 [9.72; 27.61]	1.01 [0.71; 1.46] 0.939	0.647
Western Pacific Region				
KESTREL, N'/ N	30 / 30	29 / 29		
Number of patients with at least one event, n (%)	21 (70.0)	24 (82.8)		
Median (in weeks)	23.7 [5.9; 72.1]	18.1 [6.1; 28.1]		
% of outcome-free patients[1]	26.55 [10.15; 42.95]	13.55 [0.36; 26.73]	0.72 [0.40; 1.30] 0.278	0.318

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.610			
South-East Asia Region and Eastern Mediterranean Region				
KITE, N'/ N	26 / 26	21 / 21		
Number of patients with at least one event, n (%)	21 (80.8)	19 (90.5)		
Median (in weeks)	14.4 [6.1; 24.1]	12.3 [6.3; 18.1]		
% of outcome-free patients[1]	19.23 [4.08; 34.38]	5.56 [0.00; 16.05]	0.74 [0.40; 1.38] 0.339	0.277
European Region				
KITE, N'/ N	135 / 135	132 / 132		
Number of patients with at least one event, n (%)	110 (81.5)	112 (84.8)		
Median (in weeks)	9.1 [8.1; 17.1]	12.1 [8.4; 16.1]		
% of outcome-free patients[1]	15.71 [9.37; 22.06]	12.50 [6.51; 18.49]	1.04 [0.79; 1.35] 0.790	0.664
Western Pacific Region				
KITE, N'/ N	18 / 18	28 / 28		
Number of patients with at least one event, n (%)	14 (77.8)	25 (89.3)		
Median (in weeks)	15.6 [6.7; 35.1]	12.1 [8.7; 18.1]		
% of outcome-free patients[1]	11.67 [0.00; 31.08]	0.00 [0.00; 0.00]	0.94 [0.49; 1.82] 0.858	0.600
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.644			
Region of the Americas				
Pooled Analysis, N'/ N	90 / 90	83 / 83		
Number of patients with at least one event, n (%)	73 (81.1)	72 (86.7)		
Median (in weeks)	13.0 [8.3; 20.1]	12.1 [8.0; 17.1]		
% of outcome-free patients[1]	15.55 [7.44; 23.65]	7.14 [0.00; 17.73]	0.90 [0.62; 1.32] 0.603	0.544

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
South-East Asia Region and Eastern Mediterranean Region				
Pooled Analysis, N'/ N	26 / 26	21 / 21		
Number of patients with at least one event, n (%)	21 (80.8)	19 (90.5)		
Median (in weeks)	14.4 [6.1; 24.1]	12.3 [6.3; 18.1]		
% of outcome-free patients[1]	19.23 [4.08; 34.38]	5.56 [0.00; 16.05]	0.70 [0.36; 1.34] 0.281	0.277
European Region				
Pooled Analysis, N'/ N	204 / 204	207 / 207		
Number of patients with at least one event, n (%)	168 (82.4)	172 (83.1)		
Median (in weeks)	12.0 [8.1; 16.4]	12.4 [9.0; 16.1]		
% of outcome-free patients[1]	14.02 [8.99; 19.05]	14.69 [9.65; 19.74]	1.02 [0.82; 1.27] 0.857	0.935
Western Pacific Region				
Pooled Analysis, N'/ N	48 / 48	57 / 57		
Number of patients with at least one event, n (%)	35 (72.9)	49 (86.0)		
Median (in weeks)	19.1 [8.4; 36.1]	16.1 [11.1; 20.0]		
% of outcome-free patients[1]	21.90 [9.24; 34.56]	0.00 [0.00; 0.00]	0.86 [0.55; 1.33] 0.491	0.275
Time to first gain in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.696**				
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.788			
Region of the Americas				
KESTREL, N'/ N	90 / 90	83 / 83		
Number of patients with at least one event, n (%)	51 (56.7)	50 (60.2)		
Median (in weeks)	35.4 [19.4; N.E.]	24.1 [17.9; 48.1]		
% of outcome-free patients[1]	41.49 [30.97; 52.02]	26.13 [4.02; 48.23]	0.93 [0.62; 1.37] 0.701	0.669

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
European Region				
KESTREL, N'/ N	69 / 69	75 / 75		
Number of patients with at least one event, n (%)	48 (69.6)	44 (58.7)		
Median (in weeks)	24.3 [18.1; 35.1]	29.3 [16.1; 52.9]		
% of outcome-free patients[1]	18.23 [1.84; 34.62]	34.33 [18.82; 49.83]	1.13 [0.75; 1.71] 0.557	0.297
Western Pacific Region				
KESTREL, N'/ N	30 / 30	29 / 29		
Number of patients with at least one event, n (%)	15 (50.0)	14 (48.3)		
Median (in weeks)	40.1 [12.3; N.E.]	N.E.		
% of outcome-free patients[1]	48.28 [30.09; 66.46]	50.29 [31.77; 68.80]	1.02 [0.49; 2.11] 0.965	0.809
KITE: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.323			
South-East Asia Region and Eastern Mediterranean Region				
KITE, N'/ N	26 / 26	21 / 21		
Number of patients with at least one event, n (%)	17 (65.4)	16 (76.2)		
Median (in weeks)	24.7 [12.4; 53.1]	16.4 [12.1; 32.1]		
% of outcome-free patients[1]	0.00 [0.00; 0.00]	21.43 [3.19; 39.66]	0.77 [0.39; 1.54] 0.464	0.354
European Region				
KITE, N'/ N	135 / 135	132 / 132		
Number of patients with at least one event, n (%)	92 (68.1)	82 (62.1)		
Median (in weeks)	20.1 [16.7; 28.4]	20.3 [18.4; 28.3]		
% of outcome-free patients[1]	27.69 [18.82; 36.56]	34.45 [24.79; 44.11]	1.20 [0.89; 1.62] 0.229	0.305
Western Pacific Region				
KITE, N'/ N	18 / 18	28 / 28		
Number of patients with at least one event, n (%)	10 (55.6)	19 (67.9)		
Median (in weeks)	35.1 [21.6; N.E.]	18.9 [13.3; 39.9]		
% of outcome-free patients[1]	40.40 [16.33; 64.48]	26.81 [9.47; 44.15]	0.75 [0.35; 1.62] 0.466	0.314

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.525			
Region of the Americas				
Pooled Analysis, N'/ N	90 / 90	83 / 83		
Number of patients with at least one event, n (%)	51 (56.7)	50 (60.2)		
Median (in weeks)	35.4 [19.4; N.E.]	24.1 [17.9; 48.1]		
% of outcome-free patients[1]	41.49 [30.97; 52.02]	26.13 [4.02; 48.23]	0.95 [0.60; 1.49] 0.819	0.669
South-East Asia Region and Eastern Mediterranean Region				
Pooled Analysis, N'/ N	26 / 26	21 / 21		
Number of patients with at least one event, n (%)	17 (65.4)	16 (76.2)		
Median (in weeks)	24.7 [12.4; 53.1]	16.4 [12.1; 32.1]		
% of outcome-free patients[1]	0.00 [0.00; 0.00]	21.43 [3.19; 39.66]	0.80 [0.39; 1.64] 0.539	0.354
European Region				
Pooled Analysis, N'/ N	204 / 204	207 / 207		
Number of patients with at least one event, n (%)	140 (68.6)	126 (60.9)		
Median (in weeks)	23.6 [18.1; 28.9]	24.0 [19.1; 32.0]		
% of outcome-free patients[1]	23.73 [14.32; 33.14]	34.57 [26.33; 42.80]	1.20 [0.93; 1.54] 0.163	0.149
Western Pacific Region				
Pooled Analysis, N'/ N	48 / 48	57 / 57		
Number of patients with at least one event, n (%)	25 (52.1)	33 (57.9)		
Median (in weeks)	36.3 [23.7; N.E.]	28.1 [18.1; N.E.]		
% of outcome-free patients[1]	45.66 [31.17; 60.16]	39.18 [26.12; 52.24]	0.90 [0.54; 1.52] 0.697	0.591
Time to first gain in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.933**				

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.512			
Region of the Americas				
KESTREL, N'/ N	90 / 90	83 / 83		
Number of patients with at least one event, n (%)	60 (66.7)	56 (67.5)		
Median (in weeks)	35.4 [19.4; 55.9]	24.1 [17.9; 53.9]		
% of outcome-free patients[1]	29.59 [19.49; 39.69]	29.28 [18.98; 39.58]	0.97 [0.67; 1.40] 0.855	0.807
European Region				
KESTREL, N'/ N	69 / 69	75 / 75		
Number of patients with at least one event, n (%)	55 (79.7)	49 (65.3)		
Median (in weeks)	24.3 [18.1; 35.1]	29.3 [16.1; 59.4]		
% of outcome-free patients[1]	12.31 [3.61; 21.00]	32.26 [21.32; 43.21]	1.30 [0.88; 1.91] 0.187	0.101
Western Pacific Region				
KESTREL, N'/ N	30 / 30	29 / 29		
Number of patients with at least one event, n (%)	18 (60.0)	19 (65.5)		
Median (in weeks)	40.1 [12.3; N.E.]	72.1 [20.1; 100.9]		
% of outcome-free patients[1]	36.21 [18.15; 54.26]	23.35 [1.15; 45.54]	0.97 [0.51; 1.84] 0.915	0.893
KITE: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.333			
South-East Asia Region and Eastern Mediterranean Region				
KITE, N'/ N	26 / 26	21 / 21		
Number of patients with at least one event, n (%)	17 (65.4)	16 (76.2)		
Median (in weeks)	24.7 [12.4; N.E.]	16.4 [12.1; 32.1]		
% of outcome-free patients[1]	31.32 [12.55; 50.09]	21.43 [3.19; 39.66]	0.76 [0.38; 1.51] 0.437	0.418

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
European Region				
KITE, N'/ N	135 / 135	132 / 132		
Number of patients with at least one event, n (%)	99 (73.3)	90 (68.2)		
Median (in weeks)	20.1 [16.7; 28.4]	20.3 [18.4; 28.3]		
% of outcome-free patients[1]	22.23 [14.06; 30.39]	29.36 [21.24; 37.48]	1.19 [0.89; 1.59] 0.230	0.330
Western Pacific Region				
KITE, N'/ N	18 / 18	28 / 28		
Number of patients with at least one event, n (%)	12 (66.7)	22 (78.6)		
Median (in weeks)	35.1 [21.6; 64.4]	18.9 [13.3; 39.9]		
% of outcome-free patients[1]	24.24 [1.67; 46.82]	14.08 [0.01; 28.14]	0.79 [0.39; 1.61] 0.519	0.378
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.344			
Region of the Americas				
Pooled Analysis, N'/ N	90 / 90	83 / 83		
Number of patients with at least one event, n (%)	60 (66.7)	56 (67.5)		
Median (in weeks)	35.4 [19.4; 55.9]	24.1 [17.9; 53.9]		
% of outcome-free patients[1]	29.59 [19.49; 39.69]	29.28 [18.98; 39.58]	0.95 [0.62; 1.44] 0.803	0.807
South-East Asia Region and Eastern Mediterranean Region				
Pooled Analysis, N'/ N	26 / 26	21 / 21		
Number of patients with at least one event, n (%)	17 (65.4)	16 (76.2)		
Median (in weeks)	24.7 [12.4; N.E.]	16.4 [12.1; 32.1]		
% of outcome-free patients[1]	31.32 [12.55; 50.09]	21.43 [3.19; 39.66]	0.79 [0.39; 1.62] 0.520	0.418
European Region				
Pooled Analysis, N'/ N	204 / 204	207 / 207		
Number of patients with at least one event, n (%)	154 (75.5)	139 (67.1)		
Median (in weeks)	23.6 [18.1; 28.9]	24.0 [19.1; 32.0]		
% of outcome-free patients[1]	19.10 [12.66; 25.54]	30.21 [23.65; 36.78]	1.25 [0.99; 1.59] 0.064	0.079

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Western Pacific Region				
Pooled Analysis, N'/ N	48 / 48	57 / 57		
Number of patients with at least one event, n (%)	30 (62.5)	41 (71.9)		
Median (in weeks)	36.3 [23.7; 72.1]	28.1 [18.1; 72.1]		
% of outcome-free patients[1]	32.23 [18.00; 46.46]	20.21 [7.23; 33.19]	0.90 [0.56; 1.44] 0.653	0.608

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
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Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + region + treatment * region.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + region + treatment * region.

Table 6.6 BCVA - Gain of 10 respectively 15 letters by diabetes type (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.347**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.173			
Type 1				
KESTREL, N'/ N	12 / 12	6 / 6		
Number of patients with at least one event, n (%)	9 (75.0)	3 (50.0)		
Median (in weeks)	13.1 [4.6; 31.1]	N.E.		
% of outcome-free patients[1]	20.00 [0.00; 44.27]	50.00 [9.99; 90.01]	2.12 [0.57; 7.84] 0.262	0.237
Type 2				
KESTREL, N'/ N	177 / 177	181 / 181		
Number of patients with at least one event, n (%)	131 (74.0)	143 (79.0)		
Median (in weeks)	15.1 [12.0; 18.7]	12.4 [9.1; 17.7]		
% of outcome-free patients[1]	20.21 [11.14; 29.28]	16.87 [9.85; 23.89]	0.84 [0.66; 1.07] 0.154	0.319
KITE: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.324			
Type 1				
KITE, N'/ N	19 / 19	7 / 7		
Number of patients with at least one event, n (%)	18 (94.7)	7 (100.0)		
Median (in weeks)	8.1 [5.0; 12.0]	6.1 [4.0; 8.6]		
% of outcome-free patients[1]	5.26 [0.00; 15.30]	0.00 [0.00; 0.00]	0.62 [0.26; 1.52] 0.297	0.276
Type 2				
KITE, N'/ N	160 / 160	174 / 174		
Number of patients with at least one event, n (%)	121 (75.6)	138 (79.3)		
Median (in weeks)	12.4 [8.1; 18.1]	12.4 [9.1; 16.0]		
% of outcome-free patients[1]	21.46 [14.76; 28.17]	18.42 [12.48; 24.36]	0.99 [0.77; 1.27] 0.947	0.412

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.592			
Type 1				
Pooled Analysis, N'/ N	31 / 31	13 / 13		
Number of patients with at least one event, n (%)	27 (87.1)	10 (76.9)		
Median (in weeks)	8.1 [5.1; 18.1]	8.6 [4.7; 24.7]		
% of outcome-free patients[1]	10.75 [0.00; 22.10]	23.08 [0.17; 45.98]	1.14 [0.55; 2.35] 0.733	0.974
Type 2				
Pooled Analysis, N'/ N	337 / 337	355 / 355		
Number of patients with at least one event, n (%)	252 (74.8)	281 (79.2)		
Median (in weeks)	12.9 [11.9; 18.1]	12.4 [11.6; 16.1]		
% of outcome-free patients[1]	20.07 [13.39; 26.74]	17.09 [12.18; 22.00]	0.92 [0.78; 1.10] 0.369	0.199
Time to first gain in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.583**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.108			
Type 1				
KESTREL, N'/ N	12 / 12	6 / 6		
Number of patients with at least one event, n (%)	10 (83.3)	3 (50.0)		
Median (in weeks)	13.1 [4.6; 31.1]	N.E.		
% of outcome-free patients[1]	10.00 [0.00; 28.42]	50.00 [9.99; 90.01]	2.53 [0.70; 9.23] 0.159	0.140
Type 2				
KESTREL, N'/ N	177 / 177	181 / 181		
Number of patients with at least one event, n (%)	142 (80.2)	153 (84.5)		
Median (in weeks)	15.1 [12.0; 18.7]	12.4 [9.1; 17.7]		
% of outcome-free patients[1]	15.76 [9.95; 21.57]	9.82 [1.22; 18.42]	0.86 [0.69; 1.09] 0.217	0.381

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.341			
Type 1				
KITE, N'/ N	19 / 19	7 / 7		
Number of patients with at least one event, n (%)	18 (94.7)	7 (100.0)		
Median (in weeks)	8.1 [5.0; 12.0]	6.1 [4.0; 8.6]		
% of outcome-free patients[1]	5.26 [0.00; 15.30]	0.00 [0.00; 0.00]	0.61 [0.25; 1.49] 0.280	0.276
Type 2				
KITE, N'/ N	160 / 160	174 / 174		
Number of patients with at least one event, n (%)	127 (79.4)	149 (85.6)		
Median (in weeks)	12.4 [8.1; 18.1]	12.4 [9.1; 16.0]		
% of outcome-free patients[1]	17.59 [11.43; 23.75]	9.56 [4.14; 14.99]	0.96 [0.75; 1.22] 0.725	0.249
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.427			
Type 1				
Pooled Analysis, N'/ N	31 / 31	13 / 13		
Number of patients with at least one event, n (%)	28 (90.3)	10 (76.9)		
Median (in weeks)	8.1 [5.1; 18.1]	8.6 [4.7; 24.7]		
% of outcome-free patients[1]	7.17 [0.00; 16.66]	23.08 [0.17; 45.98]	1.24 [0.60; 2.55] 0.564	0.842
Type 2				
Pooled Analysis, N'/ N	337 / 337	355 / 355		
Number of patients with at least one event, n (%)	269 (79.8)	302 (85.1)		
Median (in weeks)	12.9 [11.9; 18.1]	12.4 [11.6; 16.1]		
% of outcome-free patients[1]	16.71 [12.48; 20.94]	9.50 [4.20; 14.80]	0.92 [0.78; 1.08] 0.291	0.153
Time to first gain in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.696**				

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.215			
Type 1				
KESTREL, N'/ N	12 / 12	6 / 6		
Number of patients with at least one event, n (%)	8 (66.7)	2 (33.3)		
Median (in weeks)	20.1 [5.1; N.E.]	N.E.		
% of outcome-free patients[1]	29.17 [1.98; 56.35]	66.67 [28.95; 100.00]	2.64 [0.56; 12.50] 0.221	0.204
Type 2				
KESTREL, N'/ N	177 / 177	181 / 181		
Number of patients with at least one event, n (%)	106 (59.9)	106 (58.6)		
Median (in weeks)	31.9 [23.7; 43.1]	29.1 [20.3; 47.6]		
% of outcome-free patients[1]	33.43 [22.52; 44.34]	25.63 [4.39; 46.86]	0.98 [0.74; 1.28] 0.855	0.972
KITE: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.475			
Type 1				
KITE, N'/ N	19 / 19	7 / 7		
Number of patients with at least one event, n (%)	16 (84.2)	6 (85.7)		
Median (in weeks)	20.1 [8.1; 40.1]	12.0 [6.1; 28.3]		
% of outcome-free patients[1]	14.04 [0.00; 30.63]	14.29 [0.00; 40.21]	0.75 [0.29; 1.94] 0.548	0.568
Type 2				
KITE, N'/ N	160 / 160	174 / 174		
Number of patients with at least one event, n (%)	103 (64.4)	111 (63.8)		
Median (in weeks)	24.4 [18.1; 32.1]	20.3 [18.1; 25.1]		
% of outcome-free patients[1]	27.03 [13.74; 40.33]	32.24 [23.86; 40.63]	1.07 [0.82; 1.40] 0.625	0.896

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.653			
Type 1				
Pooled Analysis, N'/ N	31 / 31	13 / 13		
Number of patients with at least one event, n (%)	24 (77.4)	8 (61.5)		
Median (in weeks)	20.1 [8.1; 39.7]	20.1 [8.6; N.E.]		
% of outcome-free patients[1]	19.19 [4.29; 34.10]	38.46 [12.02; 64.91]	1.26 [0.56; 2.81] 0.573	0.726
Type 2				
Pooled Analysis, N'/ N	337 / 337	355 / 355		
Number of patients with at least one event, n (%)	209 (62.0)	217 (61.1)		
Median (in weeks)	28.1 [23.6; 32.6]	24.1 [19.7; 29.1]		
% of outcome-free patients[1]	30.59 [22.20; 38.98]	23.63 [4.32; 42.93]	1.04 [0.86; 1.26] 0.672	0.907
Time to first gain in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.933**				
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.141			
Type 1				
KESTREL, N'/ N	12 / 12	6 / 6		
Number of patients with at least one event, n (%)	9 (75.0)	2 (33.3)		
Median (in weeks)	20.1 [5.1; 64.0]	N.E.		
% of outcome-free patients[1]	19.44 [0.00; 43.33]	66.67 [28.95; 100.00]	3.33 [0.72; 15.45] 0.125	0.129
Type 2				
KESTREL, N'/ N	177 / 177	181 / 181		
Number of patients with at least one event, n (%)	124 (70.1)	122 (67.4)		
Median (in weeks)	31.9 [23.7; 43.1]	29.1 [20.3; 47.6]		
% of outcome-free patients[1]	24.67 [17.74; 31.59]	27.84 [20.06; 35.62]	1.03 [0.80; 1.33] 0.794	0.660

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.374			
Type 1				
KITE, N'/ N	19 / 19	7 / 7		
Number of patients with at least one event, n (%)	17 (89.5)	7 (100.0)		
Median (in weeks)	20.1 [8.1; 40.1]	12.0 [6.1; 28.3]		
% of outcome-free patients[1]	10.53 [0.00; 24.33]	0.00 [0.00; 0.00]	0.70 [0.29; 1.70] 0.429	0.524
Type 2				
KITE, N'/ N	160 / 160	174 / 174		
Number of patients with at least one event, n (%)	111 (69.4)	121 (69.5)		
Median (in weeks)	24.4 [18.1; 32.1]	20.3 [18.1; 25.1]		
% of outcome-free patients[1]	25.23 [17.11; 33.35]	27.00 [20.00; 34.00]	1.06 [0.82; 1.38] 0.651	0.943
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.578			
Type 1				
Pooled Analysis, N'/ N	31 / 31	13 / 13		
Number of patients with at least one event, n (%)	26 (83.9)	9 (69.2)		
Median (in weeks)	20.1 [8.1; 39.7]	20.1 [8.6; N.E.]		
% of outcome-free patients[1]	13.71 [1.28; 26.14]	25.64 [0.00; 52.69]	1.32 [0.62; 2.83] 0.470	0.662

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Type 2				
Pooled Analysis, N'/ N	337 / 337	355 / 355		
Number of patients with at least one event, n (%)	235 (69.7)	243 (68.5)		
Median (in weeks)	28.1 [23.6; 32.6]	24.1 [19.7; 29.1]		
% of outcome-free patients[1]	24.50 [18.76; 30.24]	27.40 [22.13; 32.66]	1.06 [0.89; 1.27] 0.527	0.715

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + diabetes type + treatment * diabetes type.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + diabetes type + treatment * diabetes type.

Table 6.7 BCVA - Gain of 10 respectively 15 letters by HbA1c (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.347**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.866			
< 7.5 %				
KESTREL, N'/ N	76 / 76	107 / 107		
Number of patients with at least one event, n (%)	60 (78.9)	86 (80.4)		
Median (in weeks)	16.4 [12.1; 20.4]	12.1 [9.1; 17.1]		
% of outcome-free patients[1]	18.32 [9.08; 27.56]	16.53 [7.87; 25.20]	0.86 [0.61; 1.20] 0.367	0.547
≥ 7.5 %				
KESTREL, N'/ N	112 / 112	80 / 80		
Number of patients with at least one event, n (%)	80 (71.4)	60 (75.0)		
Median (in weeks)	12.1 [7.1; 20.1]	16.1 [8.1; 20.1]		
% of outcome-free patients[1]	21.85 [10.09; 33.61]	21.16 [10.67; 31.66]	0.89 [0.64; 1.25] 0.512	0.841
KITE: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.394			
< 7.5 %				
KITE, N'/ N	82 / 82	96 / 96		
Number of patients with at least one event, n (%)	64 (78.0)	77 (80.2)		
Median (in weeks)	11.9 [6.6; 17.6]	12.4 [8.4; 17.1]		
% of outcome-free patients[1]	17.83 [9.16; 26.51]	17.55 [9.69; 25.42]	1.13 [0.81; 1.57] 0.487	0.874
≥ 7.5 %				
KITE, N'/ N	97 / 97	85 / 85		
Number of patients with at least one event, n (%)	75 (77.3)	68 (80.0)		
Median (in weeks)	11.9 [8.1; 20.1]	12.1 [8.9; 15.4]		
% of outcome-free patients[1]	21.32 [12.88; 29.77]	17.73 [9.38; 26.07]	0.92 [0.66; 1.28] 0.611	0.329

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.623			
< 7.5 %				
Pooled Analysis, N'/ N	158 / 158	203 / 203		
Number of patients with at least one event, n (%)	124 (78.5)	163 (80.3)		
Median (in weeks)	12.7 [10.1; 18.1]	12.1 [11.4; 16.1]		
% of outcome-free patients[1]	18.34 [12.04; 24.64]	16.09 [9.34; 22.85]	0.99 [0.79; 1.26] 0.963	0.749
≥ 7.5 %				
Pooled Analysis, N'/ N	209 / 209	165 / 165		
Number of patients with at least one event, n (%)	155 (74.2)	128 (77.6)		
Median (in weeks)	12.1 [8.1; 18.1]	12.4 [9.1; 16.6]		
% of outcome-free patients[1]	20.27 [11.43; 29.11]	19.05 [12.19; 25.91]	0.91 [0.72; 1.16] 0.458	0.404
Time to first gain in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.583**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.738			
< 7.5 %				
KESTREL, N'/ N	76 / 76	107 / 107		
Number of patients with at least one event, n (%)	63 (82.9)	91 (85.0)		
Median (in weeks)	16.4 [12.1; 20.4]	12.1 [9.1; 17.1]		
% of outcome-free patients[1]	14.03 [5.72; 22.34]	14.05 [7.40; 20.71]	0.87 [0.63; 1.20] 0.394	0.521
≥ 7.5 %				
KESTREL, N'/ N	112 / 112	80 / 80		
Number of patients with at least one event, n (%)	89 (79.5)	65 (81.3)		
Median (in weeks)	12.1 [7.1; 20.1]	16.1 [8.1; 20.1]		
% of outcome-free patients[1]	15.48 [8.10; 22.86]	0.00 [0.00; 0.00]	0.94 [0.68; 1.29] 0.698	0.980

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.289			
< 7.5 %				
KITE, N'/ N	82 / 82	96 / 96		
Number of patients with at least one event, n (%)	66 (80.5)	81 (84.4)		
Median (in weeks)	11.9 [6.6; 17.6]	12.4 [8.4; 17.1]		
% of outcome-free patients[1]	15.09 [6.96; 23.22]	9.22 [0.40; 18.04]	1.11 [0.80; 1.54] 0.534	0.991
≥ 7.5 %				
KITE, N'/ N	97 / 97	85 / 85		
Number of patients with at least one event, n (%)	79 (81.4)	75 (88.2)		
Median (in weeks)	11.9 [8.1; 20.1]	12.1 [8.9; 15.4]		
% of outcome-free patients[1]	16.94 [9.17; 24.71]	7.55 [1.43; 13.66]	0.87 [0.63; 1.19] 0.379	0.162
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.576			
< 7.5 %				
Pooled Analysis, N'/ N	158 / 158	203 / 203		
Number of patients with at least one event, n (%)	129 (81.6)	172 (84.7)		
Median (in weeks)	12.7 [10.1; 18.1]	12.1 [11.4; 16.1]		
% of outcome-free patients[1]	14.71 [8.89; 20.52]	11.64 [5.81; 17.47]	0.99 [0.79; 1.24] 0.921	0.651
≥ 7.5 %				
Pooled Analysis, N'/ N	209 / 209	165 / 165		
Number of patients with at least one event, n (%)	168 (80.4)	140 (84.8)		
Median (in weeks)	12.1 [8.1; 18.1]	12.4 [9.1; 16.6]		
% of outcome-free patients[1]	16.21 [10.85; 21.57]	6.40 [0.00; 15.66]	0.90 [0.72; 1.13] 0.367	0.332
Time to first gain in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.696**				

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.637			
< 7.5 %				
KESTREL, N'/ N	76 / 76	107 / 107		
Number of patients with at least one event, n (%)	49 (64.5)	63 (58.9)		
Median (in weeks)	24.1 [18.1; 45.1]	29.3 [18.1; 52.9]		
% of outcome-free patients[1]	33.29 [22.28; 44.30]	35.87 [23.35; 48.38]	1.10 [0.75; 1.60] 0.633	0.557
≥ 7.5 %				
KESTREL, N'/ N	112 / 112	80 / 80		
Number of patients with at least one event, n (%)	65 (58.0)	45 (56.3)		
Median (in weeks)	36.1 [24.1; 44.4]	28.9 [19.7; N.E.]		
% of outcome-free patients[1]	33.48 [19.15; 47.81]	21.39 [0.00; 51.55]	0.96 [0.66; 1.41] 0.848	0.943
KITE: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.599			
< 7.5 %				
KITE, N'/ N	82 / 82	96 / 96		
Number of patients with at least one event, n (%)	54 (65.9)	61 (63.5)		
Median (in weeks)	24.1 [17.1; 32.3]	20.9 [17.1; 32.3]		
% of outcome-free patients[1]	25.53 [11.57; 39.50]	28.68 [13.87; 43.50]	1.15 [0.80; 1.67] 0.445	0.626
≥ 7.5 %				
KITE, N'/ N	97 / 97	85 / 85		
Number of patients with at least one event, n (%)	65 (67.0)	56 (65.9)		
Median (in weeks)	23.6 [16.6; 36.3]	19.1 [16.4; 25.1]		
% of outcome-free patients[1]	21.73 [3.22; 40.24]	32.08 [21.93; 42.23]	1.01 [0.70; 1.44] 0.977	0.931

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.484			
< 7.5 %				
Pooled Analysis, N'/ N	158 / 158	203 / 203		
Number of patients with at least one event, n (%)	103 (65.2)	124 (61.1)		
Median (in weeks)	24.1 [19.0; 31.1]	25.1 [18.4; 36.3]		
% of outcome-free patients[1]	30.01 [21.39; 38.63]	32.62 [23.11; 42.13]	1.14 [0.88; 1.49] 0.317	0.448
≥ 7.5 %				
Pooled Analysis, N'/ N	209 / 209	165 / 165		
Number of patients with at least one event, n (%)	130 (62.2)	101 (61.2)		
Median (in weeks)	28.9 [21.1; 36.9]	23.9 [18.9; 28.9]		
% of outcome-free patients[1]	28.48 [17.24; 39.72]	18.67 [0.00; 44.81]	1.00 [0.77; 1.30] 0.989	0.989
Time to first gain in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.933**				
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.940			
< 7.5 %				
KESTREL, N'/ N	76 / 76	107 / 107		
Number of patients with at least one event, n (%)	54 (71.1)	73 (68.2)		
Median (in weeks)	24.1 [18.1; 45.1]	29.3 [18.1; 52.9]		
% of outcome-free patients[1]	25.75 [15.36; 36.13]	27.24 [17.07; 37.41]	1.09 [0.77; 1.56] 0.620	0.605
≥ 7.5 %				
KESTREL, N'/ N	112 / 112	80 / 80		
Number of patients with at least one event, n (%)	79 (70.5)	51 (63.8)		
Median (in weeks)	36.1 [24.1; 44.4]	28.9 [19.7; 63.9]		
% of outcome-free patients[1]	22.54 [13.94; 31.14]	32.14 [21.24; 43.04]	1.07 [0.75; 1.53] 0.695	0.474

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.544			
< 7.5 %				
KITE, N'/ N	82 / 82	96 / 96		
Number of patients with at least one event, n (%)	58 (70.7)	67 (69.8)		
Median (in weeks)	24.1 [17.1; 32.3]	20.9 [17.1; 32.3]		
% of outcome-free patients[1]	24.75 [14.92; 34.57]	26.59 [17.17; 36.02]	1.15 [0.81; 1.64] 0.430	0.659
≥ 7.5 %				
KITE, N'/ N	97 / 97	85 / 85		
Number of patients with at least one event, n (%)	70 (72.2)	61 (71.8)		
Median (in weeks)	23.6 [16.6; 36.3]	19.1 [16.4; 25.1]		
% of outcome-free patients[1]	22.21 [11.21; 33.22]	24.98 [15.30; 34.66]	0.99 [0.70; 1.40] 0.953	0.865
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.596			
< 7.5 %				
Pooled Analysis, N'/ N	158 / 158	203 / 203		
Number of patients with at least one event, n (%)	112 (70.9)	140 (69.0)		
Median (in weeks)	24.1 [19.0; 31.1]	25.1 [18.4; 36.3]		
% of outcome-free patients[1]	25.27 [18.13; 32.41]	26.80 [19.71; 33.88]	1.14 [0.89; 1.47] 0.300	0.498

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
≥ 7.5 %				
Pooled Analysis, N'/ N	209 / 209	165 / 165		
Number of patients with at least one event, n (%)	149 (71.3)	112 (67.9)		
Median (in weeks)	28.9 [21.1; 36.9]	23.9 [18.9; 28.9]		
% of outcome-free patients[1]	21.87 [14.34; 29.41]	28.37 [21.06; 35.68]	1.04 [0.81; 1.33] 0.767	0.703

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + HbA1c + treatment * HbA1c.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + HbA1c + treatment * HbA1c.

Table 6.8 BCVA - Gain of 10 respectively 15 letters by duration of DME (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.347**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.091			
≤ 3 months				
KESTREL, N'/ N	120 / 120	110 / 110		
Number of patients with at least one event, n (%)	93 (77.5)	91 (82.7)		
Median (in weeks)	12.4 [10.1; 18.1]	11.9 [6.9; 16.0]		
% of outcome-free patients[1]	17.72 [8.77; 26.67]	14.25 [7.06; 21.44]	0.77 [0.58; 1.04] 0.084	0.213
> 3 - < 12 months				
KESTREL, N'/ N	30 / 30	39 / 39		
Number of patients with at least one event, n (%)	25 (83.3)	30 (76.9)		
Median (in weeks)	7.0 [5.1; 23.9]	16.1 [8.7; 28.9]		
% of outcome-free patients[1]	12.73 [0.00; 25.66]	19.23 [4.26; 34.20]	1.49 [0.88; 2.54] 0.142	0.165
≥ 12 months				
KESTREL, N'/ N	39 / 39	38 / 38		
Number of patients with at least one event, n (%)	22 (56.4)	25 (65.8)		
Median (in weeks)	39.4 [18.0; N.E.]	22.9 [16.1; 45.0]		
% of outcome-free patients[1]	41.25 [25.21; 57.29]	33.68 [18.51; 48.86]	0.76 [0.43; 1.34] 0.339	0.437
KITE: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.162			
≤ 3 months				
KITE, N'/ N	85 / 85	92 / 92		
Number of patients with at least one event, n (%)	64 (75.3)	71 (77.2)		
Median (in weeks)	12.7 [8.1; 20.7]	14.1 [11.1; 19.1]		
% of outcome-free patients[1]	21.74 [12.53; 30.95]	22.16 [13.55; 30.77]	1.16 [0.83; 1.63] 0.391	0.890

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
> 3 - < 12 months				
KITE, N'/ N	51 / 51	49 / 49		
Number of patients with at least one event, n (%)	45 (88.2)	42 (85.7)		
Median (in weeks)	8.1 [6.1; 12.0]	11.1 [6.4; 13.1]		
% of outcome-free patients[1]	11.76 [2.92; 20.61]	11.54 [2.18; 20.89]	1.04 [0.68; 1.59] 0.871	0.984
≥ 12 months				
KITE, N'/ N	43 / 43	40 / 40		
Number of patients with at least one event, n (%)	30 (69.8)	32 (80.0)		
Median (in weeks)	17.1 [8.1; 33.9]	8.6 [6.6; 16.0]		
% of outcome-free patients[1]	25.76 [11.85; 39.67]	14.31 [2.79; 25.82]	0.65 [0.39; 1.07] 0.089	0.074
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.131			
≤ 3 months				
Pooled Analysis, N'/ N	205 / 205	202 / 202		
Number of patients with at least one event, n (%)	157 (76.6)	162 (80.2)		
Median (in weeks)	12.4 [11.1; 18.1]	12.1 [9.1; 16.1]		
% of outcome-free patients[1]	18.71 [11.62; 25.81]	17.26 [11.43; 23.10]	0.96 [0.77; 1.20] 0.718	0.391
> 3 - < 12 months				
Pooled Analysis, N'/ N	81 / 81	88 / 88		
Number of patients with at least one event, n (%)	70 (86.4)	72 (81.8)		
Median (in weeks)	8.1 [6.1; 12.0]	12.1 [9.1; 16.1]		
% of outcome-free patients[1]	12.08 [4.72; 19.43]	14.33 [5.25; 23.40]	1.20 [0.86; 1.68] 0.275	0.386
≥ 12 months				
Pooled Analysis, N'/ N	82 / 82	78 / 78		
Number of patients with at least one event, n (%)	52 (63.4)	57 (73.1)		
Median (in weeks)	21.1 [12.9; 39.4]	16.1 [8.6; 20.1]		
% of outcome-free patients[1]	33.41 [22.72; 44.10]	24.23 [14.44; 34.03]	0.72 [0.49; 1.05] 0.085	0.064

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.583**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.225			
≤ 3 months				
KESTREL, N'/ N	120 / 120	110 / 110		
Number of patients with at least one event, n (%)	99 (82.5)	93 (84.5)		
Median (in weeks)	12.4 [10.1; 18.1]	11.9 [6.9; 16.0]		
% of outcome-free patients[1]	14.49 [7.81; 21.16]	7.42 [0.00; 18.24]	0.82 [0.61; 1.09] 0.169	0.333
> 3 - < 12 months				
KESTREL, N'/ N	30 / 30	39 / 39		
Number of patients with at least one event, n (%)	25 (83.3)	33 (84.6)		
Median (in weeks)	7.0 [5.1; 23.9]	16.1 [8.7; 28.9]		
% of outcome-free patients[1]	12.73 [0.00; 25.66]	13.68 [2.31; 25.04]	1.37 [0.81; 2.30] 0.239	0.240
≥ 12 months				
KESTREL, N'/ N	39 / 39	38 / 38		
Number of patients with at least one event, n (%)	28 (71.8)	30 (78.9)		
Median (in weeks)	39.4 [18.0; 64.0]	22.9 [16.1; 45.0]		
% of outcome-free patients[1]	21.26 [6.99; 35.53]	20.26 [7.24; 33.28]	0.84 [0.50; 1.40] 0.499	0.600
KITE: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.215			
≤ 3 months				
KITE, N'/ N	85 / 85	92 / 92		
Number of patients with at least one event, n (%)	67 (78.8)	79 (85.9)		
Median (in weeks)	12.7 [8.1; 20.7]	14.1 [11.1; 19.1]		
% of outcome-free patients[1]	18.42 [9.89; 26.95]	10.64 [3.18; 18.10]	1.08 [0.78; 1.50] 0.639	0.808

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
> 3 - < 12 months				
KITE, N'/ N	51 / 51	49 / 49		
Number of patients with at least one event, n (%)	46 (90.2)	43 (87.8)		
Median (in weeks)	8.1 [6.1; 12.0]	11.1 [6.4; 13.1]		
% of outcome-free patients[1]	9.80 [1.64; 17.97]	8.65 [0.09; 17.21]	1.03 [0.68; 1.58] 0.874	0.979
≥ 12 months				
KITE, N'/ N	43 / 43	40 / 40		
Number of patients with at least one event, n (%)	32 (74.4)	34 (85.0)		
Median (in weeks)	17.1 [8.1; 33.9]	8.6 [6.6; 16.0]		
% of outcome-free patients[1]	19.63 [6.66; 32.59]	8.58 [0.00; 17.83]	0.65 [0.40; 1.06] 0.085	0.058
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.210			
≤ 3 months				
Pooled Analysis, N'/ N	205 / 205	202 / 202		
Number of patients with at least one event, n (%)	166 (81.0)	172 (85.1)		
Median (in weeks)	12.4 [11.1; 18.1]	12.1 [9.1; 16.1]		
% of outcome-free patients[1]	16.13 [10.86; 21.40]	9.52 [2.83; 16.21]	0.95 [0.77; 1.18] 0.646	0.374
> 3 - < 12 months				
Pooled Analysis, N'/ N	81 / 81	88 / 88		
Number of patients with at least one event, n (%)	71 (87.7)	76 (86.4)		
Median (in weeks)	8.1 [6.1; 12.0]	12.1 [9.1; 16.1]		
% of outcome-free patients[1]	10.57 [3.56; 17.57]	11.13 [4.16; 18.11]	1.16 [0.84; 1.61] 0.374	0.483
≥ 12 months				
Pooled Analysis, N'/ N	82 / 82	78 / 78		
Number of patients with at least one event, n (%)	60 (73.2)	64 (82.1)		
Median (in weeks)	21.1 [12.9; 39.4]	16.1 [8.6; 20.1]		
% of outcome-free patients[1]	20.57 [10.90; 30.24]	14.55 [6.42; 22.67]	0.75 [0.53; 1.07] 0.114	0.084

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.696**				
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.272			
≤ 3 months				
KESTREL, N'/ N	120 / 120	110 / 110		
Number of patients with at least one event, n (%)	80 (66.7)	71 (64.5)		
Median (in weeks)	23.4 [18.1; 35.1]	23.9 [17.0; 36.9]		
% of outcome-free patients[1]	27.97 [17.45; 38.48]	17.06 [0.00; 41.14]	0.99 [0.71; 1.36] 0.933	0.798
> 3 - < 12 months				
KESTREL, N'/ N	30 / 30	39 / 39		
Number of patients with at least one event, n (%)	20 (66.7)	20 (51.3)		
Median (in weeks)	25.1 [15.0; 40.1]	43.1 [17.7; N.E.]		
% of outcome-free patients[1]	30.15 [13.05; 47.26]	47.13 [31.08; 63.19]	1.50 [0.81; 2.80] 0.201	0.290
≥ 12 months				
KESTREL, N'/ N	39 / 39	38 / 38		
Number of patients with at least one event, n (%)	14 (35.9)	17 (44.7)		
Median (in weeks)	N.E.	52.9 [25.0; N.E.]		
% of outcome-free patients[1]	61.81 [45.93; 77.69]	28.95 [0.00; 69.83]	0.70 [0.34; 1.42] 0.325	0.365
KITE: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.178			
≤ 3 months				
KITE, N'/ N	85 / 85	92 / 92		
Number of patients with at least one event, n (%)	57 (67.1)	56 (60.9)		
Median (in weeks)	23.6 [16.1; 32.1]	24.4 [18.4; 40.6]		
% of outcome-free patients[1]	24.00 [8.43; 39.57]	38.69 [28.66; 48.72]	1.32 [0.91; 1.92] 0.140	0.308

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
> 3 - < 12 months				
KITE, N'/ N	51 / 51	49 / 49		
Number of patients with at least one event, n (%)	36 (70.6)	34 (69.4)		
Median (in weeks)	21.9 [12.1; 32.1]	18.1 [16.1; 28.6]		
% of outcome-free patients[1]	28.34 [15.82; 40.86]	20.18 [1.78; 38.58]	1.01 [0.63; 1.62] 0.967	0.893
≥ 12 months				
KITE, N'/ N	43 / 43	40 / 40		
Number of patients with at least one event, n (%)	26 (60.5)	27 (67.5)		
Median (in weeks)	28.4 [18.1; 52.6]	18.1 [16.0; 25.1]		
% of outcome-free patients[1]	28.46 [8.71; 48.20]	27.65 [13.15; 42.15]	0.71 [0.42; 1.23] 0.222	0.233
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.154			
≤ 3 months				
Pooled Analysis, N'/ N	205 / 205	202 / 202		
Number of patients with at least one event, n (%)	137 (66.8)	127 (62.9)		
Median (in weeks)	23.4 [18.1; 28.3]	24.1 [19.1; 35.4]		
% of outcome-free patients[1]	26.63 [17.95; 35.32]	18.12 [0.00; 43.46]	1.17 [0.91; 1.48] 0.216	0.390
> 3 - < 12 months				
Pooled Analysis, N'/ N	81 / 81	88 / 88		
Number of patients with at least one event, n (%)	56 (69.1)	54 (61.4)		
Median (in weeks)	24.1 [16.7; 32.1]	20.3 [17.7; 43.1]		
% of outcome-free patients[1]	29.00 [18.87; 39.12]	31.43 [17.23; 45.62]	1.19 [0.81; 1.73] 0.377	0.459
≥ 12 months				
Pooled Analysis, N'/ N	82 / 82	78 / 78		
Number of patients with at least one event, n (%)	40 (48.8)	44 (56.4)		
Median (in weeks)	41.1 [35.1; N.E.]	25.0 [18.4; N.E.]		
% of outcome-free patients[1]	44.02 [29.73; 58.31]	34.33 [16.80; 51.85]	0.73 [0.48; 1.13] 0.157	0.134

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.933**				
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.432			
≤ 3 months				
KESTREL, N'/ N	120 / 120	110 / 110		
Number of patients with at least one event, n (%)	92 (76.7)	74 (67.3)		
Median (in weeks)	23.4 [18.1; 35.1]	23.9 [17.0; 36.9]		
% of outcome-free patients[1]	19.25 [11.67; 26.83]	28.31 [18.63; 38.00]	1.12 [0.82; 1.53] 0.468	0.327
> 3 - < 12 months				
KESTREL, N'/ N	30 / 30	39 / 39		
Number of patients with at least one event, n (%)	21 (70.0)	26 (66.7)		
Median (in weeks)	25.1 [15.0; 40.1]	43.1 [17.7; 65.1]		
% of outcome-free patients[1]	24.12 [6.83; 41.42]	26.44 [10.96; 41.91]	1.28 [0.72; 2.29] 0.399	0.582
≥ 12 months				
KESTREL, N'/ N	39 / 39	38 / 38		
Number of patients with at least one event, n (%)	20 (51.3)	24 (63.2)		
Median (in weeks)	60.3 [40.1; N.E.]	69.6 [25.0; N.E.]		
% of outcome-free patients[1]	42.04 [25.07; 59.00]	36.01 [20.51; 51.51]	0.77 [0.42; 1.39] 0.381	0.531
KITE: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.329			
≤ 3 months				
KITE, N'/ N	85 / 85	92 / 92		
Number of patients with at least one event, n (%)	60 (70.6)	63 (68.5)		
Median (in weeks)	23.6 [16.1; 32.1]	24.4 [18.4; 40.6]		
% of outcome-free patients[1]	26.56 [16.81; 36.31]	29.00 [19.19; 38.81]	1.26 [0.88; 1.80] 0.210	0.458

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
> 3 - < 12 months				
KITE, N'/ N	51 / 51	49 / 49		
Number of patients with at least one event, n (%)	39 (76.5)	37 (75.5)		
Median (in weeks)	21.9 [12.1; 32.1]	18.1 [16.1; 28.6]		
% of outcome-free patients[1]	21.58 [9.93; 33.23]	20.75 [8.70; 32.80]	0.99 [0.63; 1.55] 0.954	0.941
≥ 12 months				
KITE, N'/ N	43 / 43	40 / 40		
Number of patients with at least one event, n (%)	29 (67.4)	28 (70.0)		
Median (in weeks)	28.4 [18.1; 55.1]	18.1 [16.0; 25.1]		
% of outcome-free patients[1]	19.87 [1.27; 38.48]	24.20 [10.01; 38.38]	0.79 [0.47; 1.33] 0.368	0.362
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.198			
≤ 3 months				
Pooled Analysis, N'/ N	205 / 205	202 / 202		
Number of patients with at least one event, n (%)	152 (74.1)	137 (67.8)		
Median (in weeks)	23.4 [18.1; 28.3]	24.1 [19.1; 35.4]		
% of outcome-free patients[1]	22.26 [16.23; 28.28]	28.57 [21.61; 35.53]	1.21 [0.96; 1.53] 0.105	0.220
> 3 - < 12 months				
Pooled Analysis, N'/ N	81 / 81	88 / 88		
Number of patients with at least one event, n (%)	60 (74.1)	63 (71.6)		
Median (in weeks)	24.1 [16.7; 32.1]	20.3 [17.7; 43.1]		
% of outcome-free patients[1]	22.48 [12.81; 32.16]	23.48 [13.88; 33.08]	1.11 [0.78; 1.59] 0.568	0.692

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
≥ 12 months				
Pooled Analysis, N'/ N	82 / 82	78 / 78		
Number of patients with at least one event, n (%)	49 (59.8)	52 (66.7)		
Median (in weeks)	41.1 [35.1; 64.0]	25.0 [18.4; 72.1]		
% of outcome-free patients[1]	28.58 [13.18; 43.99]	30.17 [19.59; 40.76]	0.80 [0.54; 1.18] 0.260	0.272

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + duration of DME + treatment * duration of DME.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + duration of DME + treatment * duration of DME.

Table 6.9 BCVA - Gain of 10 respectively 15 letters by DME type (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.347**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.074			
focal				
KESTREL, N'/ N	59 / 59	48 / 48		
Number of patients with at least one event, n (%)	42 (71.2)	30 (62.5)		
Median (in weeks)	12.3 [8.1; 28.0]	20.1 [12.4; 40.1]		
% of outcome-free patients[1]	21.90 [6.61; 37.20]	34.74 [20.93; 48.54]	1.28 [0.80; 2.06] 0.299	0.469
diffuse				
KESTREL, N'/ N	127 / 127	134 / 134		
Number of patients with at least one event, n (%)	96 (75.6)	112 (83.6)		
Median (in weeks)	15.7 [11.4; 20.1]	12.1 [8.1; 16.1]		
% of outcome-free patients[1]	21.27 [13.80; 28.74]	13.40 [6.35; 20.44]	0.78 [0.59; 1.03] 0.076	0.307
KITE: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.776			
focal				
KITE, N'/ N	63 / 63	66 / 66		
Number of patients with at least one event, n (%)	51 (81.0)	55 (83.3)		
Median (in weeks)	12.1 [8.1; 20.7]	16.1 [12.4; 18.1]		
% of outcome-free patients[1]	13.94 [4.45; 23.42]	15.50 [6.68; 24.33]	1.06 [0.72; 1.55] 0.773	0.962
diffuse				
KITE, N'/ N	115 / 115	109 / 109		
Number of patients with at least one event, n (%)	88 (76.5)	87 (79.8)		
Median (in weeks)	8.4 [6.6; 17.6]	9.1 [7.1; 12.3]		
% of outcome-free patients[1]	21.84 [14.11; 29.56]	18.66 [11.17; 26.14]	0.99 [0.73; 1.33] 0.927	0.441

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.206			
focal				
Pooled Analysis, N'/ N	122 / 122	114 / 114		
Number of patients with at least one event, n (%)	93 (76.2)	85 (74.6)		
Median (in weeks)	12.3 [8.4; 20.1]	17.0 [12.9; 19.1]		
% of outcome-free patients[1]	17.11 [7.35; 26.87]	23.37 [15.46; 31.29]	1.12 [0.83; 1.50] 0.458	0.618
diffuse				
Pooled Analysis, N'/ N	242 / 242	243 / 243		
Number of patients with at least one event, n (%)	184 (76.0)	199 (81.9)		
Median (in weeks)	12.3 [8.1; 17.1]	11.4 [8.4; 12.6]		
% of outcome-free patients[1]	21.62 [16.24; 26.99]	14.96 [9.49; 20.42]	0.89 [0.73; 1.09] 0.246	0.203
Time to first gain in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.583**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.083			
focal				
KESTREL, N'/ N	59 / 59	48 / 48		
Number of patients with at least one event, n (%)	47 (79.7)	35 (72.9)		
Median (in weeks)	12.3 [8.1; 28.0]	20.1 [12.4; 40.1]		
% of outcome-free patients[1]	15.81 [5.48; 26.15]	22.49 [9.95; 35.02]	1.27 [0.81; 1.97] 0.296	0.418
diffuse				
KESTREL, N'/ N	127 / 127	134 / 134		
Number of patients with at least one event, n (%)	102 (80.3)	117 (87.3)		
Median (in weeks)	15.7 [11.4; 20.1]	12.1 [8.1; 16.1]		
% of outcome-free patients[1]	15.61 [8.84; 22.38]	8.96 [0.82; 17.09]	0.80 [0.61; 1.05] 0.105	0.339

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.878			
focal				
KITE, N'/ N	63 / 63	66 / 66		
Number of patients with at least one event, n (%)	52 (82.5)	59 (89.4)		
Median (in weeks)	12.1 [8.1; 20.7]	16.1 [12.4; 18.1]		
% of outcome-free patients[1]	13.81 [4.97; 22.64]	0.00 [0.00; 0.00]	1.00 [0.69; 1.45] 0.998	0.775
diffuse				
KITE, N'/ N	115 / 115	109 / 109		
Number of patients with at least one event, n (%)	93 (80.9)	94 (86.2)		
Median (in weeks)	8.4 [6.6; 17.6]	9.1 [7.1; 12.3]		
% of outcome-free patients[1]	16.58 [9.46; 23.70]	9.91 [3.64; 16.18]	0.96 [0.72; 1.29] 0.801	0.306
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.249			
focal				
Pooled Analysis, N'/ N	122 / 122	114 / 114		
Number of patients with at least one event, n (%)	99 (81.1)	94 (82.5)		
Median (in weeks)	12.3 [8.4; 20.1]	17.0 [12.9; 19.1]		
% of outcome-free patients[1]	15.21 [8.43; 21.99]	10.52 [0.92; 20.11]	1.08 [0.82; 1.44] 0.579	0.754
diffuse				
Pooled Analysis, N'/ N	242 / 242	243 / 243		
Number of patients with at least one event, n (%)	195 (80.6)	211 (86.8)		
Median (in weeks)	12.3 [8.1; 17.1]	11.4 [8.4; 12.6]		
% of outcome-free patients[1]	16.09 [11.18; 21.01]	9.77 [4.31; 15.24]	0.88 [0.73; 1.08] 0.218	0.163
Time to first gain in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.696**				

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.127			
focal				
KESTREL, N'/ N	59 / 59	48 / 48		
Number of patients with at least one event, n (%)	37 (62.7)	23 (47.9)		
Median (in weeks)	31.9 [16.0; 49.1]	36.9 [20.3; N.E.]		
% of outcome-free patients[1]	31.01 [15.65; 46.36]	49.89 [35.39; 64.39]	1.47 [0.87; 2.49] 0.149	0.263
diffuse				
KESTREL, N'/ N	127 / 127	134 / 134		
Number of patients with at least one event, n (%)	76 (59.8)	82 (61.2)		
Median (in weeks)	28.3 [20.4; 40.1]	28.9 [19.3; 45.1]		
% of outcome-free patients[1]	37.45 [28.72; 46.19]	23.80 [3.66; 43.95]	0.91 [0.67; 1.25] 0.575	0.930
KITE: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.165			
focal				
KITE, N'/ N	63 / 63	66 / 66		
Number of patients with at least one event, n (%)	43 (68.3)	39 (59.1)		
Median (in weeks)	21.9 [16.1; 32.3]	21.0 [18.4; N.E.]		
% of outcome-free patients[1]	27.42 [15.86; 38.99]	40.10 [28.18; 52.02]	1.38 [0.89; 2.13] 0.150	0.149
diffuse				
KITE, N'/ N	115 / 115	109 / 109		
Number of patients with at least one event, n (%)	76 (66.1)	75 (68.8)		
Median (in weeks)	24.4 [17.1; 32.1]	18.1 [13.3; 24.4]		
% of outcome-free patients[1]	23.29 [8.16; 38.41]	26.71 [16.29; 37.12]	0.94 [0.68; 1.30] 0.704	0.507

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.051			
focal				
Pooled Analysis, N'/ N	122 / 122	114 / 114		
Number of patients with at least one event, n (%)	80 (65.6)	62 (54.4)		
Median (in weeks)	24.1 [16.6; 33.3]	28.1 [20.1; N.E.]		
% of outcome-free patients[1]	27.70 [16.51; 38.88]	44.17 [34.92; 53.43]	1.42 [1.02; 1.98] 0.039 *	0.068
diffuse				
Pooled Analysis, N'/ N	242 / 242	243 / 243		
Number of patients with at least one event, n (%)	152 (62.8)	157 (64.6)		
Median (in weeks)	27.1 [21.1; 35.1]	20.6 [18.1; 28.9]		
% of outcome-free patients[1]	29.76 [19.90; 39.62]	21.10 [3.55; 38.65]	0.95 [0.76; 1.19] 0.669	0.599
Time to first gain in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.933**				
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.350			
focal				
KESTREL, N'/ N	59 / 59	48 / 48		
Number of patients with at least one event, n (%)	42 (71.2)	31 (64.6)		
Median (in weeks)	31.9 [16.0; 53.1]	59.4 [20.3; 81.4]		
% of outcome-free patients[1]	24.49 [12.64; 36.35]	24.85 [7.26; 42.44]	1.31 [0.82; 2.10] 0.254	0.383
diffuse				
KESTREL, N'/ N	127 / 127	134 / 134		
Number of patients with at least one event, n (%)	89 (70.1)	90 (67.2)		
Median (in weeks)	28.3 [20.4; 43.1]	28.9 [19.3; 45.1]		
% of outcome-free patients[1]	24.65 [16.52; 32.78]	30.49 [22.41; 38.57]	1.01 [0.75; 1.36] 0.954	0.655

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.470			
focal				
KITE, N'/ N	63 / 63	66 / 66		
Number of patients with at least one event, n (%)	45 (71.4)	47 (71.2)		
Median (in weeks)	21.9 [16.1; 32.3]	21.0 [18.4; 56.1]		
% of outcome-free patients[1]	23.89 [12.80; 34.98]	26.33 [15.26; 37.41]	1.21 [0.80; 1.82] 0.369	0.330
diffuse				
KITE, N'/ N	115 / 115	109 / 109		
Number of patients with at least one event, n (%)	83 (72.2)	78 (71.6)		
Median (in weeks)	24.4 [17.1; 32.1]	18.1 [13.3; 24.4]		
% of outcome-free patients[1]	22.79 [13.36; 32.23]	25.72 [17.08; 34.36]	1.00 [0.73; 1.37] 0.992	0.717
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.269			
focal				
Pooled Analysis, N'/ N	122 / 122	114 / 114		
Number of patients with at least one event, n (%)	87 (71.3)	78 (68.4)		
Median (in weeks)	24.1 [16.6; 33.3]	28.1 [20.1; 59.4]		
% of outcome-free patients[1]	24.37 [16.24; 32.49]	23.89 [12.61; 35.18]	1.26 [0.93; 1.72] 0.137	0.191

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
diffuse				
Pooled Analysis, N'/ N	242 / 242	243 / 243		
Number of patients with at least one event, n (%)	172 (71.1)	168 (69.1)		
Median (in weeks)	27.1 [21.1; 35.1]	20.6 [18.1; 28.9]		
% of outcome-free patients[1]	23.06 [16.23; 29.89]	28.42 [22.52; 34.32]	1.02 [0.83; 1.27] 0.837	0.940

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
*: $p < 0.05$
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + DME type + treatment * DME type.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + DME type + treatment * DME type.

Table 6.10 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.347**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.227			
< 450 µm				
KESTREL, N'/ N	107 / 107	96 / 96		
Number of patients with at least one event, n (%)	78 (72.9)	71 (74.0)		
Median (in weeks)	12.1 [8.1; 18.1]	16.1 [11.9; 19.7]		
% of outcome-free patients[1]	24.73 [16.15; 33.32]	22.22 [12.95; 31.50]	0.97 [0.70; 1.34] 0.859	0.822
≥ 450 - < 650 µm				
KESTREL, N'/ N	70 / 70	71 / 71		
Number of patients with at least one event, n (%)	51 (72.9)	56 (78.9)		
Median (in weeks)	20.1 [12.4; 28.0]	16.1 [8.1; 20.9]		
% of outcome-free patients[1]	19.89 [6.10; 33.67]	16.84 [4.84; 28.83]	0.85 [0.58; 1.24] 0.396	0.441
≥ 650 µm				
KESTREL, N'/ N	12 / 12	20 / 20		
Number of patients with at least one event, n (%)	11 (91.7)	19 (95.0)		
Median (in weeks)	11.6 [4.6; 21.0]	6.2 [4.1; 12.1]		
% of outcome-free patients[1]	8.33 [0.00; 23.97]	5.00 [0.00; 14.55]	0.47 [0.22; 1.01] 0.053	0.282
KITE: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.031 *			
< 450 µm				
KITE, N'/ N	85 / 85	82 / 82		
Number of patients with at least one event, n (%)	57 (67.1)	62 (75.6)		
Median (in weeks)	19.1 [12.0; 28.4]	16.0 [11.1; 19.1]		
% of outcome-free patients[1]	30.26 [20.16; 40.36]	20.56 [11.39; 29.74]	0.80 [0.56; 1.15] 0.221	0.181

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
≥ 450 - < 650 µm				
KITE, N'/ N	74 / 74	79 / 79		
Number of patients with at least one event, n (%)	65 (87.8)	66 (83.5)		
Median (in weeks)	8.1 [6.6; 12.0]	12.1 [8.4; 16.1]		
% of outcome-free patients[1]	8.28 [0.99; 15.57]	16.08 [7.90; 24.27]	1.44 [1.01; 2.05] 0.044 *	0.293
≥ 650 µm				
KITE, N'/ N	20 / 20	19 / 19		
Number of patients with at least one event, n (%)	17 (85.0)	16 (84.2)		
Median (in weeks)	8.1 [5.3; 18.1]	6.1 [4.1; 9.1]		
% of outcome-free patients[1]	15.00 [0.00; 30.65]	13.16 [0.00; 29.41]	0.66 [0.33; 1.31] 0.232	0.362
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.049 *			
< 450 µm				
Pooled Analysis, N'/ N	192 / 192	178 / 178		
Number of patients with at least one event, n (%)	135 (70.3)	133 (74.7)		
Median (in weeks)	16.1 [12.0; 19.1]	16.1 [12.1; 19.0]		
% of outcome-free patients[1]	27.16 [20.61; 33.71]	20.45 [13.36; 27.53]	0.90 [0.71; 1.14] 0.374	0.471
≥ 450 - < 650 µm				
Pooled Analysis, N'/ N	144 / 144	150 / 150		
Number of patients with at least one event, n (%)	116 (80.6)	122 (81.3)		
Median (in weeks)	12.1 [8.4; 18.1]	12.4 [9.1; 16.1]		
% of outcome-free patients[1]	13.99 [5.93; 22.04]	16.37 [9.03; 23.71]	1.14 [0.88; 1.47] 0.330	0.799
≥ 650 µm				
Pooled Analysis, N'/ N	32 / 32	39 / 39		
Number of patients with at least one event, n (%)	28 (87.5)	35 (89.7)		
Median (in weeks)	8.1 [5.6; 16.1]	6.1 [4.1; 8.0]		
% of outcome-free patients[1]	12.50 [1.04; 23.96]	8.46 [0.00; 17.52]	0.57 [0.35; 0.94] 0.028 *	0.161

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.583**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.283			
< 450 µm				
KESTREL, N'/ N	107 / 107	96 / 96		
Number of patients with at least one event, n (%)	84 (78.5)	78 (81.3)		
Median (in weeks)	12.1 [8.1; 18.1]	16.1 [11.9; 19.7]		
% of outcome-free patients[1]	17.50 [9.65; 25.36]	8.69 [0.00; 21.34]	0.96 [0.71; 1.31] 0.808	0.927
≥ 450 - < 650 µm				
KESTREL, N'/ N	70 / 70	71 / 71		
Number of patients with at least one event, n (%)	57 (81.4)	59 (83.1)		
Median (in weeks)	20.1 [12.4; 28.0]	16.1 [8.1; 20.9]		
% of outcome-free patients[1]	14.73 [5.92; 23.54]	16.68 [7.95; 25.42]	0.92 [0.64; 1.32] 0.647	0.707
≥ 650 µm				
KESTREL, N'/ N	12 / 12	20 / 20		
Number of patients with at least one event, n (%)	11 (91.7)	19 (95.0)		
Median (in weeks)	11.6 [4.6; 21.0]	6.2 [4.1; 12.1]		
% of outcome-free patients[1]	8.33 [0.00; 23.97]	5.00 [0.00; 14.55]	0.50 [0.24; 1.06] 0.072	0.282
KITE: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.078			
< 450 µm				
KITE, N'/ N	85 / 85	82 / 82		
Number of patients with at least one event, n (%)	61 (71.8)	64 (78.0)		
Median (in weeks)	19.1 [12.0; 28.4]	16.0 [11.1; 19.1]		
% of outcome-free patients[1]	24.55 [14.91; 34.20]	17.77 [9.05; 26.49]	0.82 [0.58; 1.17] 0.281	0.235

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
≥ 450 - < 650 µm				
KITE, N'/ N	74 / 74	79 / 79		
Number of patients with at least one event, n (%)	66 (89.2)	74 (93.7)		
Median (in weeks)	8.1 [6.6; 12.0]	12.1 [8.4; 16.1]		
% of outcome-free patients[1]	8.61 [2.05; 15.16]	0.00 [0.00; 0.00]	1.31 [0.93; 1.84] 0.128	0.597
≥ 650 µm				
KITE, N'/ N	20 / 20	19 / 19		
Number of patients with at least one event, n (%)	18 (90.0)	17 (89.5)		
Median (in weeks)	8.1 [5.3; 18.1]	6.1 [4.1; 9.1]		
% of outcome-free patients[1]	10.00 [0.00; 23.15]	6.58 [0.00; 18.79]	0.64 [0.33; 1.25] 0.196	0.311
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.068			
< 450 µm				
Pooled Analysis, N'/ N	192 / 192	178 / 178		
Number of patients with at least one event, n (%)	145 (75.5)	142 (79.8)		
Median (in weeks)	16.1 [12.0; 19.1]	16.1 [12.1; 19.0]		
% of outcome-free patients[1]	20.66 [14.54; 26.79]	13.16 [4.52; 21.79]	0.90 [0.72; 1.14] 0.397	0.476
≥ 450 - < 650 µm				
Pooled Analysis, N'/ N	144 / 144	150 / 150		
Number of patients with at least one event, n (%)	123 (85.4)	133 (88.7)		
Median (in weeks)	12.1 [8.4; 18.1]	12.4 [9.1; 16.1]		
% of outcome-free patients[1]	11.64 [6.15; 17.13]	7.30 [0.51; 14.10]	1.10 [0.86; 1.41] 0.446	0.895
≥ 650 µm				
Pooled Analysis, N'/ N	32 / 32	39 / 39		
Number of patients with at least one event, n (%)	29 (90.6)	36 (92.3)		
Median (in weeks)	8.1 [5.6; 16.1]	6.1 [4.1; 8.0]		
% of outcome-free patients[1]	8.33 [0.00; 18.47]	5.64 [0.00; 13.18]	0.58 [0.35; 0.94] 0.029 *	0.140

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.696**				
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.022 *			
< 450 µm				
KESTREL, N'/ N	107 / 107	96 / 96		
Number of patients with at least one event, n (%)	70 (65.4)	52 (54.2)		
Median (in weeks)	20.4 [16.0; 33.3]	36.3 [21.0; N.E.]		
% of outcome-free patients[1]	31.82 [22.58; 41.06]	22.48 [0.00; 54.04]	1.33 [0.93; 1.91] 0.123	0.121
≥ 450 - < 650 µm				
KESTREL, N'/ N	70 / 70	71 / 71		
Number of patients with at least one event, n (%)	36 (51.4)	39 (54.9)		
Median (in weeks)	40.1 [31.1; N.E.]	43.1 [20.0; N.E.]		
% of outcome-free patients[1]	39.99 [22.50; 57.47]	39.65 [24.99; 54.30]	0.87 [0.55; 1.37] 0.551	0.567
≥ 650 µm				
KESTREL, N'/ N	12 / 12	20 / 20		
Number of patients with at least one event, n (%)	8 (66.7)	17 (85.0)		
Median (in weeks)	30.6 [20.4; N.E.]	16.6 [6.1; 20.1]		
% of outcome-free patients[1]	30.00 [2.63; 57.37]	13.33 [0.00; 29.16]	0.39 [0.17; 0.90] 0.027 *	0.074
KITE: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.095			
< 450 µm				
KITE, N'/ N	85 / 85	82 / 82		
Number of patients with at least one event, n (%)	48 (56.5)	48 (58.5)		
Median (in weeks)	32.1 [23.6; N.E.]	24.0 [18.9; 39.9]		
% of outcome-free patients[1]	33.43 [16.39; 50.47]	38.70 [27.81; 49.58]	0.91 [0.61; 1.35] 0.633	0.684

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
≥ 450 - < 650 µm				
KITE, N'/ N	74 / 74	79 / 79		
Number of patients with at least one event, n (%)	57 (77.0)	54 (68.4)		
Median (in weeks)	17.1 [11.9; 24.7]	19.9 [17.1; 32.1]		
% of outcome-free patients[1]	14.89 [1.33; 28.46]	28.03 [15.74; 40.32]	1.44 [0.99; 2.11] 0.058	0.104
≥ 650 µm				
KITE, N'/ N	20 / 20	19 / 19		
Number of patients with at least one event, n (%)	14 (70.0)	14 (73.7)		
Median (in weeks)	20.0 [8.1; N.E.]	8.1 [5.7; 28.6]		
% of outcome-free patients[1]	30.00 [9.92; 50.08]	23.68 [3.80; 43.57]	0.66 [0.31; 1.38] 0.269	0.257
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.035 *			
< 450 µm				
Pooled Analysis, N'/ N	192 / 192	178 / 178		
Number of patients with at least one event, n (%)	118 (61.5)	100 (56.2)		
Median (in weeks)	25.1 [19.0; 36.1]	28.3 [20.6; 48.1]		
% of outcome-free patients[1]	32.95 [24.04; 41.86]	21.06 [0.00; 50.49]	1.14 [0.87; 1.48] 0.346	0.375
≥ 450 - < 650 µm				
Pooled Analysis, N'/ N	144 / 144	150 / 150		
Number of patients with at least one event, n (%)	93 (64.6)	93 (62.0)		
Median (in weeks)	27.3 [20.1; 36.1]	24.4 [18.4; 47.6]		
% of outcome-free patients[1]	27.07 [15.76; 38.38]	33.41 [23.88; 42.94]	1.18 [0.88; 1.57] 0.268	0.378
≥ 650 µm				
Pooled Analysis, N'/ N	32 / 32	39 / 39		
Number of patients with at least one event, n (%)	22 (68.8)	31 (79.5)		
Median (in weeks)	28.6 [18.1; 44.1]	13.1 [6.1; 19.3]		
% of outcome-free patients[1]	30.13 [13.95; 46.32]	18.46 [5.89; 31.04]	0.54 [0.31; 0.93] 0.025 *	0.039 *

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.933**				
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.043 *			
< 450 µm				
KESTREL, N'/ N	107 / 107	96 / 96		
Number of patients with at least one event, n (%)	80 (74.8)	62 (64.6)		
Median (in weeks)	20.4 [16.0; 33.3]	36.3 [21.0; 64.1]		
% of outcome-free patients[1]	19.93 [11.62; 28.24]	32.03 [22.27; 41.78]	1.36 [0.98; 1.90] 0.070	0.072
≥ 450 - < 650 µm				
KESTREL, N'/ N	70 / 70	71 / 71		
Number of patients with at least one event, n (%)	44 (62.9)	45 (63.4)		
Median (in weeks)	40.1 [31.1; 87.1]	43.1 [20.0; 75.4]		
% of outcome-free patients[1]	32.18 [20.37; 43.99]	27.87 [12.48; 43.27]	0.93 [0.61; 1.41] 0.730	0.797
≥ 650 µm				
KESTREL, N'/ N	12 / 12	20 / 20		
Number of patients with at least one event, n (%)	9 (75.0)	17 (85.0)		
Median (in weeks)	30.6 [20.4; 60.1]	16.6 [6.1; 20.1]		
% of outcome-free patients[1]	15.00 [0.00; 39.89]	15.00 [0.00; 30.65]	0.47 [0.21; 1.07] 0.072	0.137
KITE: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.169			
< 450 µm				
KITE, N'/ N	85 / 85	82 / 82		
Number of patients with at least one event, n (%)	55 (64.7)	54 (65.9)		
Median (in weeks)	32.1 [23.6; 55.1]	24.0 [18.9; 39.9]		
% of outcome-free patients[1]	27.65 [15.93; 39.37]	29.16 [18.58; 39.74]	0.94 [0.65; 1.37] 0.749	0.811

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
≥ 450 - < 650 µm				
KITE, N'/ N	74 / 74	79 / 79		
Number of patients with at least one event, n (%)	58 (78.4)	59 (74.7)		
Median (in weeks)	17.1 [11.9; 24.7]	19.9 [17.1; 32.1]		
% of outcome-free patients[1]	19.54 [10.27; 28.80]	23.75 [13.95; 33.56]	1.37 [0.94; 1.98] 0.098	0.200
≥ 650 µm				
KITE, N'/ N	20 / 20	19 / 19		
Number of patients with at least one event, n (%)	15 (75.0)	14 (73.7)		
Median (in weeks)	20.0 [8.1; 85.1]	8.1 [5.7; 28.6]		
% of outcome-free patients[1]	24.00 [4.80; 43.20]	23.68 [3.80; 43.57]	0.69 [0.33; 1.43] 0.315	0.332
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.064			
< 450 µm				
Pooled Analysis, N'/ N	192 / 192	178 / 178		
Number of patients with at least one event, n (%)	135 (70.3)	116 (65.2)		
Median (in weeks)	25.1 [19.0; 36.1]	28.3 [20.6; 48.1]		
% of outcome-free patients[1]	22.65 [15.07; 30.22]	30.56 [23.35; 37.77]	1.16 [0.91; 1.49] 0.232	0.233
≥ 450 - < 650 µm				
Pooled Analysis, N'/ N	144 / 144	150 / 150		
Number of patients with at least one event, n (%)	102 (70.8)	104 (69.3)		
Median (in weeks)	27.3 [20.1; 36.1]	24.4 [18.4; 47.6]		
% of outcome-free patients[1]	25.85 [18.32; 33.37]	25.76 [16.75; 34.77]	1.15 [0.88; 1.52] 0.305	0.430

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
≥ 650 µm				
Pooled Analysis, N'/ N	32 / 32	39 / 39		
Number of patients with at least one event, n (%)	24 (75.0)	31 (79.5)		
Median (in weeks)	28.6 [18.1; 44.1]	13.1 [6.1; 19.3]		
% of outcome-free patients[1]	21.97 [6.67; 37.28]	18.85 [6.33; 31.36]	0.59 [0.35; 1.01] 0.053	0.083

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
*: $p < 0.05$
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + CSFT + treatment * CSFT.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + CSFT + treatment * CSFT.

Table 6.11 BCVA - Gain of 10 respectively 15 letters by status of SRF (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.347**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.977			
presence				
KESTREL, N'/ N	62 / 62	61 / 61		
Number of patients with at least one event, n (%)	56 (90.3)	54 (88.5)		
Median (in weeks)	12.0 [6.1; 18.1]	8.1 [6.4; 12.6]		
% of outcome-free patients[1]	8.85 [1.44; 16.26]	10.00 [2.41; 17.59]	0.87 [0.60; 1.27] 0.476	0.756
absence				
KESTREL, N'/ N	127 / 127	126 / 126		
Number of patients with at least one event, n (%)	84 (66.1)	92 (73.0)		
Median (in weeks)	16.3 [12.1; 29.3]	17.7 [12.1; 20.1]		
% of outcome-free patients[1]	27.35 [16.34; 38.37]	21.39 [11.66; 31.12]	0.87 [0.64; 1.16] 0.339	0.454
KITE: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.539			
presence				
KITE, N'/ N	56 / 56	67 / 67		
Number of patients with at least one event, n (%)	48 (85.7)	58 (86.6)		
Median (in weeks)	6.4 [5.1; 8.3]	9.0 [6.3; 12.1]		
% of outcome-free patients[1]	12.00 [3.18; 20.81]	10.49 [2.78; 18.21]	1.14 [0.78; 1.68] 0.495	0.585
absence				
KITE, N'/ N	123 / 123	114 / 114		
Number of patients with at least one event, n (%)	91 (74.0)	87 (76.3)		
Median (in weeks)	18.1 [11.9; 24.1]	13.1 [12.1; 18.1]		
% of outcome-free patients[1]	23.19 [15.35; 31.03]	21.73 [13.97; 29.50]	0.98 [0.73; 1.32] 0.903	0.434

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.687			
presence				
Pooled Analysis, N'/ N	118 / 118	128 / 128		
Number of patients with at least one event, n (%)	104 (88.1)	112 (87.5)		
Median (in weeks)	8.1 [6.1; 12.0]	8.4 [7.0; 11.9]		
% of outcome-free patients[1]	10.23 [4.57; 15.89]	10.21 [4.81; 15.62]	0.99 [0.76; 1.30] 0.971	0.878
absence				
Pooled Analysis, N'/ N	250 / 250	240 / 240		
Number of patients with at least one event, n (%)	175 (70.0)	179 (74.6)		
Median (in weeks)	18.0 [12.1; 21.9]	16.1 [12.4; 18.1]		
% of outcome-free patients[1]	24.02 [15.92; 32.12]	20.26 [13.07; 27.44]	0.93 [0.75; 1.14] 0.481	0.279
Time to first gain in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.583**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.716			
presence				
KESTREL, N'/ N	62 / 62	61 / 61		
Number of patients with at least one event, n (%)	60 (96.8)	55 (90.2)		
Median (in weeks)	12.0 [6.1; 18.1]	8.1 [6.4; 12.6]		
% of outcome-free patients[1]	1.84 [0.00; 5.39]	8.33 [1.34; 15.33]	0.95 [0.66; 1.37] 0.784	0.946
absence				
KESTREL, N'/ N	127 / 127	126 / 126		
Number of patients with at least one event, n (%)	92 (72.4)	101 (80.2)		
Median (in weeks)	16.3 [12.1; 29.3]	17.7 [12.1; 20.1]		
% of outcome-free patients[1]	22.68 [14.75; 30.62]	12.91 [1.56; 24.26]	0.87 [0.66; 1.16] 0.339	0.438

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.666			
presence				
KITE, N'/ N	56 / 56	67 / 67		
Number of patients with at least one event, n (%)	48 (85.7)	61 (91.0)		
Median (in weeks)	6.4 [5.1; 8.3]	9.0 [6.3; 12.1]		
% of outcome-free patients[1]	12.00 [3.18; 20.81]	4.66 [0.00; 10.38]	1.07 [0.73; 1.56] 0.729	0.806
absence				
KITE, N'/ N	123 / 123	114 / 114		
Number of patients with at least one event, n (%)	97 (78.9)	95 (83.3)		
Median (in weeks)	18.1 [11.9; 24.1]	13.1 [12.1; 18.1]		
% of outcome-free patients[1]	18.30 [11.20; 25.39]	11.63 [4.17; 19.09]	0.96 [0.72; 1.28] 0.797	0.333
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.629			
presence				
Pooled Analysis, N'/ N	118 / 118	128 / 128		
Number of patients with at least one event, n (%)	108 (91.5)	116 (90.6)		
Median (in weeks)	8.1 [6.1; 12.0]	8.4 [7.0; 11.9]		
% of outcome-free patients[1]	6.14 [1.47; 10.80]	6.57 [2.03; 11.11]	1.00 [0.77; 1.30] 0.975	0.827
absence				
Pooled Analysis, N'/ N	250 / 250	240 / 240		
Number of patients with at least one event, n (%)	189 (75.6)	196 (81.7)		
Median (in weeks)	18.0 [12.1; 21.9]	16.1 [12.4; 18.1]		
% of outcome-free patients[1]	20.54 [15.22; 25.86]	11.55 [3.84; 19.26]	0.92 [0.75; 1.12] 0.400	0.218
Time to first gain in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.696**				

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.193			
presence				
KESTREL, N'/ N	62 / 62	61 / 61		
Number of patients with at least one event, n (%)	43 (69.4)	45 (73.8)		
Median (in weeks)	24.0 [19.4; 40.1]	17.1 [12.1; 32.9]		
% of outcome-free patients[1]	29.34 [17.73; 40.95]	0.00 [0.00; 0.00]	0.81 [0.53; 1.23] 0.327	0.445
absence				
KESTREL, N'/ N	127 / 127	126 / 126		
Number of patients with at least one event, n (%)	71 (55.9)	63 (50.0)		
Median (in weeks)	36.1 [24.1; 53.1]	47.6 [27.9; N.E.]		
% of outcome-free patients[1]	37.49 [25.73; 49.25]	48.39 [39.45; 57.34]	1.16 [0.83; 1.63] 0.394	0.372
KITE: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.557			
presence				
KITE, N'/ N	56 / 56	67 / 67		
Number of patients with at least one event, n (%)	45 (80.4)	50 (74.6)		
Median (in weeks)	12.4 [8.1; 20.1]	16.1 [12.1; 19.1]		
% of outcome-free patients[1]	9.56 [0.00; 23.83]	21.14 [10.05; 32.24]	1.22 [0.82; 1.83] 0.328	0.378
absence				
KITE, N'/ N	123 / 123	114 / 114		
Number of patients with at least one event, n (%)	74 (60.2)	67 (58.8)		
Median (in weeks)	28.4 [23.6; 40.1]	25.0 [19.7; 48.1]		
% of outcome-free patients[1]	34.85 [24.51; 45.19]	39.60 [30.45; 48.76]	1.05 [0.75; 1.46] 0.794	0.921

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.561			
presence				
Pooled Analysis, N'/ N	118 / 118	128 / 128		
Number of patients with at least one event, n (%)	88 (74.6)	95 (74.2)		
Median (in weeks)	20.1 [16.1; 24.1]	16.4 [13.1; 20.1]		
% of outcome-free patients[1]	16.34 [2.23; 30.45]	0.00 [0.00; 0.00]	1.00 [0.74; 1.33] 0.983	0.920
absence				
Pooled Analysis, N'/ N	250 / 250	240 / 240		
Number of patients with at least one event, n (%)	145 (58.0)	130 (54.2)		
Median (in weeks)	32.1 [25.1; 40.1]	28.9 [24.1; N.E.]		
% of outcome-free patients[1]	35.37 [26.67; 44.07]	44.22 [37.80; 50.65]	1.11 [0.88; 1.41] 0.370	0.487
Time to first gain in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.933**				
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.585			
presence				
KESTREL, N'/ N	62 / 62	61 / 61		
Number of patients with at least one event, n (%)	52 (83.9)	47 (77.0)		
Median (in weeks)	24.0 [19.4; 40.1]	17.1 [12.1; 32.9]		
% of outcome-free patients[1]	12.23 [3.37; 21.08]	21.43 [10.98; 31.88]	0.98 [0.66; 1.46] 0.922	0.994
absence				
KESTREL, N'/ N	127 / 127	126 / 126		
Number of patients with at least one event, n (%)	81 (63.8)	77 (61.1)		
Median (in weeks)	36.1 [24.1; 60.1]	47.6 [27.9; 72.1]		
% of outcome-free patients[1]	30.77 [22.01; 39.54]	33.12 [23.23; 43.01]	1.13 [0.83; 1.54] 0.448	0.460

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.524			
presence				
KITE, N'/ N	56 / 56	67 / 67		
Number of patients with at least one event, n (%)	46 (82.1)	52 (77.6)		
Median (in weeks)	12.4 [8.1; 20.1]	16.1 [12.1; 19.1]		
% of outcome-free patients[1]	13.77 [3.65; 23.89]	19.00 [9.01; 29.00]	1.22 [0.82; 1.82] 0.327	0.415
absence				
KITE, N'/ N	123 / 123	114 / 114		
Number of patients with at least one event, n (%)	82 (66.7)	76 (66.7)		
Median (in weeks)	28.4 [23.6; 40.1]	25.0 [19.7; 48.1]		
% of outcome-free patients[1]	27.79 [18.22; 37.36]	29.75 [20.84; 38.65]	1.03 [0.75; 1.42] 0.833	0.981
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.971			
presence				
Pooled Analysis, N'/ N	118 / 118	128 / 128		
Number of patients with at least one event, n (%)	98 (83.1)	99 (77.3)		
Median (in weeks)	20.1 [16.1; 24.1]	16.4 [13.1; 20.1]		
% of outcome-free patients[1]	12.81 [6.14; 19.47]	20.16 [12.96; 27.35]	1.08 [0.82; 1.43] 0.580	0.564

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
absence				
Pooled Analysis, N'/ N	250 / 250	240 / 240		
Number of patients with at least one event, n (%)	163 (65.2)	153 (63.8)		
Median (in weeks)	32.1 [25.1; 40.1]	28.9 [24.1; 56.6]		
% of outcome-free patients[1]	28.59 [21.40; 35.79]	31.39 [24.61; 38.17]	1.09 [0.87; 1.36] 0.447	0.590

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + status of SRF + treatment * status of SRF.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + status of SRF + treatment * status of SRF.

Table 6.12 BCVA - Gain of 10 respectively 15 letters by exposure (week 52) (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by exposure (week 52) (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.347**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.025 *			
Non-exposed				
KESTREL, N'/ N	71 / 71	75 / 75		
Number of patients with at least one event, n (%)	53 (74.6)	63 (84.0)		
Median (in weeks)	15.7 [11.4; 23.4]	11.4 [6.4; 16.1]		
% of outcome-free patients[1]	20.87 [10.79; 30.95]	9.57 [1.11; 18.03]	0.62 [0.43; 0.89] 0.011 *	0.153
Exposed				
KESTREL, N'/ N	118 / 118	112 / 112		
Number of patients with at least one event, n (%)	87 (73.7)	83 (74.1)		
Median (in weeks)	14.1 [8.9; 20.1]	16.6 [12.1; 20.1]		
% of outcome-free patients[1]	22.16 [12.50; 31.81]	25.57 [17.43; 33.71]	1.07 [0.79; 1.44] 0.683	0.805
KITE: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.697			
Non-exposed				
KITE, N'/ N	85 / 85	90 / 90		
Number of patients with at least one event, n (%)	69 (81.2)	72 (80.0)		
Median (in weeks)	8.1 [6.7; 17.1]	9.0 [8.0; 13.1]		
% of outcome-free patients[1]	13.21 [5.41; 21.01]	15.86 [7.80; 23.92]	0.96 [0.69; 1.34] 0.810	0.743
Exposed				
KITE, N'/ N	94 / 94	91 / 91		
Number of patients with at least one event, n (%)	70 (74.5)	73 (80.2)		
Median (in weeks)	16.1 [8.1; 20.7]	13.1 [11.9; 19.1]		
% of outcome-free patients[1]	24.71 [15.72; 33.70]	19.72 [11.53; 27.91]	1.05 [0.76; 1.47] 0.758	0.583

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by exposure (week 52) (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.069			
Non-exposed				
Pooled Analysis, N'/ N	156 / 156	165 / 165		
Number of patients with at least one event, n (%)	122 (78.2)	135 (81.8)		
Median (in weeks)	12.0 [8.1; 17.1]	9.1 [8.0; 12.4]		
% of outcome-free patients[1]	16.80 [10.50; 23.09]	11.26 [4.68; 17.85]	0.79 [0.62; 1.01] 0.058	0.227
Exposed				
Pooled Analysis, N'/ N	212 / 212	203 / 203		
Number of patients with at least one event, n (%)	157 (74.1)	156 (76.8)		
Median (in weeks)	15.6 [11.4; 18.9]	16.1 [12.3; 19.1]		
% of outcome-free patients[1]	22.48 [15.01; 29.96]	22.95 [17.14; 28.77]	1.07 [0.86; 1.34] 0.534	0.851
Time to first gain in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.696**				
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.007 *			
Non-exposed				
KESTREL, N'/ N	71 / 71	75 / 75		
Number of patients with at least one event, n (%)	41 (57.7)	49 (65.3)		
Median (in weeks)	36.1 [18.1; N.E.]	20.0 [16.1; 29.1]		
% of outcome-free patients[1]	38.66 [26.76; 50.55]	27.65 [14.99; 40.30]	0.63 [0.42; 0.97] 0.035 *	0.208
Exposed				
KESTREL, N'/ N	118 / 118	112 / 112		
Number of patients with at least one event, n (%)	73 (61.9)	59 (52.7)		
Median (in weeks)	29.3 [20.3; 44.1]	45.1 [27.9; N.E.]		
% of outcome-free patients[1]	32.98 [21.92; 44.03]	31.76 [5.60; 57.93]	1.34 [0.95; 1.90] 0.093	0.147

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by exposure (week 52) (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.881			
Non-exposed				
KITE, N'/ N	85 / 85	90 / 90		
Number of patients with at least one event, n (%)	59 (69.4)	58 (64.4)		
Median (in weeks)	21.6 [16.1; 32.0]	18.1 [16.1; 21.0]		
% of outcome-free patients[1]	17.54 [2.02; 33.06]	27.92 [14.85; 41.00]	1.05 [0.73; 1.51] 0.780	0.727
Exposed				
KITE, N'/ N	94 / 94	91 / 91		
Number of patients with at least one event, n (%)	60 (63.8)	59 (64.8)		
Median (in weeks)	24.9 [18.1; 36.9]	25.0 [19.1; 32.3]		
% of outcome-free patients[1]	29.72 [14.52; 44.91]	35.04 [25.21; 44.87]	1.10 [0.76; 1.58] 0.625	0.880
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.053			
Non-exposed				
Pooled Analysis, N'/ N	156 / 156	165 / 165		
Number of patients with at least one event, n (%)	100 (64.1)	107 (64.8)		
Median (in weeks)	23.9 [18.1; 35.1]	18.1 [16.1; 24.0]		
% of outcome-free patients[1]	27.46 [16.84; 38.09]	27.93 [18.88; 36.98]	0.86 [0.65; 1.13] 0.282	0.569
Exposed				
Pooled Analysis, N'/ N	212 / 212	203 / 203		
Number of patients with at least one event, n (%)	133 (62.7)	118 (58.1)		
Median (in weeks)	28.1 [20.4; 35.4]	32.1 [24.4; 48.1]		
% of outcome-free patients[1]	31.88 [23.01; 40.75]	27.99 [5.13; 50.84]	1.24 [0.97; 1.59] 0.088	0.248

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by exposure (week 52) (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
*: $p < 0.05$
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + exposure (week 52) + treatment * exposure (week 52).
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).

Table 6.13 BCVA - Gain of 10 respectively 15 letters by exposure (week 100) (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first gain in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.583**				
KESTREL: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.016 *			
Non-exposed				
KESTREL, N'/ N	12 / 12	13 / 13		
Number of patients with at least one event, n (%)	6 (50.0)	11 (84.6)		
Median (in weeks)	23.9 [8.0; N.E.]	6.9 [5.1; 16.6]		
% of outcome-free patients[1]	25.45 [0.00; 64.16]	0.00 [0.00; 0.00]	0.27 [0.10; 0.74] 0.011 *	0.050
Exposed				
KESTREL, N'/ N	177 / 177	174 / 174		
Number of patients with at least one event, n (%)	146 (82.5)	145 (83.3)		
Median (in weeks)	13.1 [11.4; 18.4]	13.1 [11.9; 18.1]		
% of outcome-free patients[1]	15.30 [9.71; 20.89]	11.21 [1.49; 20.94]	0.96 [0.76; 1.21] 0.722	0.906
KITE: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.951			
Non-exposed				
KITE, N'/ N	17 / 17	12 / 12		
Number of patients with at least one event, n (%)	10 (58.8)	6 (50.0)		
Median (in weeks)	18.1 [8.3; 35.1]	15.4 [6.6; N.E.]		
% of outcome-free patients[1]	0.00 [0.00; 0.00]	35.71 [0.60; 70.82]	0.95 [0.34; 2.64] 0.922	0.645
Exposed				
KITE, N'/ N	162 / 162	169 / 169		
Number of patients with at least one event, n (%)	135 (83.3)	150 (88.8)		
Median (in weeks)	10.3 [8.1; 17.1]	12.1 [9.0; 15.1]		
% of outcome-free patients[1]	16.44 [10.69; 22.20]	9.12 [3.92; 14.33]	0.98 [0.78; 1.24] 0.876	0.364

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first gain in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.067			
Non-exposed				
Pooled Analysis, N'/ N	29 / 29	25 / 25		
Number of patients with at least one event, n (%)	16 (55.2)	17 (68.0)		
Median (in weeks)	18.7 [11.1; 35.1]	11.1 [6.1; 16.6]		
% of outcome-free patients[1]	14.39 [0.00; 37.48]	0.00 [0.00; 0.00]	0.50 [0.25; 1.00] 0.050 *	0.079
Exposed				
Pooled Analysis, N'/ N	339 / 339	343 / 343		
Number of patients with at least one event, n (%)	281 (82.9)	295 (86.0)		
Median (in weeks)	12.1 [8.9; 16.4]	12.4 [11.9; 16.1]		
% of outcome-free patients[1]	15.92 [11.91; 19.94]	10.15 [4.60; 15.69]	0.97 [0.83; 1.15] 0.747	0.471
Time to first gain in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.933**				
KESTREL: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.344			
Non-exposed				
KESTREL, N'/ N	12 / 12	13 / 13		
Number of patients with at least one event, n (%)	5 (41.7)	6 (46.2)		
Median (in weeks)	28.9 [19.0; N.E.]	29.1 [16.6; N.E.]		
% of outcome-free patients[1]	33.67 [0.00; 70.19]	20.62 [0.00; 55.09]	0.61 [0.19; 2.02] 0.420	0.878
Exposed				
KESTREL, N'/ N	177 / 177	174 / 174		
Number of patients with at least one event, n (%)	128 (72.3)	118 (67.8)		
Median (in weeks)	31.1 [20.4; 41.1]	29.3 [20.3; 48.1]		
% of outcome-free patients[1]	24.36 [17.64; 31.07]	29.47 [21.76; 37.17]	1.10 [0.86; 1.42] 0.447	0.387

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.564			
Non-exposed				
KITE, N'/ N	17 / 17	12 / 12		
Number of patients with at least one event, n (%)	8 (47.1)	6 (50.0)		
Median (in weeks)	21.1 [12.3; N.E.]	21.0 [15.4; 28.6]		
% of outcome-free patients[1]	21.28 [0.00; 54.27]	0.00 [0.00; 0.00]	0.78 [0.27; 2.28] 0.656	0.598
Exposed				
KITE, N'/ N	162 / 162	169 / 169		
Number of patients with at least one event, n (%)	120 (74.1)	122 (72.2)		
Median (in weeks)	24.1 [18.1; 32.0]	19.9 [18.1; 25.1]		
% of outcome-free patients[1]	23.58 [15.95; 31.21]	26.27 [19.36; 33.18]	1.08 [0.84; 1.40] 0.540	0.772
Pooled Analysis: Time to first gain in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.312			
Non-exposed				
Pooled Analysis, N'/ N	29 / 29	25 / 25		
Number of patients with at least one event, n (%)	13 (44.8)	12 (48.0)		
Median (in weeks)	23.9 [18.1; N.E.]	21.0 [16.6; 40.9]		
% of outcome-free patients[1]	27.56 [3.27; 51.85]	12.43 [0.00; 34.38]	0.73 [0.33; 1.60] 0.431	0.625

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Exposed				
Pooled Analysis, N'/ N	339 / 339	343 / 343		
Number of patients with at least one event, n (%)	248 (73.2)	240 (70.0)		
Median (in weeks)	27.3 [21.6; 32.1]	24.1 [19.1; 29.3]		
% of outcome-free patients[1]	23.64 [18.24; 29.04]	27.82 [22.60; 33.05]	1.11 [0.93; 1.32] 0.268	0.413

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
*: $p < 0.05$
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + exposure (week 100) + treatment * exposure (week 100).
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).

7 BCVA: Time-to-event analysis (Loss)

Table 7.1 BCVA - Loss of 10 respectively 15 letters (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first loss in BCVA of ≥10 letters, Week 52				
KESTREL, N'/ N	189 / 189	187 / 187		
Number of patients with at least one event, n (%)	12 (6.3)	8 (4.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.36 [89.73; 97.00]	90.94 [80.91; 100.00]	1.55 [0.63; 3.79] 0.338	0.380
KITE, N'/ N	179 / 179	181 / 181		
Number of patients with at least one event, n (%)	10 (5.6)	10 (5.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.13 [90.60; 97.66]	90.46 [81.90; 99.03]	0.95 [0.39; 2.30] 0.915	0.952
Pooled Analysis, N'/ N	368 / 368	368 / 368		
Number of patients with at least one event, n (%)	22 (6.0)	18 (4.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1] p_H=0.453	93.74 [91.21; 96.28]	90.74 [84.22; 97.25]	1.22 [0.65; 2.28] 0.535	0.507
Time to first loss in BCVA of ≥10 letters, Week 100				
KESTREL, N'/ N	189 / 189	187 / 187		
Number of patients with at least one event, n (%)	21 (11.1)	15 (8.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	87.70 [82.74; 92.65]	91.09 [86.77; 95.42]	1.43 [0.74; 2.78] 0.287	0.310
KITE, N'/ N	179 / 179	181 / 181		
Number of patients with at least one event, n (%)	15 (8.4)	22 (12.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	90.67 [86.14; 95.20]	82.73 [74.31; 91.15]	0.65 [0.34; 1.25] 0.199	0.303

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis, N'/ N	368 / 368	368 / 368		
Number of patients with at least one event, n (%)	36 (9.8)	37 (10.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1] p_H=0.100	89.15 [85.79; 92.52]	86.43 [81.20; 91.66]	0.99 [0.62; 1.58] 0.972	0.984
Time to first loss in BCVA of ≥15 letters, Week 52				
KESTREL, N'/ N	189 / 189	187 / 187		
Number of patients with at least one event, n (%)	4 (2.1)	1 (0.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.76 [95.58; 99.93]	99.46 [98.39; 100.00]	4.36 [0.48; 39.20] 0.189	0.180
KITE, N'/ N	179 / 179	181 / 181		
Number of patients with at least one event, n (%)	7 (3.9)	6 (3.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.91 [92.93; 98.88]	92.80 [84.62; 100.00]	1.09 [0.36; 3.27] 0.876	0.720
Pooled Analysis, N'/ N	368 / 368	368 / 368		
Number of patients with at least one event, n (%)	11 (3.0)	7 (1.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1] p_H=0.296	96.86 [95.03; 98.69]	95.92 [91.36; 100.00]	2.17 [0.63; 7.50] 0.220	0.312
Time to first loss in BCVA of ≥15 letters, Week 100				
KESTREL, N'/ N	189 / 189	187 / 187		
Number of patients with at least one event, n (%)	10 (5.3)	4 (2.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.98 [90.35; 97.61]	97.55 [95.17; 99.93]	2.65 [0.83; 8.46] 0.100	0.102

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE, N'/ N	179 / 179	181 / 181		
Number of patients with at least one event, n (%)	8 (4.5)	13 (7.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.21 [91.96; 98.46]	90.53 [84.94; 96.12]	0.58 [0.24; 1.40] 0.225	0.326
Pooled Analysis, N'/ N	368 / 368	368 / 368		
Number of patients with at least one event, n (%)	18 (4.9)	17 (4.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1] p_H=0.045 *	94.59 [92.15; 97.03]	93.85 [90.56; 97.13]	1.27 [0.61; 2.63] 0.529	0.784

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
*: $p < 0.05$
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study.

Table 7.2 BCVA - Loss of 10 respectively 15 letters by age (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first loss in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.453**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.218			
< 65 years				
KESTREL, N'/ N	104 / 104	93 / 93		
Number of patients with at least one event, n (%)	3 (2.9)	4 (4.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.05 [93.75; 100.00]	87.09 [68.80; 100.00]	0.72 [0.16; 3.25] 0.672	0.569
≥ 65 years				
KESTREL, N'/ N	85 / 85	94 / 94		
Number of patients with at least one event, n (%)	9 (10.6)	4 (4.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	88.75 [81.81; 95.69]	95.06 [90.25; 99.88]	2.41 [0.74; 7.85] 0.144	0.113
KITE: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.380			
< 65 years				
KITE, N'/ N	100 / 100	102 / 102		
Number of patients with at least one event, n (%)	6 (6.0)	4 (3.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.44 [88.36; 98.52]	95.32 [90.67; 99.96]	1.43 [0.40; 5.11] 0.583	0.483
≥ 65 years				
KITE, N'/ N	79 / 79	79 / 79		
Number of patients with at least one event, n (%)	4 (5.1)	6 (7.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.87 [89.97; 99.77]	84.10 [66.02; 100.00]	0.64 [0.18; 2.27] 0.489	0.509

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.781			
< 65 years				
Pooled Analysis, N'/ N	204 / 204	195 / 195		
Number of patients with at least one event, n (%)	9 (4.4)	8 (4.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.35 [92.37; 98.32]	91.89 [83.41; 100.00]	1.10 [0.42; 2.86] 0.844	0.862
≥ 65 years				
Pooled Analysis, N'/ N	164 / 164	173 / 173		
Number of patients with at least one event, n (%)	13 (7.9)	10 (5.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.79 [87.52; 96.07]	89.39 [79.32; 99.46]	1.32 [0.58; 3.01] 0.516	0.451
Time to first loss in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.100**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.119			
< 65 years				
KESTREL, N'/ N	104 / 104	93 / 93		
Number of patients with at least one event, n (%)	8 (7.7)	9 (9.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.46 [85.79; 97.14]	89.40 [82.82; 95.98]	0.82 [0.31; 2.13] 0.680	0.644
≥ 65 years				
KESTREL, N'/ N	85 / 85	94 / 94		
Number of patients with at least one event, n (%)	13 (15.3)	6 (6.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	83.06 [74.61; 91.52]	92.88 [87.36; 98.40]	2.44 [0.92; 6.43] 0.072	0.061

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.357			
< 65 years				
KITE, N'/ N	100 / 100	102 / 102		
Number of patients with at least one event, n (%)	8 (8.0)	9 (8.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	90.90 [84.86; 96.95]	84.70 [72.75; 96.64]	0.91 [0.35; 2.36] 0.839	0.999
≥ 65 years				
KITE, N'/ N	79 / 79	79 / 79		
Number of patients with at least one event, n (%)	7 (8.9)	13 (16.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	90.30 [83.42; 97.17]	81.06 [71.66; 90.45]	0.49 [0.19; 1.22] 0.123	0.134
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.779			
< 65 years				
Pooled Analysis, N'/ N	204 / 204	195 / 195		
Number of patients with at least one event, n (%)	16 (7.8)	18 (9.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.19 [87.04; 95.33]	86.12 [78.13; 94.10]	0.92 [0.47; 1.83] 0.820	0.745
≥ 65 years				
Pooled Analysis, N'/ N	164 / 164	173 / 173		
Number of patients with at least one event, n (%)	20 (12.2)	19 (11.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	86.67 [81.20; 92.15]	87.23 [81.78; 92.68]	1.05 [0.56; 1.99] 0.870	0.813
Time to first loss in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.296**				

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.995			
< 65 years				
KESTREL, N'/ N	104 / 104	93 / 93		
Number of patients with at least one event, n (%)	0 (0.0)	1 (1.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	100.00 [100.00; 100.00]	98.92 [96.83; 100.00]	0.00 [0.00; N.E.] 0.996	0.293
≥ 65 years				
KESTREL, N'/ N	85 / 85	94 / 94		
Number of patients with at least one event, n (%)	4 (4.7)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.89 [90.00; 99.78]	100.00 [100.00; 100.00]	N.E.	0.034 *
KITE: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.066			
< 65 years				
KITE, N'/ N	100 / 100	102 / 102		
Number of patients with at least one event, n (%)	5 (5.0)	1 (1.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.58 [89.95; 99.21]	98.33 [95.09; 100.00]	4.73 [0.55; 40.83] 0.158	0.085
≥ 65 years				
KITE, N'/ N	79 / 79	79 / 79		
Number of patients with at least one event, n (%)	2 (2.5)	5 (6.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.44 [93.93; 100.00]	85.29 [67.10; 100.00]	0.38 [0.07; 1.94] 0.242	0.244

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.458			
< 65 years				
Pooled Analysis, N'/ N	204 / 204	195 / 195		
Number of patients with at least one event, n (%)	5 (2.5)	2 (1.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.41 [95.16; 99.65]	98.66 [96.76; 100.00]	3.55 [0.56; 22.34] 0.177	0.232
≥ 65 years				
Pooled Analysis, N'/ N	164 / 164	173 / 173		
Number of patients with at least one event, n (%)	6 (3.7)	5 (2.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.18 [93.19; 99.18]	92.70 [83.11; 100.00]	1.65 [0.40; 6.85] 0.490	0.727
Time to first loss in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.045 ***				
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.712			
< 65 years				
KESTREL, N'/ N	104 / 104	93 / 93		
Number of patients with at least one event, n (%)	4 (3.8)	1 (1.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.50 [91.19; 99.81]	98.92 [96.83; 100.00]	3.71 [0.41; 33.52] 0.242	0.212
≥ 65 years				
KESTREL, N'/ N	85 / 85	94 / 94		
Number of patients with at least one event, n (%)	6 (7.1)	3 (3.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	92.08 [85.98; 98.18]	96.08 [91.74; 100.00]	2.27 [0.56; 9.14] 0.249	0.232

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.127			
< 65 years				
KITE, N'/ N	100 / 100	102 / 102		
Number of patients with at least one event, n (%)	5 (5.0)	4 (3.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.59 [89.98; 99.21]	93.65 [86.70; 100.00]	1.27 [0.34; 4.75] 0.728	0.586
≥ 65 years				
KITE, N'/ N	79 / 79	79 / 79		
Number of patients with at least one event, n (%)	3 (3.8)	9 (11.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.89 [91.31; 100.00]	86.95 [78.88; 95.02]	0.30 [0.08; 1.10] 0.070	0.066
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.158			
< 65 years				
Pooled Analysis, N'/ N	204 / 204	195 / 195		
Number of patients with at least one event, n (%)	9 (4.4)	5 (2.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.04 [91.86; 98.21]	95.73 [91.24; 100.00]	2.35 [0.74; 7.39] 0.145	0.236

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by age (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
≥ 65 years				
Pooled Analysis, N'/ N	164 / 164	173 / 173		
Number of patients with at least one event, n (%)	9 (5.5)	12 (6.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.03 [90.23; 97.83]	91.71 [87.13; 96.28]	0.86 [0.34; 2.14] 0.742	0.543

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
*: $p < 0.05$
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + baseline category + age + treatment * age.
Pooled analysis: log(hazard ratio) = treatment + baseline category + study + treatment * study + age + treatment * age.

Table 7.3 BCVA - Loss of 10 respectively 15 letters by gender (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first loss in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.453**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.644			
Male				
KESTREL, N'/ N	110 / 110	126 / 126		
Number of patients with at least one event, n (%)	5 (4.5)	5 (4.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.28 [91.23; 99.32]	95.92 [92.42; 99.42]	1.21 [0.35; 4.17] 0.768	0.836
Female				
KESTREL, N'/ N	79 / 79	61 / 61		
Number of patients with at least one event, n (%)	7 (8.9)	3 (4.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	90.74 [84.19; 97.29]	77.01 [43.01; 100.00]	1.86 [0.48; 7.19] 0.369	0.349
KITE: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.059			
Male				
KITE, N'/ N	120 / 120	115 / 115		
Number of patients with at least one event, n (%)	5 (4.2)	9 (7.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.54 [91.71; 99.36]	86.60 [74.61; 98.58]	0.51 [0.17; 1.53] 0.231	0.252
Female				
KITE, N'/ N	59 / 59	66 / 66		
Number of patients with at least one event, n (%)	5 (8.5)	1 (1.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.25 [83.91; 98.58]	98.41 [95.33; 100.00]	5.25 [0.61; 45.45] 0.132	0.070

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.079			
Male				
Pooled Analysis, N'/ N	230 / 230	241 / 241		
Number of patients with at least one event, n (%)	10 (4.3)	14 (5.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.42 [92.64; 98.19]	91.04 [84.28; 97.80]	0.76 [0.34; 1.72] 0.510	0.458
Female				
Pooled Analysis, N'/ N	138 / 138	127 / 127		
Number of patients with at least one event, n (%)	12 (8.7)	4 (3.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	90.98 [86.10; 95.85]	89.20 [73.73; 100.00]	2.67 [0.85; 8.34] 0.091	0.064
Time to first loss in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.100**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.239			
Male				
KESTREL, N'/ N	110 / 110	126 / 126		
Number of patients with at least one event, n (%)	8 (7.3)	10 (7.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.97 [86.61; 97.33]	90.90 [85.48; 96.32]	0.93 [0.37; 2.37] 0.886	0.844
Female				
KESTREL, N'/ N	79 / 79	61 / 61		
Number of patients with at least one event, n (%)	13 (16.5)	5 (8.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	82.08 [73.21; 90.96]	91.45 [84.28; 98.62]	2.15 [0.77; 6.04] 0.146	0.136

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.222			
Male				
KITE, N'/ N	120 / 120	115 / 115		
Number of patients with at least one event, n (%)	9 (7.5)	17 (14.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.54 [86.22; 96.85]	79.11 [68.27; 89.94]	0.49 [0.22; 1.11] 0.087	0.096
Female				
KITE, N'/ N	59 / 59	66 / 66		
Number of patients with at least one event, n (%)	6 (10.2)	5 (7.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	88.97 [80.56; 97.37]	91.38 [84.15; 98.61]	1.21 [0.37; 4.03] 0.751	0.523
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.056			
Male				
Pooled Analysis, N'/ N	230 / 230	241 / 241		
Number of patients with at least one event, n (%)	17 (7.4)	27 (11.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.75 [87.97; 95.52]	84.32 [77.47; 91.18]	0.68 [0.37; 1.25] 0.216	0.159
Female				
Pooled Analysis, N'/ N	138 / 138	127 / 127		
Number of patients with at least one event, n (%)	19 (13.8)	10 (7.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	84.88 [78.57; 91.19]	91.39 [86.28; 96.50]	1.77 [0.82; 3.86] 0.148	0.117
Time to first loss in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.296**				

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.995			
Male				
KESTREL, N'/ N	110 / 110	126 / 126		
Number of patients with at least one event, n (%)	3 (2.7)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.10 [93.87; 100.00]	100.00 [100.00; 100.00]	N.E.	0.063
Female				
KESTREL, N'/ N	79 / 79	61 / 61		
Number of patients with at least one event, n (%)	1 (1.3)	1 (1.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	98.65 [96.02; 100.00]	98.36 [95.17; 100.00]	0.86 [0.05; 13.82] 0.912	0.863
KITE: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.990			
Male				
KITE, N'/ N	120 / 120	115 / 115		
Number of patients with at least one event, n (%)	3 (2.5)	6 (5.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.35 [94.38; 100.00]	89.43 [78.04; 100.00]	0.47 [0.12; 1.87] 0.281	0.307
Female				
KITE, N'/ N	59 / 59	66 / 66		
Number of patients with at least one event, n (%)	4 (6.8)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	92.97 [86.33; 99.62]	100.00 [100.00; 100.00]	N.E.	0.033 *

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.241			
Male				
Pooled Analysis, N'/ N	230 / 230	241 / 241		
Number of patients with at least one event, n (%)	6 (2.6)	6 (2.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.23 [95.03; 99.42]	94.53 [88.29; 100.00]	1.45 [0.36; 5.86] 0.598	0.965
Female				
Pooled Analysis, N'/ N	138 / 138	127 / 127		
Number of patients with at least one event, n (%)	5 (3.6)	1 (0.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.25 [93.03; 99.48]	99.19 [97.62; 100.00]	6.26 [0.63; 62.29] 0.118	0.099
Time to first loss in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.045 ***				
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.804			
Male				
KESTREL, N'/ N	110 / 110	126 / 126		
Number of patients with at least one event, n (%)	6 (5.5)	3 (2.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.81 [89.00; 98.63]	97.06 [93.77; 100.00]	2.45 [0.61; 9.80] 0.206	0.214
Female				
KESTREL, N'/ N	79 / 79	61 / 61		
Number of patients with at least one event, n (%)	4 (5.1)	1 (1.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.19 [88.66; 99.73]	98.36 [95.17; 100.00]	3.40 [0.38; 30.47] 0.274	0.263

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.203			
Male				
KITE, N'/ N	120 / 120	115 / 115		
Number of patients with at least one event, n (%)	4 (3.3)	10 (8.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.33 [92.79; 99.88]	88.45 [80.79; 96.11]	0.37 [0.12; 1.19] 0.096	0.097
Female				
KITE, N'/ N	59 / 59	66 / 66		
Number of patients with at least one event, n (%)	4 (6.8)	3 (4.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	92.97 [86.33; 99.62]	94.67 [88.81; 100.00]	1.29 [0.28; 5.88] 0.742	0.519
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.310			
Male				
Pooled Analysis, N'/ N	230 / 230	241 / 241		
Number of patients with at least one event, n (%)	10 (4.3)	13 (5.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.16 [92.22; 98.10]	92.58 [88.10; 97.06]	0.99 [0.41; 2.39] 0.985	0.602

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by gender (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Female				
Pooled Analysis, N'/ N	138 / 138	127 / 127		
Number of patients with at least one event, n (%)	8 (5.8)	4 (3.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.65 [89.37; 97.93]	96.47 [93.07; 99.87]	2.12 [0.61; 7.41] 0.239	0.225

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
*: $p < 0.05$
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + gender + treatment * gender.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + gender + treatment * gender.

Table 7.4 BCVA - Loss of 10 respectively 15 letters by BCVA (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first loss in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.453**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.992			
≤ 65 letters				
KESTREL, N'/ N	74 / 74	64 / 64		
Number of patients with at least one event, n (%)	3 (4.1)	2 (3.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.77 [91.07; 100.00]	96.88 [92.61; 100.00]	1.56 [0.26; 9.43] 0.627	0.769
> 65 letters				
KESTREL, N'/ N	115 / 115	123 / 123		
Number of patients with at least one event, n (%)	9 (7.8)	6 (4.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.84 [86.72; 96.96]	88.67 [75.28; 100.00]	1.54 [0.55; 4.34] 0.410	0.371
KITE: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.163			
≤ 65 letters				
KITE, N'/ N	65 / 65	91 / 91		
Number of patients with at least one event, n (%)	1 (1.5)	5 (5.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	98.31 [95.01; 100.00]	93.75 [88.31; 99.19]	0.27 [0.03; 2.29] 0.228	0.211
> 65 letters				
KITE, N'/ N	114 / 114	90 / 90		
Number of patients with at least one event, n (%)	9 (7.9)	5 (5.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.75 [86.59; 96.92]	89.04 [76.32; 100.00]	1.49 [0.50; 4.44] 0.478	0.483

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.271			
≤ 65 letters				
Pooled Analysis, N'/ N	139 / 139	155 / 155		
Number of patients with at least one event, n (%)	4 (2.9)	7 (4.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.98 [94.05; 99.90]	94.99 [91.30; 98.69]	0.68 [0.20; 2.33] 0.536	0.472
> 65 letters				
Pooled Analysis, N'/ N	229 / 229	213 / 213		
Number of patients with at least one event, n (%)	18 (7.9)	11 (5.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.80 [88.17; 95.43]	88.88 [79.67; 98.10]	1.52 [0.72; 3.23] 0.272	0.258
Time to first loss in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.100**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.903			
≤ 65 letters				
KESTREL, N'/ N	74 / 74	64 / 64		
Number of patients with at least one event, n (%)	7 (9.5)	5 (7.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	89.18 [81.56; 96.79]	91.45 [84.26; 98.65]	1.35 [0.42; 4.31] 0.610	0.690
> 65 letters				
KESTREL, N'/ N	115 / 115	123 / 123		
Number of patients with at least one event, n (%)	14 (12.2)	10 (8.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	86.77 [80.29; 93.26]	90.90 [85.50; 96.31]	1.48 [0.66; 3.33] 0.347	0.322

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.208			
≤ 65 letters				
KITE, N'/ N	65 / 65	91 / 91		
Number of patients with at least one event, n (%)	2 (3.1)	9 (9.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.35 [91.36; 100.00]	88.76 [81.74; 95.78]	0.28 [0.06; 1.30] 0.105	0.116
> 65 letters				
KITE, N'/ N	114 / 114	90 / 90		
Number of patients with at least one event, n (%)	13 (11.4)	13 (14.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	87.44 [81.01; 93.87]	79.03 [66.64; 91.41]	0.85 [0.39; 1.83] 0.673	0.669
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.485			
≤ 65 letters				
Pooled Analysis, N'/ N	139 / 139	155 / 155		
Number of patients with at least one event, n (%)	9 (6.5)	14 (9.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	92.54 [87.83; 97.26]	89.63 [84.38; 94.89]	0.77 [0.33; 1.80] 0.550	0.429
> 65 letters				
Pooled Analysis, N'/ N	229 / 229	213 / 213		
Number of patients with at least one event, n (%)	27 (11.8)	23 (10.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	87.12 [82.55; 91.68]	84.84 [77.65; 92.04]	1.11 [0.63; 1.94] 0.722	0.704
Time to first loss in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.296**				

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.995			
≤ 65 letters				
KESTREL, N'/ N	74 / 74	64 / 64		
Number of patients with at least one event, n (%)	1 (1.4)	1 (1.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	98.51 [95.60; 100.00]	98.44 [95.40; 100.00]	1.23 [0.08; 20.15] 0.885	0.928
> 65 letters				
KESTREL, N'/ N	115 / 115	123 / 123		
Number of patients with at least one event, n (%)	3 (2.6)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.27 [94.22; 100.00]	100.00 [100.00; 100.00]	N.E.	0.073
KITE: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.647			
≤ 65 letters				
KITE, N'/ N	65 / 65	91 / 91		
Number of patients with at least one event, n (%)	1 (1.5)	2 (2.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	98.31 [95.01; 100.00]	97.11 [93.06; 100.00]	0.67 [0.06; 7.39] 0.742	0.789
> 65 letters				
KITE, N'/ N	114 / 114	90 / 90		
Number of patients with at least one event, n (%)	6 (5.3)	4 (4.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.54 [90.29; 98.79]	90.48 [78.47; 100.00]	1.26 [0.35; 4.47] 0.721	0.730

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.465			
≤ 65 letters				
Pooled Analysis, N'/ N	139 / 139	155 / 155		
Number of patients with at least one event, n (%)	2 (1.4)	3 (1.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	98.41 [96.22; 100.00]	97.62 [94.87; 100.00]	1.21 [0.16; 8.96] 0.850	0.792
> 65 letters				
Pooled Analysis, N'/ N	229 / 229	213 / 213		
Number of patients with at least one event, n (%)	9 (3.9)	4 (1.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.91 [93.30; 98.53]	95.35 [89.01; 100.00]	2.70 [0.67; 10.86] 0.161	0.243
Time to first loss in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.045 ***				
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.527			
≤ 65 letters				
KESTREL, N'/ N	74 / 74	64 / 64		
Number of patients with at least one event, n (%)	3 (4.1)	2 (3.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.19 [89.87; 100.00]	96.65 [92.07; 100.00]	1.66 [0.27; 10.14] 0.583	0.731
> 65 letters				
KESTREL, N'/ N	115 / 115	123 / 123		
Number of patients with at least one event, n (%)	7 (6.1)	2 (1.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.22 [88.35; 98.08]	98.01 [95.28; 100.00]	3.61 [0.75; 17.38] 0.110	0.074

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.876			
≤ 65 letters				
KITE, N'/ N	65 / 65	91 / 91		
Number of patients with at least one event, n (%)	2 (3.1)	4 (4.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.35 [91.36; 100.00]	95.10 [90.40; 99.80]	0.65 [0.12; 3.56] 0.619	0.693
> 65 letters				
KITE, N'/ N	114 / 114	90 / 90		
Number of patients with at least one event, n (%)	6 (5.3)	9 (10.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.54 [90.29; 98.79]	86.64 [77.46; 95.82]	0.55 [0.20; 1.56] 0.263	0.253
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.949			
≤ 65 letters				
Pooled Analysis, N'/ N	139 / 139	155 / 155		
Number of patients with at least one event, n (%)	5 (3.6)	6 (3.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.74 [92.07; 99.41]	95.74 [92.39; 99.09]	1.31 [0.38; 4.55] 0.673	0.955

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
> 65 letters				
Pooled Analysis, N'/ N	229 / 229	213 / 213		
Number of patients with at least one event, n (%)	13 (5.7)	11 (5.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.87 [90.64; 97.11]	92.74 [87.97; 97.50]	1.25 [0.53; 2.92] 0.609	0.845

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + BCVA + treatment * BCVA.
Pooled analysis: log(hazard ratio) = treatment + age category + study + treatment * study + BCVA + treatment * BCVA.

Table 7.5 BCVA - Loss of 10 respectively 15 letters by region (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first loss in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.453**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.752			
Region of the Americas				
KESTREL, N'/ N	90 / 90	83 / 83		
Number of patients with at least one event, n (%)	6 (6.7)	4 (4.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.13 [87.82; 98.45]	84.10 [61.75; 100.00]	1.35 [0.38; 4.84] 0.642	0.573
European Region				
KESTREL, N'/ N	69 / 69	75 / 75		
Number of patients with at least one event, n (%)	2 (2.9)	4 (5.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.99 [92.87; 100.00]	94.56 [89.37; 99.74]	0.60 [0.11; 3.26] 0.551	0.459
Western Pacific Region				
KESTREL, N'/ N	30 / 30	29 / 29		
Number of patients with at least one event, n (%)	4 (13.3)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	86.21 [73.66; 98.76]	100.00 [100.00; 100.00]	N.E.	0.047 *
KITE: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.460			
South-East Asia Region and Eastern Mediterranean Region				
KITE, N'/ N	26 / 26	21 / 21		
Number of patients with at least one event, n (%)	1 (3.8)	2 (9.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.65 [87.32; 100.00]	90.48 [77.92; 100.00]	0.37 [0.03; 4.03] 0.411	0.436

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
European Region				
KITE, N'/ N	135 / 135	132 / 132		
Number of patients with at least one event, n (%)	5 (3.7)	5 (3.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.16 [92.85; 99.46]	91.41 [81.19; 100.00]	0.93 [0.27; 3.21] 0.903	0.993
Western Pacific Region				
KITE, N'/ N	18 / 18	28 / 28		
Number of patients with at least one event, n (%)	4 (22.2)	3 (10.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	77.04 [57.23; 96.84]	88.71 [76.67; 100.00]	2.06 [0.46; 9.29] 0.345	0.341
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.298			
Region of the Americas				
Pooled Analysis, N'/ N	90 / 90	83 / 83		
Number of patients with at least one event, n (%)	6 (6.7)	4 (4.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.13 [87.82; 98.45]	84.10 [61.75; 100.00]	1.54 [0.34; 6.97] 0.574	0.573
South-East Asia Region and Eastern Mediterranean Region				
Pooled Analysis, N'/ N	26 / 26	21 / 21		
Number of patients with at least one event, n (%)	1 (3.8)	2 (9.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.65 [87.32; 100.00]	90.48 [77.92; 100.00]	0.33 [0.03; 4.20] 0.393	0.436
European Region				
Pooled Analysis, N'/ N	204 / 204	207 / 207		
Number of patients with at least one event, n (%)	7 (3.4)	9 (4.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.44 [93.85; 99.03]	92.19 [84.81; 99.58]	0.72 [0.24; 2.16] 0.563	0.656

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Western Pacific Region				
Pooled Analysis, N'/ N	48 / 48	57 / 57		
Number of patients with at least one event, n (%)	8 (16.7)	3 (5.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	82.73 [71.84; 93.62]	94.41 [88.25; 100.00]	3.26 [0.86; 12.33] 0.082	0.049 *
Time to first loss in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.100**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.581			
Region of the Americas				
KESTREL, N'/ N	90 / 90	83 / 83		
Number of patients with at least one event, n (%)	11 (12.2)	7 (8.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	86.24 [78.61; 93.86]	90.56 [83.85; 97.26]	1.48 [0.57; 3.84] 0.418	0.387
European Region				
KESTREL, N'/ N	69 / 69	75 / 75		
Number of patients with at least one event, n (%)	5 (7.2)	6 (8.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.81 [84.90; 98.72]	91.40 [84.80; 98.01]	0.92 [0.28; 3.03] 0.894	0.837
Western Pacific Region				
KESTREL, N'/ N	30 / 30	29 / 29		
Number of patients with at least one event, n (%)	5 (16.7)	2 (6.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	82.61 [68.75; 96.48]	92.44 [82.37; 100.00]	2.67 [0.51; 13.91] 0.242	0.253

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.626			
South-East Asia Region and Eastern Mediterranean Region				
KITE, N'/ N	26 / 26	21 / 21		
Number of patients with at least one event, n (%)	3 (11.5)	2 (9.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	84.02 [67.22; 100.00]	90.48 [77.92; 100.00]	1.20 [0.20; 7.20] 0.842	0.812
European Region				
KITE, N'/ N	135 / 135	132 / 132		
Number of patients with at least one event, n (%)	8 (5.9)	13 (9.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.51 [89.14; 97.88]	88.80 [83.01; 94.58]	0.55 [0.23; 1.33] 0.184	0.268
Western Pacific Region				
KITE, N'/ N	18 / 18	28 / 28		
Number of patients with at least one event, n (%)	4 (22.2)	7 (25.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	77.04 [57.23; 96.84]	58.32 [28.07; 88.57]	1.00 [0.29; 3.46] 0.997	0.733
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.772			
Region of the Americas				
Pooled Analysis, N'/ N	90 / 90	83 / 83		
Number of patients with at least one event, n (%)	11 (12.2)	7 (8.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	86.24 [78.61; 93.86]	90.56 [83.85; 97.26]	1.13 [0.37; 3.51] 0.827	0.387

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
South-East Asia Region and Eastern Mediterranean Region				
Pooled Analysis, N'/ N	26 / 26	21 / 21		
Number of patients with at least one event, n (%)	3 (11.5)	2 (9.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	84.02 [67.22; 100.00]	90.48 [77.92; 100.00]	1.61 [0.24; 10.77] 0.621	0.812
European Region				
Pooled Analysis, N'/ N	204 / 204	207 / 207		
Number of patients with at least one event, n (%)	13 (6.4)	19 (9.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	92.95 [89.24; 96.66]	89.57 [85.08; 94.06]	0.77 [0.36; 1.67] 0.511	0.309
Western Pacific Region				
Pooled Analysis, N'/ N	48 / 48	57 / 57		
Number of patients with at least one event, n (%)	9 (18.8)	9 (15.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	80.37 [68.85; 91.89]	71.11 [49.10; 93.13]	1.32 [0.51; 3.38] 0.567	0.310
Time to first loss in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.296**				
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=1.000			
Region of the Americas				
KESTREL, N'/ N	90 / 90	83 / 83		
Number of patients with at least one event, n (%)	2 (2.2)	1 (1.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.68 [94.51; 100.00]	98.80 [96.45; 100.00]	1.56 [0.14; 17.31] 0.717	0.603

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
European Region				
KESTREL, N'/ N	69 / 69	75 / 75		
Number of patients with at least one event, n (%)	1 (1.4)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	98.44 [95.40; 100.00]	100.00 [100.00; 100.00]	N.E.	0.296
Western Pacific Region				
KESTREL, N'/ N	30 / 30	29 / 29		
Number of patients with at least one event, n (%)	1 (3.3)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.55 [89.91; 100.00]	100.00 [100.00; 100.00]	N.E.	0.335
KITE: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.284			
South-East Asia Region and Eastern Mediterranean Region				
KITE, N'/ N	26 / 26	21 / 21		
Number of patients with at least one event, n (%)	1 (3.8)	2 (9.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.65 [87.32; 100.00]	90.48 [77.92; 100.00]	0.36 [0.03; 3.96] 0.403	0.436
European Region				
KITE, N'/ N	135 / 135	132 / 132		
Number of patients with at least one event, n (%)	3 (2.2)	3 (2.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.70 [95.12; 100.00]	93.13 [83.41; 100.00]	0.91 [0.18; 4.53] 0.909	0.975
Western Pacific Region				
KITE, N'/ N	18 / 18	28 / 28		
Number of patients with at least one event, n (%)	3 (16.7)	1 (3.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	82.96 [65.37; 100.00]	96.15 [88.76; 100.00]	4.87 [0.50; 47.40] 0.173	0.137

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.607			
Region of the Americas				
Pooled Analysis, N'/ N	90 / 90	83 / 83		
Number of patients with at least one event, n (%)	2 (2.2)	1 (1.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.68 [94.51; 100.00]	98.80 [96.45; 100.00]	0.00 [0.00; N.E.] 0.992	0.603
South-East Asia Region and Eastern Mediterranean Region				
Pooled Analysis, N'/ N	26 / 26	21 / 21		
Number of patients with at least one event, n (%)	1 (3.8)	2 (9.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.65 [87.32; 100.00]	90.48 [77.92; 100.00]	471.79 [0.00; N.E.] 0.992	0.436
European Region				
Pooled Analysis, N'/ N	204 / 204	207 / 207		
Number of patients with at least one event, n (%)	4 (2.0)	3 (1.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.95 [95.96; 99.94]	95.29 [88.50; 100.00]	1446.80 [0.00; N.E.] 0.991	0.672
Western Pacific Region				
Pooled Analysis, N'/ N	48 / 48	57 / 57		
Number of patients with at least one event, n (%)	4 (8.3)	1 (1.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.39 [83.33; 99.46]	98.11 [94.45; 100.00]	4701.77 [0.00; N.E.] 0.989	0.078
Time to first loss in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.045 ***				

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.626			
Region of the Americas				
KESTREL, N'/ N	90 / 90	83 / 83		
Number of patients with at least one event, n (%)	5 (5.6)	1 (1.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.62 [88.17; 99.06]	98.80 [96.45; 100.00]	4.51 [0.52; 38.72] 0.170	0.115
European Region				
KESTREL, N'/ N	69 / 69	75 / 75		
Number of patients with at least one event, n (%)	3 (4.3)	3 (4.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.98 [89.42; 100.00]	95.26 [90.02; 100.00]	1.19 [0.24; 5.94] 0.830	0.921
Western Pacific Region				
KESTREL, N'/ N	30 / 30	29 / 29		
Number of patients with at least one event, n (%)	2 (6.7)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	92.84 [83.26; 100.00]	100.00 [100.00; 100.00]	N.E.	0.169
KITE: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.522			
South-East Asia Region and Eastern Mediterranean Region				
KITE, N'/ N	26 / 26	21 / 21		
Number of patients with at least one event, n (%)	2 (7.7)	2 (9.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	89.67 [75.90; 100.00]	90.48 [77.92; 100.00]	0.78 [0.11; 5.54] 0.802	0.838

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
European Region				
KITE, N'/ N	135 / 135	132 / 132		
Number of patients with at least one event, n (%)	3 (2.2)	7 (5.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.70 [95.13; 100.00]	93.80 [89.31; 98.30]	0.38 [0.10; 1.47] 0.162	0.202
Western Pacific Region				
KITE, N'/ N	18 / 18	28 / 28		
Number of patients with at least one event, n (%)	3 (16.7)	4 (14.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	82.96 [65.37; 100.00]	79.62 [59.80; 99.43]	1.22 [0.27; 5.51] 0.797	0.541
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.723			
Region of the Americas				
Pooled Analysis, N'/ N	90 / 90	83 / 83		
Number of patients with at least one event, n (%)	5 (5.6)	1 (1.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.62 [88.17; 99.06]	98.80 [96.45; 100.00]	3.01 [0.29; 31.08] 0.355	0.115
South-East Asia Region and Eastern Mediterranean Region				
Pooled Analysis, N'/ N	26 / 26	21 / 21		
Number of patients with at least one event, n (%)	2 (7.7)	2 (9.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	89.67 [75.90; 100.00]	90.48 [77.92; 100.00]	1.22 [0.14; 10.71] 0.860	0.838
European Region				
Pooled Analysis, N'/ N	204 / 204	207 / 207		
Number of patients with at least one event, n (%)	6 (2.9)	10 (4.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.80 [94.27; 99.33]	94.24 [90.73; 97.76]	0.76 [0.24; 2.42] 0.640	0.343

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by region (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Western Pacific Region				
Pooled Analysis, N'/ N	48 / 48	57 / 57		
Number of patients with at least one event, n (%)	5 (10.4)	4 (7.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	88.99 [79.86; 98.12]	88.65 [76.52; 100.00]	1.71 [0.44; 6.62] 0.438	0.222

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
*: $p < 0.05$
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + region + treatment * region.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + region + treatment * region.

Table 7.6 BCVA - Loss of 10 respectively 15 letters by diabetes type (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first loss in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.453**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.991			
Type 1				
KESTREL, N'/ N	12 / 12	6 / 6		
Number of patients with at least one event, n (%)	0 (0.0)	1 (16.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	100.00 [100.00; 100.00]	83.33 [53.51; 100.00]	0.00 [0.00; N.E.] 0.992	0.157
Type 2				
KESTREL, N'/ N	177 / 177	181 / 181		
Number of patients with at least one event, n (%)	12 (6.8)	7 (3.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	92.92 [89.05; 96.79]	91.34 [81.29; 100.00]	1.83 [0.72; 4.65] 0.204	0.221
KITE: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.990			
Type 1				
KITE, N'/ N	19 / 19	7 / 7		
Number of patients with at least one event, n (%)	1 (5.3)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.74 [84.70; 100.00]	100.00 [100.00; 100.00]	N.E.	0.544
Type 2				
KITE, N'/ N	160 / 160	174 / 174		
Number of patients with at least one event, n (%)	9 (5.6)	10 (5.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.05 [90.27; 97.82]	90.06 [81.14; 98.98]	0.92 [0.37; 2.28] 0.859	0.996

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.458			
Type 1				
Pooled Analysis, N'/ N	31 / 31	13 / 13		
Number of patients with at least one event, n (%)	1 (3.2)	1 (7.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.77 [90.55; 100.00]	92.31 [77.82; 100.00]	0.44 [0.03; 7.06] 0.560	0.539
Type 2				
Pooled Analysis, N'/ N	337 / 337	355 / 355		
Number of patients with at least one event, n (%)	21 (6.2)	17 (4.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.46 [90.75; 96.17]	90.72 [84.06; 97.39]	1.29 [0.68; 2.45] 0.440	0.389
Time to first loss in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.100**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.988			
Type 1				
KESTREL, N'/ N	12 / 12	6 / 6		
Number of patients with at least one event, n (%)	0 (0.0)	1 (16.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	100.00 [100.00; 100.00]	83.33 [53.51; 100.00]	0.00 [0.00; N.E.] 0.989	0.157
Type 2				
KESTREL, N'/ N	177 / 177	181 / 181		
Number of patients with at least one event, n (%)	21 (11.9)	14 (7.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	86.87 [81.61; 92.14]	91.38 [87.04; 95.71]	1.59 [0.81; 3.14] 0.177	0.185

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.986			
Type 1				
KITE, N'/ N	19 / 19	7 / 7		
Number of patients with at least one event, n (%)	2 (10.5)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	88.82 [74.16; 100.00]	100.00 [100.00; 100.00]	N.E.	0.369
Type 2				
KITE, N'/ N	160 / 160	174 / 174		
Number of patients with at least one event, n (%)	13 (8.1)	22 (12.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	90.84 [86.06; 95.62]	82.10 [73.44; 90.76]	0.60 [0.30; 1.19] 0.144	0.242
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.911			
Type 1				
Pooled Analysis, N'/ N	31 / 31	13 / 13		
Number of patients with at least one event, n (%)	2 (6.5)	1 (7.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.05 [83.73; 100.00]	92.31 [77.82; 100.00]	0.88 [0.08; 9.77] 0.916	0.907
Type 2				
Pooled Analysis, N'/ N	337 / 337	355 / 355		
Number of patients with at least one event, n (%)	34 (10.1)	36 (10.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	88.77 [85.19; 92.35]	86.25 [80.90; 91.60]	1.01 [0.63; 1.63] 0.964	0.912
Time to first loss in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.296**				

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=1.000			
Type 1				
KESTREL, N'/ N	12 / 12	6 / 6		
Number of patients with at least one event, n (%)	0 (0.0)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	100.00 [100.00; 100.00]	100.00 [100.00; 100.00]	1.32 [0.00; N.E.] 1.000	N.E.
Type 2				
KESTREL, N'/ N	177 / 177	181 / 181		
Number of patients with at least one event, n (%)	4 (2.3)	1 (0.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.61 [95.29; 99.93]	99.44 [98.34; 100.00]	4.44 [0.49; 39.93] 0.184	0.169
KITE: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.992			
Type 1				
KITE, N'/ N	19 / 19	7 / 7		
Number of patients with at least one event, n (%)	1 (5.3)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.74 [84.70; 100.00]	100.00 [100.00; 100.00]	N.E.	0.544
Type 2				
KITE, N'/ N	160 / 160	174 / 174		
Number of patients with at least one event, n (%)	6 (3.8)	6 (3.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.04 [92.94; 99.15]	92.50 [83.98; 100.00]	1.00 [0.32; 3.11] 0.994	0.829

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.991			
Type 1				
Pooled Analysis, N'/ N	31 / 31	13 / 13		
Number of patients with at least one event, n (%)	1 (3.2)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.77 [90.55; 100.00]	100.00 [100.00; 100.00]	N.E.	0.544
Type 2				
Pooled Analysis, N'/ N	337 / 337	355 / 355		
Number of patients with at least one event, n (%)	10 (3.0)	7 (2.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.87 [94.95; 98.78]	95.74 [90.97; 100.00]	2.05 [0.59; 7.19] 0.260	0.353
Time to first loss in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.045 ***				
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.991			
Type 1				
KESTREL, N'/ N	12 / 12	6 / 6		
Number of patients with at least one event, n (%)	0 (0.0)	1 (16.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	100.00 [100.00; 100.00]	75.00 [32.57; 100.00]	0.00 [0.00; N.E.] 0.992	0.114
Type 2				
KESTREL, N'/ N	177 / 177	181 / 181		
Number of patients with at least one event, n (%)	10 (5.6)	3 (1.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.58 [89.71; 97.44]	98.14 [96.05; 100.00]	3.62 [1.00; 13.16] 0.051	0.042 *

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.989			
Type 1				
KITE, N'/ N	19 / 19	7 / 7		
Number of patients with at least one event, n (%)	1 (5.3)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.74 [84.70; 100.00]	100.00 [100.00; 100.00]	N.E.	0.544
Type 2				
KITE, N'/ N	160 / 160	174 / 174		
Number of patients with at least one event, n (%)	7 (4.4)	13 (7.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.24 [91.79; 98.70]	90.19 [84.44; 95.94]	0.54 [0.21; 1.35] 0.187	0.293
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.595			
Type 1				
Pooled Analysis, N'/ N	31 / 31	13 / 13		
Number of patients with at least one event, n (%)	1 (3.2)	1 (7.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.77 [90.55; 100.00]	90.91 [73.92; 100.00]	0.61 [0.04; 9.99] 0.726	0.482

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Type 2				
Pooled Analysis, N'/ N	337 / 337	355 / 355		
Number of patients with at least one event, n (%)	17 (5.0)	16 (4.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.37 [91.76; 96.98]	93.95 [90.60; 97.30]	1.32 [0.62; 2.79] 0.472	0.644

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
*: $p < 0.05$
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + diabetes type + treatment * diabetes type.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + diabetes type + treatment * diabetes type.

Table 7.7 BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first loss in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.453**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.024 *			
< 7.5 %				
KESTREL, N'/ N	76 / 76	107 / 107		
Number of patients with at least one event, n (%)	1 (1.3)	6 (5.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	98.65 [96.02; 100.00]	83.32 [61.21; 100.00]	0.22 [0.03; 1.86] 0.165	0.113
≥ 7.5 %				
KESTREL, N'/ N	112 / 112	80 / 80		
Number of patients with at least one event, n (%)	11 (9.8)	2 (2.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	89.62 [83.80; 95.44]	97.03 [92.93; 100.00]	4.51 [1.00; 20.47] 0.051	0.043 *
KITE: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.158			
< 7.5 %				
KITE, N'/ N	82 / 82	96 / 96		
Number of patients with at least one event, n (%)	2 (2.4)	6 (6.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.42 [93.88; 100.00]	93.03 [87.53; 98.53]	0.38 [0.08; 1.90] 0.239	0.233
≥ 7.5 %				
KITE, N'/ N	97 / 97	85 / 85		
Number of patients with at least one event, n (%)	8 (8.2)	4 (4.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.35 [85.61; 97.09]	86.67 [68.39; 100.00]	1.62 [0.48; 5.42] 0.437	0.329

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.009 *			
< 7.5 %				
Pooled Analysis, N'/ N	158 / 158	203 / 203		
Number of patients with at least one event, n (%)	3 (1.9)	12 (5.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	98.02 [95.80; 100.00]	89.65 [80.48; 98.82]	0.32 [0.09; 1.12] 0.075	0.051
≥ 7.5 %				
Pooled Analysis, N'/ N	209 / 209	165 / 165		
Number of patients with at least one event, n (%)	19 (9.1)	6 (3.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	90.46 [86.36; 94.55]	92.05 [82.82; 100.00]	2.55 [1.01; 6.43] 0.047 *	0.033 *
Time to first loss in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.100**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.077			
< 7.5 %				
KESTREL, N'/ N	76 / 76	107 / 107		
Number of patients with at least one event, n (%)	6 (7.9)	11 (10.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	90.94 [83.99; 97.89]	88.89 [82.68; 95.10]	0.75 [0.28; 2.04] 0.577	0.571
≥ 7.5 %				
KESTREL, N'/ N	112 / 112	80 / 80		
Number of patients with at least one event, n (%)	15 (13.4)	4 (5.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	85.31 [78.41; 92.22]	94.11 [88.48; 99.74]	2.89 [0.96; 8.75] 0.060	0.056

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.092			
< 7.5 %				
KITE, N'/ N	82 / 82	96 / 96		
Number of patients with at least one event, n (%)	4 (4.9)	14 (14.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.28 [88.79; 99.76]	80.86 [70.24; 91.48]	0.32 [0.11; 0.98] 0.046 *	0.043 *
≥ 7.5 %				
KITE, N'/ N	97 / 97	85 / 85		
Number of patients with at least one event, n (%)	11 (11.3)	8 (9.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	87.63 [80.74; 94.53]	84.46 [70.82; 98.10]	1.11 [0.44; 2.79] 0.818	0.621
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.018 *			
< 7.5 %				
Pooled Analysis, N'/ N	158 / 158	203 / 203		
Number of patients with at least one event, n (%)	10 (6.3)	25 (12.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	92.64 [88.22; 97.05]	84.95 [78.79; 91.10]	0.52 [0.25; 1.09] 0.084	0.065
≥ 7.5 %				
Pooled Analysis, N'/ N	209 / 209	165 / 165		
Number of patients with at least one event, n (%)	26 (12.4)	12 (7.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	86.42 [81.54; 91.31]	87.81 [78.08; 97.55]	1.77 [0.88; 3.54] 0.108	0.090
Time to first loss in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.296**				

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.996			
< 7.5 %				
KESTREL, N'/ N	76 / 76	107 / 107		
Number of patients with at least one event, n (%)	1 (1.3)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	98.65 [96.02; 100.00]	100.00 [100.00; 100.00]	N.E.	0.240
≥ 7.5 %				
KESTREL, N'/ N	112 / 112	80 / 80		
Number of patients with at least one event, n (%)	3 (2.7)	1 (1.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.13 [93.92; 100.00]	98.73 [96.27; 100.00]	2.72 [0.27; 26.86] 0.393	0.492
KITE: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.668			
< 7.5 %				
KITE, N'/ N	82 / 82	96 / 96		
Number of patients with at least one event, n (%)	2 (2.4)	3 (3.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.42 [93.88; 100.00]	96.24 [91.94; 100.00]	0.77 [0.13; 4.64] 0.779	0.803
≥ 7.5 %				
KITE, N'/ N	97 / 97	85 / 85		
Number of patients with at least one event, n (%)	5 (5.2)	3 (3.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.63 [90.04; 99.22]	88.62 [71.76; 100.00]	1.28 [0.30; 5.42] 0.737	0.561

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.815			
< 7.5 %				
Pooled Analysis, N'/ N	158 / 158	203 / 203		
Number of patients with at least one event, n (%)	3 (1.9)	3 (1.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	98.02 [95.80; 100.00]	98.17 [96.04; 100.00]	1.74 [0.29; 10.37] 0.545	0.805
≥ 7.5 %				
Pooled Analysis, N'/ N	209 / 209	165 / 165		
Number of patients with at least one event, n (%)	8 (3.8)	4 (2.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.96 [93.21; 98.71]	93.63 [84.85; 100.00]	2.21 [0.52; 9.40] 0.284	0.384
Time to first loss in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.045 ***				
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.876			
< 7.5 %				
KESTREL, N'/ N	76 / 76	107 / 107		
Number of patients with at least one event, n (%)	4 (5.3)	2 (1.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.24 [88.76; 99.73]	97.88 [94.98; 100.00]	2.86 [0.52; 15.65] 0.226	0.198
≥ 7.5 %				
KESTREL, N'/ N	112 / 112	80 / 80		
Number of patients with at least one event, n (%)	6 (5.4)	2 (2.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.81 [89.00; 98.63]	97.12 [93.14; 100.00]	2.37 [0.47; 11.87] 0.294	0.342

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.385			
< 7.5 %				
KITE, N'/ N	82 / 82	96 / 96		
Number of patients with at least one event, n (%)	2 (2.4)	7 (7.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.42 [93.88; 100.00]	88.69 [79.02; 98.35]	0.33 [0.07; 1.58] 0.164	0.168
≥ 7.5 %				
KITE, N'/ N	97 / 97	85 / 85		
Number of patients with at least one event, n (%)	6 (6.2)	6 (7.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.38 [88.23; 98.53]	92.13 [86.07; 98.19]	0.78 [0.25; 2.43] 0.662	0.860
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.661			
< 7.5 %				
Pooled Analysis, N'/ N	158 / 158	203 / 203		
Number of patients with at least one event, n (%)	6 (3.8)	9 (4.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.86 [92.61; 99.11]	93.33 [88.20; 98.45]	1.03 [0.35; 3.02] 0.952	0.791

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
≥ 7.5 %				
Pooled Analysis, N'/ N	209 / 209	165 / 165		
Number of patients with at least one event, n (%)	12 (5.7)	8 (4.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.62 [90.10; 97.13]	94.44 [90.69; 98.20]	1.40 [0.54; 3.66] 0.487	0.646

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
*: $p < 0.05$
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + HbA1c + treatment * HbA1c.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + HbA1c + treatment * HbA1c.

Table 7.8 BCVA - Loss of 10 respectively 15 letters by duration of DME (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first loss in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.453**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.756			
≤ 3 months				
KESTREL, N'/ N	120 / 120	110 / 110		
Number of patients with at least one event, n (%)	5 (4.2)	4 (3.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.71 [92.03; 99.39]	89.46 [75.06; 100.00]	1.19 [0.32; 4.45] 0.792	0.857
> 3 - < 12 months				
KESTREL, N'/ N	30 / 30	39 / 39		
Number of patients with at least one event, n (%)	4 (13.3)	3 (7.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	86.31 [73.84; 98.78]	92.24 [83.80; 100.00]	1.67 [0.37; 7.51] 0.503	0.473
≥ 12 months				
KESTREL, N'/ N	39 / 39	38 / 38		
Number of patients with at least one event, n (%)	3 (7.7)	1 (2.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.53 [82.33; 100.00]	97.30 [92.07; 100.00]	3.22 [0.34; 31.02] 0.311	0.312
KITE: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.376			
≤ 3 months				
KITE, N'/ N	85 / 85	92 / 92		
Number of patients with at least one event, n (%)	4 (4.7)	7 (7.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.00 [90.22; 99.78]	85.69 [71.27; 100.00]	0.53 [0.15; 1.85] 0.323	0.426

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
> 3 - < 12 months				
KITE, N'/ N	51 / 51	49 / 49		
Number of patients with at least one event, n (%)	3 (5.9)	2 (4.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.88 [87.16; 100.00]	95.83 [90.18; 100.00]	1.43 [0.24; 8.61] 0.697	0.707
≥ 12 months				
KITE, N'/ N	43 / 43	40 / 40		
Number of patients with at least one event, n (%)	3 (7.0)	1 (2.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	92.86 [85.07; 100.00]	97.30 [92.07; 100.00]	2.95 [0.30; 28.54] 0.351	0.345
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.249			
≤ 3 months				
Pooled Analysis, N'/ N	205 / 205	202 / 202		
Number of patients with at least one event, n (%)	9 (4.4)	11 (5.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.43 [92.51; 98.35]	87.66 [77.47; 97.84]	0.74 [0.31; 1.81] 0.514	0.638
> 3 - < 12 months				
Pooled Analysis, N'/ N	81 / 81	88 / 88		
Number of patients with at least one event, n (%)	7 (8.6)	5 (5.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.10 [84.81; 97.40]	94.23 [89.31; 99.14]	1.61 [0.51; 5.13] 0.418	0.429
≥ 12 months				
Pooled Analysis, N'/ N	82 / 82	78 / 78		
Number of patients with at least one event, n (%)	6 (7.3)	2 (2.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	92.34 [86.45; 98.24]	97.28 [93.56; 100.00]	3.18 [0.64; 15.81] 0.158	0.167

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first loss in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.100**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.766			
≤ 3 months				
KESTREL, N'/ N	120 / 120	110 / 110		
Number of patients with at least one event, n (%)	12 (10.0)	7 (6.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	89.01 [83.12; 94.90]	92.82 [87.67; 97.97]	1.58 [0.62; 4.02] 0.337	0.363
> 3 - < 12 months				
KESTREL, N'/ N	30 / 30	39 / 39		
Number of patients with at least one event, n (%)	4 (13.3)	5 (12.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	86.31 [73.84; 98.78]	85.38 [73.35; 97.42]	0.99 [0.26; 3.70] 0.988	0.982
≥ 12 months				
KESTREL, N'/ N	39 / 39	38 / 38		
Number of patients with at least one event, n (%)	5 (12.8)	3 (7.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	84.49 [71.84; 97.14]	91.81 [82.93; 100.00]	1.98 [0.47; 8.30] 0.351	0.360
KITE: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.961			
≤ 3 months				
KITE, N'/ N	85 / 85	92 / 92		
Number of patients with at least one event, n (%)	8 (9.4)	12 (13.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	88.59 [81.06; 96.13]	83.05 [72.82; 93.28]	0.64 [0.26; 1.57] 0.328	0.536

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
> 3 - < 12 months				
KITE, N'/ N	51 / 51	49 / 49		
Number of patients with at least one event, n (%)	4 (7.8)	6 (12.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.79 [84.08; 99.50]	86.63 [76.64; 96.62]	0.58 [0.16; 2.07] 0.404	0.464
≥ 12 months				
KITE, N'/ N	43 / 43	40 / 40		
Number of patients with at least one event, n (%)	3 (7.0)	4 (10.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	92.86 [85.07; 100.00]	75.55 [47.20; 100.00]	0.77 [0.17; 3.45] 0.732	0.721
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.786			
≤ 3 months				
Pooled Analysis, N'/ N	205 / 205	202 / 202		
Number of patients with at least one event, n (%)	20 (9.8)	19 (9.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	88.88 [84.25; 93.51]	88.13 [82.37; 93.89]	0.98 [0.52; 1.86] 0.963	0.848
> 3 - < 12 months				
Pooled Analysis, N'/ N	81 / 81	88 / 88		
Number of patients with at least one event, n (%)	8 (9.9)	11 (12.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	89.74 [83.00; 96.48]	85.96 [78.21; 93.72]	0.80 [0.32; 2.01] 0.637	0.605
≥ 12 months				
Pooled Analysis, N'/ N	82 / 82	78 / 78		
Number of patients with at least one event, n (%)	8 (9.8)	7 (9.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	89.20 [82.07; 96.33]	83.66 [68.10; 99.21]	1.30 [0.47; 3.60] 0.613	0.673

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first loss in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.296**				
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=1.000			
≤ 3 months				
KESTREL, N'/ N	120 / 120	110 / 110		
Number of patients with at least one event, n (%)	2 (1.7)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	98.27 [95.90; 100.00]	100.00 [100.00; 100.00]	N.E.	0.175
> 3 - < 12 months				
KESTREL, N'/ N	30 / 30	39 / 39		
Number of patients with at least one event, n (%)	1 (3.3)	1 (2.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.43 [89.55; 100.00]	97.44 [92.48; 100.00]	1.14 [0.07; 18.24] 0.927	0.863
≥ 12 months				
KESTREL, N'/ N	39 / 39	38 / 38		
Number of patients with at least one event, n (%)	1 (2.6)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.06 [91.38; 100.00]	100.00 [100.00; 100.00]	N.E.	0.303
KITE: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.711			
≤ 3 months				
KITE, N'/ N	85 / 85	92 / 92		
Number of patients with at least one event, n (%)	4 (4.7)	3 (3.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.00 [90.22; 99.78]	90.32 [76.72; 100.00]	1.22 [0.27; 5.56] 0.796	0.612

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
> 3 - < 12 months				
KITE, N'/ N	51 / 51	49 / 49		
Number of patients with at least one event, n (%)	1 (2.0)	2 (4.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.96 [94.00; 100.00]	95.83 [90.18; 100.00]	0.48 [0.04; 5.34] 0.549	0.527
≥ 12 months				
KITE, N'/ N	43 / 43	40 / 40		
Number of patients with at least one event, n (%)	2 (4.7)	1 (2.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.24 [88.80; 100.00]	97.30 [92.07; 100.00]	1.91 [0.17; 21.37] 0.598	0.604
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.583			
≤ 3 months				
Pooled Analysis, N'/ N	205 / 205	202 / 202		
Number of patients with at least one event, n (%)	6 (2.9)	3 (1.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.93 [94.52; 99.35]	95.17 [88.15; 100.00]	2.49 [0.52; 11.99] 0.257	0.277
> 3 - < 12 months				
Pooled Analysis, N'/ N	81 / 81	88 / 88		
Number of patients with at least one event, n (%)	2 (2.5)	3 (3.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.40 [93.85; 100.00]	96.54 [92.69; 100.00]	1.02 [0.14; 7.50] 0.988	0.702
≥ 12 months				
Pooled Analysis, N'/ N	82 / 82	78 / 78		
Number of patients with at least one event, n (%)	3 (3.7)	1 (1.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.16 [91.89; 100.00]	98.63 [95.96; 100.00]	4.35 [0.39; 48.16] 0.231	0.335

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first loss in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.045 ***				
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.342			
≤ 3 months				
KESTREL, N'/ N	120 / 120	110 / 110		
Number of patients with at least one event, n (%)	6 (5.0)	1 (0.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.52 [90.24; 98.79]	98.89 [96.72; 100.00]	5.81 [0.70; 48.35] 0.104	0.078
> 3 - < 12 months				
KESTREL, N'/ N	30 / 30	39 / 39		
Number of patients with at least one event, n (%)	1 (3.3)	2 (5.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.43 [89.55; 100.00]	94.19 [86.30; 100.00]	0.58 [0.05; 6.42] 0.657	0.715
≥ 12 months				
KESTREL, N'/ N	39 / 39	38 / 38		
Number of patients with at least one event, n (%)	3 (7.7)	1 (2.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	90.13 [79.47; 100.00]	97.22 [91.85; 100.00]	3.77 [0.39; 36.27] 0.251	0.223
KITE: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.309			
≤ 3 months				
KITE, N'/ N	85 / 85	92 / 92		
Number of patients with at least one event, n (%)	5 (5.9)	7 (7.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.43 [87.81; 99.04]	88.17 [78.33; 98.01]	0.67 [0.21; 2.16] 0.507	0.772

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
> 3 - < 12 months				
KITE, N'/ N	51 / 51	49 / 49		
Number of patients with at least one event, n (%)	1 (2.0)	5 (10.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.96 [94.00; 100.00]	88.68 [79.28; 98.07]	0.17 [0.02; 1.46] 0.106	0.081
≥ 12 months				
KITE, N'/ N	43 / 43	40 / 40		
Number of patients with at least one event, n (%)	2 (4.7)	1 (2.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.24 [88.80; 100.00]	97.30 [92.07; 100.00]	2.02 [0.18; 22.35] 0.567	0.609
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.150			
≤ 3 months				
Pooled Analysis, N'/ N	205 / 205	202 / 202		
Number of patients with at least one event, n (%)	11 (5.4)	8 (4.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.04 [90.61; 97.47]	93.70 [88.65; 98.76]	1.48 [0.57; 3.83] 0.424	0.400
> 3 - < 12 months				
Pooled Analysis, N'/ N	81 / 81	88 / 88		
Number of patients with at least one event, n (%)	2 (2.5)	7 (8.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.40 [93.85; 100.00]	91.04 [84.66; 97.42]	0.37 [0.07; 1.85] 0.225	0.101

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
≥ 12 months				
Pooled Analysis, N'/ N	82 / 82	78 / 78		
Number of patients with at least one event, n (%)	5 (6.1)	2 (2.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.05 [87.12; 98.97]	97.26 [93.51; 100.00]	3.31 [0.62; 17.57] 0.159	0.209

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + duration of DME + treatment * duration of DME.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + duration of DME + treatment * duration of DME.

Table 7.9 BCVA - Loss of 10 respectively 15 letters by DME type (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first loss in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.453**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.184			
focal				
KESTREL, N'/ N	59 / 59	48 / 48		
Number of patients with at least one event, n (%)	3 (5.1)	4 (8.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.79 [89.05; 100.00]	77.90 [49.40; 100.00]	0.55 [0.12; 2.46] 0.431	0.456
diffuse				
KESTREL, N'/ N	127 / 127	134 / 134		
Number of patients with at least one event, n (%)	7 (5.5)	4 (3.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.22 [90.05; 98.38]	96.72 [93.51; 99.92]	2.04 [0.60; 6.99] 0.255	0.294
KITE: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.893			
focal				
KITE, N'/ N	63 / 63	66 / 66		
Number of patients with at least one event, n (%)	3 (4.8)	3 (4.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.11 [89.70; 100.00]	84.76 [62.25; 100.00]	1.08 [0.22; 5.37] 0.924	0.852
diffuse				
KITE, N'/ N	115 / 115	109 / 109		
Number of patients with at least one event, n (%)	7 (6.1)	6 (5.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.59 [89.00; 98.19]	93.83 [88.95; 98.71]	0.95 [0.31; 2.85] 0.922	0.870

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.466			
focal				
Pooled Analysis, N'/ N	122 / 122	114 / 114		
Number of patients with at least one event, n (%)	6 (4.9)	7 (6.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.91 [90.94; 98.88]	81.83 [64.02; 99.64]	0.82 [0.27; 2.45] 0.716	0.676
diffuse				
Pooled Analysis, N'/ N	242 / 242	243 / 243		
Number of patients with at least one event, n (%)	14 (5.8)	10 (4.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.91 [90.82; 97.01]	95.38 [92.52; 98.23]	1.36 [0.60; 3.06] 0.462	0.406
Time to first loss in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.100**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.034 *			
focal				
KESTREL, N'/ N	59 / 59	48 / 48		
Number of patients with at least one event, n (%)	4 (6.8)	7 (14.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	92.90 [86.17; 99.62]	83.85 [72.81; 94.88]	0.42 [0.12; 1.44] 0.167	0.169
diffuse				
KESTREL, N'/ N	127 / 127	134 / 134		
Number of patients with at least one event, n (%)	15 (11.8)	8 (6.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	86.55 [80.18; 92.93]	93.40 [88.95; 97.84]	2.14 [0.90; 5.06] 0.084	0.089

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.737			
focal				
KITE, N'/ N	63 / 63	66 / 66		
Number of patients with at least one event, n (%)	5 (7.9)	10 (15.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.10 [83.60; 98.60]	69.59 [46.78; 92.40]	0.54 [0.18; 1.57] 0.255	0.240
diffuse				
KITE, N'/ N	115 / 115	109 / 109		
Number of patients with at least one event, n (%)	9 (7.8)	11 (10.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.39 [85.98; 96.80]	88.79 [82.49; 95.08]	0.68 [0.28; 1.66] 0.397	0.605
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.074			
focal				
Pooled Analysis, N'/ N	122 / 122	114 / 114		
Number of patients with at least one event, n (%)	9 (7.4)	17 (14.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	92.03 [87.02; 97.05]	75.84 [61.51; 90.18]	0.50 [0.22; 1.14] 0.100	0.074
diffuse				
Pooled Analysis, N'/ N	242 / 242	243 / 243		
Number of patients with at least one event, n (%)	24 (9.9)	19 (7.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	88.86 [84.63; 93.09]	91.17 [87.34; 95.00]	1.27 [0.69; 2.32] 0.439	0.373
Time to first loss in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.296**				

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=1.000			
focal				
KESTREL, N'/ N	59 / 59	48 / 48		
Number of patients with at least one event, n (%)	0 (0.0)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	100.00 [100.00; 100.00]	100.00 [100.00; 100.00]	0.93 [0.00; N.E.] 1.000	N.E.
diffuse				
KESTREL, N'/ N	127 / 127	134 / 134		
Number of patients with at least one event, n (%)	2 (1.6)	1 (0.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	98.35 [96.08; 100.00]	99.25 [97.78; 100.00]	2.34 [0.21; 25.99] 0.489	0.525
KITE: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.878			
focal				
KITE, N'/ N	63 / 63	66 / 66		
Number of patients with at least one event, n (%)	2 (3.2)	2 (3.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.72 [92.25; 100.00]	86.09 [63.37; 100.00]	1.07 [0.15; 7.61] 0.947	0.841
diffuse				
KITE, N'/ N	115 / 115	109 / 109		
Number of patients with at least one event, n (%)	5 (4.3)	3 (2.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.45 [91.55; 99.35]	96.67 [92.87; 100.00]	1.29 [0.31; 5.47] 0.728	0.518

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.770			
focal				
Pooled Analysis, N'/ N	122 / 122	114 / 114		
Number of patients with at least one event, n (%)	2 (1.6)	2 (1.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	98.33 [96.04; 100.00]	92.45 [79.83; 100.00]	1.23 [0.14; 11.04] 0.850	0.841
diffuse				
Pooled Analysis, N'/ N	242 / 242	243 / 243		
Number of patients with at least one event, n (%)	7 (2.9)	4 (1.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.96 [94.74; 99.18]	98.04 [96.09; 100.00]	1.75 [0.40; 7.65] 0.459	0.377
Time to first loss in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.045 ***				
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.098			
focal				
KESTREL, N'/ N	59 / 59	48 / 48		
Number of patients with at least one event, n (%)	1 (1.7)	2 (4.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	98.08 [94.34; 100.00]	95.06 [88.38; 100.00]	0.36 [0.03; 4.05] 0.412	0.429
diffuse				
KESTREL, N'/ N	127 / 127	134 / 134		
Number of patients with at least one event, n (%)	7 (5.5)	2 (1.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.60 [88.99; 98.21]	98.39 [96.16; 100.00]	4.17 [0.86; 20.16] 0.076	0.071

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.246			
focal				
KITE, N'/ N	63 / 63	66 / 66		
Number of patients with at least one event, n (%)	2 (3.2)	7 (10.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.72 [92.25; 100.00]	82.48 [67.48; 97.47]	0.30 [0.06; 1.47] 0.138	0.127
diffuse				
KITE, N'/ N	115 / 115	109 / 109		
Number of patients with at least one event, n (%)	6 (5.2)	5 (4.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.34 [89.92; 98.76]	95.00 [90.72; 99.28]	0.98 [0.30; 3.25] 0.974	0.805
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.044 *			
focal				
Pooled Analysis, N'/ N	122 / 122	114 / 114		
Number of patients with at least one event, n (%)	3 (2.5)	9 (7.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.39 [94.46; 100.00]	87.58 [78.19; 96.97]	0.39 [0.10; 1.50] 0.168	0.086

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
diffuse				
Pooled Analysis, N'/ N	242 / 242	243 / 243		
Number of patients with at least one event, n (%)	13 (5.4)	7 (2.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.95 [90.75; 97.16]	96.85 [94.54; 99.15]	2.01 [0.78; 5.19] 0.147	0.163

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
*: $p < 0.05$
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + DME type + treatment * DME type.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + DME type + treatment * DME type.

Table 7.10 BCVA - Loss of 10 respectively 15 letters by CSFT (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first loss in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.453**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.989			
< 450 µm				
KESTREL, N'/ N	107 / 107	96 / 96		
Number of patients with at least one event, n (%)	8 (7.5)	5 (5.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	92.03 [86.72; 97.34]	94.63 [90.06; 99.21]	1.54 [0.50; 4.72] 0.450	0.543
≥ 450 - < 650 µm				
KESTREL, N'/ N	70 / 70	71 / 71		
Number of patients with at least one event, n (%)	4 (5.7)	3 (4.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.18 [88.65; 99.72]	72.52 [31.35; 100.00]	1.34 [0.30; 6.00] 0.706	0.804
≥ 650 µm				
KESTREL, N'/ N	12 / 12	20 / 20		
Number of patients with at least one event, n (%)	0 (0.0)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	100.00 [100.00; 100.00]	100.00 [100.00; 100.00]	1.20 [0.00; N.E.] 1.000	N.E.
KITE: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.214			
< 450 µm				
KITE, N'/ N	85 / 85	82 / 82		
Number of patients with at least one event, n (%)	8 (9.4)	5 (6.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	90.09 [83.56; 96.62]	86.26 [69.54; 100.00]	1.62 [0.53; 5.00] 0.399	0.382

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
≥ 450 - < 650 µm				
KITE, N'/ N	74 / 74	79 / 79		
Number of patients with at least one event, n (%)	1 (1.4)	5 (6.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	98.59 [95.85; 100.00]	92.94 [86.84; 99.05]	0.18 [0.02; 1.59] 0.123	0.115
≥ 650 µm				
KITE, N'/ N	20 / 20	19 / 19		
Number of patients with at least one event, n (%)	1 (5.0)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.44 [83.86; 100.00]	100.00 [100.00; 100.00]	N.E.	0.331
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.386			
< 450 µm				
Pooled Analysis, N'/ N	192 / 192	178 / 178		
Number of patients with at least one event, n (%)	16 (8.3)	10 (5.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.17 [87.03; 95.31]	90.63 [82.11; 99.15]	1.58 [0.71; 3.51] 0.258	0.294
≥ 450 - < 650 µm				
Pooled Analysis, N'/ N	144 / 144	150 / 150		
Number of patients with at least one event, n (%)	5 (3.5)	8 (5.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.44 [93.38; 99.51]	86.75 [71.52; 100.00]	0.60 [0.19; 1.85] 0.373	0.367
≥ 650 µm				
Pooled Analysis, N'/ N	32 / 32	39 / 39		
Number of patients with at least one event, n (%)	1 (3.1)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.55 [89.91; 100.00]	100.00 [100.00; 100.00]	N.E.	0.331
Time to first loss in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.100**				

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.720			
< 450 µm				
KESTREL, N'/ N	107 / 107	96 / 96		
Number of patients with at least one event, n (%)	13 (12.1)	7 (7.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	86.57 [79.75; 93.40]	92.14 [86.53; 97.75]	1.75 [0.70; 4.40] 0.233	0.260
≥ 450 - < 650 µm				
KESTREL, N'/ N	70 / 70	71 / 71		
Number of patients with at least one event, n (%)	7 (10.0)	7 (9.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	89.16 [81.53; 96.78]	88.66 [80.73; 96.60]	1.01 [0.35; 2.89] 0.983	0.994
≥ 650 µm				
KESTREL, N'/ N	12 / 12	20 / 20		
Number of patients with at least one event, n (%)	1 (8.3)	1 (5.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	87.50 [64.58; 100.00]	93.75 [81.89; 100.00]	1.99 [0.12; 32.15] 0.628	0.582
KITE: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.652			
< 450 µm				
KITE, N'/ N	85 / 85	82 / 82		
Number of patients with at least one event, n (%)	9 (10.6)	11 (13.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	88.66 [81.66; 95.66]	76.27 [60.25; 92.29]	0.81 [0.33; 1.96] 0.637	0.611

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
≥ 450 - < 650 µm				
KITE, N'/ N	74 / 74	79 / 79		
Number of patients with at least one event, n (%)	5 (6.8)	11 (13.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.95 [85.16; 98.74]	85.43 [77.45; 93.41]	0.42 [0.14; 1.22] 0.112	0.177
≥ 650 µm				
KITE, N'/ N	20 / 20	19 / 19		
Number of patients with at least one event, n (%)	1 (5.0)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.44 [83.86; 100.00]	100.00 [100.00; 100.00]	N.E.	0.331
Pooled Analysis: Time to first loss in BCVA ≥10 letters, Week 100				
Interaction test	p=0.357			
< 450 µm				
Pooled Analysis, N'/ N	192 / 192	178 / 178		
Number of patients with at least one event, n (%)	22 (11.5)	18 (10.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	87.43 [82.49; 92.37]	84.25 [75.44; 93.06]	1.18 [0.63; 2.22] 0.603	0.662
≥ 450 - < 650 µm				
Pooled Analysis, N'/ N	144 / 144	150 / 150		
Number of patients with at least one event, n (%)	12 (8.3)	18 (12.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	90.64 [85.57; 95.71]	86.88 [81.21; 92.55]	0.68 [0.32; 1.42] 0.306	0.321
≥ 650 µm				
Pooled Analysis, N'/ N	32 / 32	39 / 39		
Number of patients with at least one event, n (%)	2 (6.3)	1 (2.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	92.35 [82.10; 100.00]	96.88 [90.85; 100.00]	2.86 [0.26; 31.60] 0.392	0.305

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first loss in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.296**				
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=1.000			
< 450 µm				
KESTREL, N'/ N	107 / 107	96 / 96		
Number of patients with at least one event, n (%)	2 (1.9)	1 (1.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.97 [95.18; 100.00]	98.92 [96.83; 100.00]	1.98 [0.18; 21.95] 0.577	0.630
≥ 450 - < 650 µm				
KESTREL, N'/ N	70 / 70	71 / 71		
Number of patients with at least one event, n (%)	2 (2.9)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.03 [92.98; 100.00]	100.00 [100.00; 100.00]	N.E.	0.151
≥ 650 µm				
KESTREL, N'/ N	12 / 12	20 / 20		
Number of patients with at least one event, n (%)	0 (0.0)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	100.00 [100.00; 100.00]	100.00 [100.00; 100.00]	0.99 [0.00; N.E.] 1.000	N.E.
KITE: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.755			
< 450 µm				
KITE, N'/ N	85 / 85	82 / 82		
Number of patients with at least one event, n (%)	5 (5.9)	4 (4.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.87 [88.67; 99.08]	87.39 [70.59; 100.00]	1.27 [0.34; 4.76] 0.728	0.692

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
≥ 450 - < 650 µm				
KITE, N'/ N	74 / 74	79 / 79		
Number of patients with at least one event, n (%)	1 (1.4)	2 (2.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	98.59 [95.85; 100.00]	96.76 [92.23; 100.00]	0.44 [0.04; 4.92] 0.506	0.602
≥ 650 µm				
KITE, N'/ N	20 / 20	19 / 19		
Number of patients with at least one event, n (%)	1 (5.0)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.44 [83.86; 100.00]	100.00 [100.00; 100.00]	N.E.	0.331
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.999			
< 450 µm				
Pooled Analysis, N'/ N	192 / 192	178 / 178		
Number of patients with at least one event, n (%)	7 (3.6)	5 (2.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.18 [93.39; 98.96]	93.57 [85.46; 100.00]	1.95 [0.49; 7.80] 0.345	0.559
≥ 450 - < 650 µm				
Pooled Analysis, N'/ N	144 / 144	150 / 150		
Number of patients with at least one event, n (%)	3 (2.1)	2 (1.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.82 [95.39; 100.00]	98.24 [95.77; 100.00]	2.03 [0.28; 14.83] 0.486	0.614
≥ 650 µm				
Pooled Analysis, N'/ N	32 / 32	39 / 39		
Number of patients with at least one event, n (%)	1 (3.1)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.55 [89.91; 100.00]	100.00 [100.00; 100.00]	N.E.	0.331
Time to first loss in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.045 ***				

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.774			
< 450 µm				
KESTREL, N'/ N	107 / 107	96 / 96		
Number of patients with at least one event, n (%)	5 (4.7)	3 (3.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.72 [90.21; 99.23]	96.47 [92.53; 100.00]	1.63 [0.39; 6.82] 0.506	0.552
≥ 450 - < 650 µm				
KESTREL, N'/ N	70 / 70	71 / 71		
Number of patients with at least one event, n (%)	4 (5.7)	1 (1.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.59 [87.48; 99.70]	98.31 [95.01; 100.00]	4.23 [0.47; 37.91] 0.197	0.171
≥ 650 µm				
KESTREL, N'/ N	12 / 12	20 / 20		
Number of patients with at least one event, n (%)	1 (8.3)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	87.50 [64.58; 100.00]	100.00 [100.00; 100.00]	N.E.	0.157
KITE: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.892			
< 450 µm				
KITE, N'/ N	85 / 85	82 / 82		
Number of patients with at least one event, n (%)	5 (5.9)	8 (9.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.87 [88.67; 99.08]	85.19 [73.89; 96.50]	0.61 [0.20; 1.87] 0.385	0.370

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
≥ 450 - < 650 µm				
KITE, N'/ N	74 / 74	79 / 79		
Number of patients with at least one event, n (%)	2 (2.7)	5 (6.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.94 [92.74; 100.00]	93.33 [87.67; 98.99]	0.37 [0.07; 1.95] 0.243	0.315
≥ 650 µm				
KITE, N'/ N	20 / 20	19 / 19		
Number of patients with at least one event, n (%)	1 (5.0)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.44 [83.86; 100.00]	100.00 [100.00; 100.00]	N.E.	0.331
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.959			
< 450 µm				
Pooled Analysis, N'/ N	192 / 192	178 / 178		
Number of patients with at least one event, n (%)	10 (5.2)	11 (6.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.34 [90.91; 97.76]	90.99 [84.93; 97.06]	1.01 [0.41; 2.52] 0.977	0.735
≥ 450 - < 650 µm				
Pooled Analysis, N'/ N	144 / 144	150 / 150		
Number of patients with at least one event, n (%)	6 (4.2)	6 (4.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.33 [91.66; 99.00]	95.57 [92.10; 99.04]	1.25 [0.38; 4.10] 0.712	0.906

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
≥ 650 µm				
Pooled Analysis, N'/ N	32 / 32	39 / 39		
Number of patients with at least one event, n (%)	2 (6.3)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	92.35 [82.10; 100.00]	100.00 [100.00; 100.00]	N.E.	0.093

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + CSFT + treatment * CSFT.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + CSFT + treatment * CSFT.

Table 7.11 BCVA - Loss of 10 respectively 15 letters by status of SRF (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first loss in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.453**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.341			
presence				
KESTREL, N'/ N	62 / 62	61 / 61		
Number of patients with at least one event, n (%)	4 (6.5)	1 (1.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.44 [87.22; 99.66]	98.33 [95.09; 100.00]	3.90 [0.44; 34.97] 0.224	0.182
absence				
KESTREL, N'/ N	127 / 127	126 / 126		
Number of patients with at least one event, n (%)	8 (6.3)	7 (5.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.35 [88.89; 97.81]	87.52 [73.28; 100.00]	1.20 [0.44; 3.33] 0.720	0.822
KITE: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.489			
presence				
KITE, N'/ N	56 / 56	67 / 67		
Number of patients with at least one event, n (%)	3 (5.4)	5 (7.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.25 [87.94; 100.00]	91.70 [84.60; 98.80]	0.65 [0.16; 2.73] 0.559	0.629
absence				
KITE, N'/ N	123 / 123	114 / 114		
Number of patients with at least one event, n (%)	7 (5.7)	5 (4.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.07 [89.81; 98.34]	90.68 [79.41; 100.00]	1.25 [0.39; 3.95] 0.707	0.583

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.998			
presence				
Pooled Analysis, N'/ N	118 / 118	128 / 128		
Number of patients with at least one event, n (%)	7 (5.9)	6 (4.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.84 [89.42; 98.26]	94.78 [90.62; 98.93]	1.22 [0.41; 3.66] 0.719	0.652
absence				
Pooled Analysis, N'/ N	250 / 250	240 / 240		
Number of patients with at least one event, n (%)	15 (6.0)	12 (5.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.70 [90.62; 96.79]	89.18 [80.28; 98.07]	1.22 [0.57; 2.62] 0.609	0.594
Time to first loss in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.100**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.181			
presence				
KESTREL, N'/ N	62 / 62	61 / 61		
Number of patients with at least one event, n (%)	9 (14.5)	3 (4.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	84.37 [74.95; 93.79]	94.38 [88.17; 100.00]	2.97 [0.80; 10.96] 0.103	0.089
absence				
KESTREL, N'/ N	127 / 127	126 / 126		
Number of patients with at least one event, n (%)	12 (9.4)	12 (9.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	89.48 [83.81; 95.15]	89.51 [83.87; 95.15]	1.04 [0.47; 2.32] 0.922	0.973

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.982			
presence				
KITE, N'/ N	56 / 56	67 / 67		
Number of patients with at least one event, n (%)	5 (8.9)	9 (13.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	89.73 [81.14; 98.32]	79.35 [62.73; 95.97]	0.65 [0.22; 1.95] 0.446	0.484
absence				
KITE, N'/ N	123 / 123	114 / 114		
Number of patients with at least one event, n (%)	10 (8.1)	13 (11.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.09 [85.78; 96.39]	84.16 [74.58; 93.74]	0.66 [0.29; 1.52] 0.331	0.452
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.429			
presence				
Pooled Analysis, N'/ N	118 / 118	128 / 128		
Number of patients with at least one event, n (%)	14 (11.9)	12 (9.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	86.88 [80.43; 93.32]	84.96 [73.12; 96.80]	1.28 [0.59; 2.79] 0.536	0.518
absence				
Pooled Analysis, N'/ N	250 / 250	240 / 240		
Number of patients with at least one event, n (%)	22 (8.8)	25 (10.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	90.27 [86.39; 94.16]	86.79 [81.21; 92.38]	0.87 [0.49; 1.55] 0.629	0.616
Time to first loss in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.296**				

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.995			
presence				
KESTREL, N'/ N	62 / 62	61 / 61		
Number of patients with at least one event, n (%)	3 (4.8)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.00 [89.49; 100.00]	100.00 [100.00; 100.00]	N.E.	0.083
absence				
KESTREL, N'/ N	127 / 127	126 / 126		
Number of patients with at least one event, n (%)	1 (0.8)	1 (0.8)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	99.21 [97.66; 100.00]	99.19 [97.62; 100.00]	1.14 [0.07; 18.21] 0.928	0.993
KITE: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.556			
presence				
KITE, N'/ N	56 / 56	67 / 67		
Number of patients with at least one event, n (%)	2 (3.6)	3 (4.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.22 [91.07; 100.00]	94.76 [88.88; 100.00]	0.73 [0.12; 4.37] 0.729	0.805
absence				
KITE, N'/ N	123 / 123	114 / 114		
Number of patients with at least one event, n (%)	5 (4.1)	3 (2.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.77 [92.14; 99.40]	92.38 [81.15; 100.00]	1.45 [0.35; 6.12] 0.610	0.471

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.793			
presence				
Pooled Analysis, N'/ N	118 / 118	128 / 128		
Number of patients with at least one event, n (%)	5 (4.2)	3 (2.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.51 [91.67; 99.36]	97.18 [93.96; 100.00]	2.52 [0.48; 13.16] 0.274	0.385
absence				
Pooled Analysis, N'/ N	250 / 250	240 / 240		
Number of patients with at least one event, n (%)	6 (2.4)	4 (1.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.51 [95.53; 99.48]	95.51 [89.21; 100.00]	1.95 [0.44; 8.61] 0.379	0.521
Time to first loss in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.045 ***				
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.992			
presence				
KESTREL, N'/ N	62 / 62	61 / 61		
Number of patients with at least one event, n (%)	7 (11.3)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	87.71 [79.16; 96.26]	100.00 [100.00; 100.00]	N.E.	0.008 *
absence				
KESTREL, N'/ N	127 / 127	126 / 126		
Number of patients with at least one event, n (%)	3 (2.4)	4 (3.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.30 [94.27; 100.00]	96.37 [92.86; 99.87]	0.82 [0.18; 3.68] 0.797	0.734

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.762			
presence				
KITE, N'/ N	56 / 56	67 / 67		
Number of patients with at least one event, n (%)	3 (5.4)	5 (7.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.91 [87.17; 100.00]	91.95 [85.16; 98.73]	0.70 [0.17; 2.94] 0.630	0.687
absence				
KITE, N'/ N	123 / 123	114 / 114		
Number of patients with at least one event, n (%)	5 (4.1)	8 (7.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.78 [92.15; 99.40]	89.02 [80.11; 97.93]	0.53 [0.17; 1.63] 0.269	0.357
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.077			
presence				
Pooled Analysis, N'/ N	118 / 118	128 / 128		
Number of patients with at least one event, n (%)	10 (8.5)	5 (3.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	90.53 [84.92; 96.14]	95.71 [92.01; 99.40]	2.67 [0.86; 8.29] 0.088	0.129

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
absence				
Pooled Analysis, N'/ N	250 / 250	240 / 240		
Number of patients with at least one event, n (%)	8 (3.2)	12 (5.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.57 [94.23; 98.91]	92.70 [87.86; 97.54]	0.76 [0.29; 1.94] 0.560	0.346

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
*: $p < 0.05$
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + status of SRF + treatment * status of SRF.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + status of SRF + treatment * status of SRF.

Table 7.12 BCVA - Loss of 10 respectively 15 letters by exposure (week 52) (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by exposure (week 52) (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first loss in BCVA of ≥10 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.453**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.624			
Non-exposed				
KESTREL, N'/ N	71 / 71	75 / 75		
Number of patients with at least one event, n (%)	4 (5.6)	4 (5.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.81 [87.93; 99.70]	93.81 [87.82; 99.80]	1.19 [0.30; 4.79] 0.805	0.960
Exposed				
KESTREL, N'/ N	118 / 118	112 / 112		
Number of patients with at least one event, n (%)	8 (6.8)	4 (3.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.06 [88.42; 97.70]	89.20 [73.74; 100.00]	1.89 [0.57; 6.28] 0.300	0.280
KITE: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.764			
Non-exposed				
KITE, N'/ N	85 / 85	90 / 90		
Number of patients with at least one event, n (%)	5 (5.9)	6 (6.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.60 [88.15; 99.04]	92.34 [86.32; 98.36]	0.85 [0.26; 2.81] 0.793	0.840
Exposed				
KITE, N'/ N	94 / 94	91 / 91		
Number of patients with at least one event, n (%)	5 (5.3)	4 (4.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.61 [90.01; 99.21]	89.26 [74.85; 100.00]	1.12 [0.30; 4.20] 0.868	0.756

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by exposure (week 52) (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 52				
Interaction test	p=0.569			
Non-exposed				
Pooled Analysis, N'/ N	156 / 156	165 / 165		
Number of patients with at least one event, n (%)	9 (5.8)	10 (6.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.74 [89.77; 97.71]	92.99 [88.70; 97.28]	1.02 [0.41; 2.53] 0.970	0.904
Exposed				
Pooled Analysis, N'/ N	212 / 212	203 / 203		
Number of patients with at least one event, n (%)	13 (6.1)	8 (3.9)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.74 [90.44; 97.04]	89.27 [78.73; 99.81]	1.47 [0.61; 3.57] 0.392	0.308
Time to first loss in BCVA of ≥15 letters, Week 52				
Test of heterogeneity in main analysis: **p_H=0.296**				
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.996			
Non-exposed				
KESTREL, N'/ N	71 / 71	75 / 75		
Number of patients with at least one event, n (%)	2 (2.8)	1 (1.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.88 [92.61; 100.00]	98.61 [95.91; 100.00]	2.56 [0.23; 28.64] 0.445	0.549
Exposed				
KESTREL, N'/ N	118 / 118	112 / 112		
Number of patients with at least one event, n (%)	2 (1.7)	0 (0.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	98.25 [95.85; 100.00]	100.00 [100.00; 100.00]	N.E.	0.163

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by exposure (week 52) (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.399			
Non-exposed				
KITE, N'/ N	85 / 85	90 / 90		
Number of patients with at least one event, n (%)	4 (4.7)	5 (5.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	94.95 [90.13; 99.78]	93.47 [87.81; 99.12]	0.83 [0.22; 3.12] 0.781	0.815
Exposed				
KITE, N'/ N	94 / 94	91 / 91		
Number of patients with at least one event, n (%)	3 (3.2)	1 (1.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.75 [93.13; 100.00]	92.31 [77.82; 100.00]	2.57 [0.27; 24.83] 0.416	0.311
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 52				
Interaction test	p=0.296			
Non-exposed				
Pooled Analysis, N'/ N	156 / 156	165 / 165		
Number of patients with at least one event, n (%)	6 (3.8)	6 (3.6)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.82 [92.54; 99.10]	95.70 [92.23; 99.16]	1.58 [0.39; 6.41] 0.526	0.923
Exposed				
Pooled Analysis, N'/ N	212 / 212	203 / 203		
Number of patients with at least one event, n (%)	5 (2.4)	1 (0.5)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	97.57 [95.47; 99.68]	96.00 [88.32; 100.00]	5.77 [0.60; 55.39] 0.129	0.103

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by exposure (week 52) (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + exposure (week 52) + treatment * exposure (week 52).
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).

Table 7.13 BCVA - Loss of 10 respectively 15 letters by exposure (week 100) (FAS), time-to-event analysis, week 100

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Time to first loss in BCVA of ≥10 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.100**				
KESTREL: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.989			
Non-exposed				
KESTREL, N'/ N	12 / 12	13 / 13		
Number of patients with at least one event, n (%)	0 (0.0)	1 (7.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	100.00 [100.00; 100.00]	90.00 [71.41; 100.00]	0.00 [0.00; N.E.] 0.989	0.294
Exposed				
KESTREL, N'/ N	177 / 177	174 / 174		
Number of patients with at least one event, n (%)	21 (11.9)	14 (8.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	87.42 [82.38; 92.47]	91.46 [87.18; 95.75]	1.54 [0.78; 3.02] 0.213	0.225
KITE: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.586			
Non-exposed				
KITE, N'/ N	17 / 17	12 / 12		
Number of patients with at least one event, n (%)	2 (11.8)	1 (8.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	85.56 [66.93; 100.00]	85.71 [59.79; 100.00]	1.20 [0.11; 13.57] 0.883	0.903
Exposed				
KITE, N'/ N	162 / 162	169 / 169		
Number of patients with at least one event, n (%)	13 (8.0)	21 (12.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.52 [87.09; 95.95]	83.07 [74.64; 91.50]	0.59 [0.30; 1.19] 0.143	0.223

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Pooled Analysis: Time to first loss in BCVA of ≥10 letters, Week 100				
Interaction test	p=0.847			
Non-exposed				
Pooled Analysis, N'/ N	29 / 29	25 / 25		
Number of patients with at least one event, n (%)	2 (6.9)	2 (8.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.78 [80.84; 100.00]	88.24 [72.92; 100.00]	0.81 [0.11; 5.88] 0.839	0.664
Exposed				
Pooled Analysis, N'/ N	339 / 339	343 / 343		
Number of patients with at least one event, n (%)	34 (10.0)	35 (10.2)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	89.40 [86.02; 92.78]	86.79 [81.56; 92.02]	1.00 [0.62; 1.61] 0.985	0.993
Time to first loss in BCVA of ≥15 letters, Week 100				
Test of heterogeneity in main analysis: **p_H=0.045 ***				
KESTREL: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.990			
Non-exposed				
KESTREL, N'/ N	12 / 12	13 / 13		
Number of patients with at least one event, n (%)	0 (0.0)	1 (7.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	100.00 [100.00; 100.00]	90.00 [71.41; 100.00]	0.00 [0.00; N.E.] 0.991	0.294
Exposed				
KESTREL, N'/ N	177 / 177	174 / 174		
Number of patients with at least one event, n (%)	10 (5.6)	3 (1.7)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	93.88 [90.20; 97.56]	98.08 [95.93; 100.00]	3.54 [0.97; 12.87] 0.055	0.047 *

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
KITE: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.501			
Non-exposed				
KITE, N'/ N	17 / 17	12 / 12		
Number of patients with at least one event, n (%)	2 (11.8)	1 (8.3)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	85.56 [66.93; 100.00]	85.71 [59.79; 100.00]	1.17 [0.10; 13.51] 0.900	0.903
Exposed				
KITE, N'/ N	162 / 162	169 / 169		
Number of patients with at least one event, n (%)	6 (3.7)	12 (7.1)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	96.18 [93.18; 99.19]	90.99 [85.44; 96.54]	0.47 [0.18; 1.27] 0.137	0.201
Pooled Analysis: Time to first loss in BCVA of ≥15 letters, Week 100				
Interaction test	p=0.799			
Non-exposed				
Pooled Analysis, N'/ N	29 / 29	25 / 25		
Number of patients with at least one event, n (%)	2 (6.9)	2 (8.0)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	91.78 [80.84; 100.00]	88.24 [72.92; 100.00]	0.98 [0.13; 7.34] 0.982	0.664

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**HR [95% CI] p-value**	**p-value[2]**
Exposed				
Pooled Analysis, N'/ N	339 / 339	343 / 343		
Number of patients with at least one event, n (%)	16 (4.7)	15 (4.4)		
Median (in weeks)	N.E.	N.E.		
% of outcome-free patients[1]	95.00 [92.61; 97.40]	94.34 [91.11; 97.57]	1.29 [0.59; 2.79] 0.521	0.754

N': Number of patients
N': Number of patients in the analysis
CI: Confidence Interval
HR: Hazard Ratio
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
[1]: Kaplan-Meier estimate of outcome-free patients
[2]: p-value obtained by Log-rank test (in the pooled analysis stratified by study)
*: $p < 0.05$
.....

Hazard ratio obtained by Cox proportional hazards model:
KESTREL and KITE: log(hazard ratio) = treatment + age category + baseline category + exposure (week 100) + treatment * exposure (week 100).
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).

8 VFQ: Continuous analysis

Table 8.0 VFQ (FAS), return rates, Week 100

	Treatment Groups		
VFQ (FAS)	**Brolucizumab**	**Aflibercept**	**Total**
KESTREL: VFQ			
N	189	187	376
Baseline Returns, n (%)	188 (99.5)	187 (100.0)	375 (99.7)
Week 28 Returns, n (%)	174 (92.1)	169 (90.4)	343 (91.2)
Week 52 Returns, n (%)	149 (78.8)	158 (84.5)	307 (81.6)
Week 100 Returns, n (%)	144 (76.2)	146 (78.1)	290 (77.1)
KITE: VFQ			
N	179	181	360
Baseline Returns, n (%)	178 (99.4)	181 (100.0)	359 (99.7)
Week 28 Returns, n (%)	167 (93.3)	168 (92.8)	335 (93.1)
Week 52 Returns, n (%)	145 (81.0)	150 (82.9)	295 (81.9)
Week 100 Returns, n (%)	132 (73.7)	146 (80.7)	278 (77.2)
Pooled Analysis: VFQ			
N	368	368	736
Baseline Returns, n (%)	366 (99.5)	368 (100.0)	734 (99.7)
Week 28 Returns, n (%)	341 (92.7)	337 (91.6)	678 (92.1)
Week 52 Returns, n (%)	294 (79.9)	308 (83.7)	602 (81.8)
Week 100 Returns, n (%)	276 (75.0)	292 (79.3)	568 (77.2)

N: Number of patients
n (%): Number and percentage of patients with available data for the total score
.....
The return rate is the proportion of patients with available data for the total score at the given visit based on the whole study population.

Table 8.1 VFQ (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
VFQ (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KESTREL: Composite Score				
N'/ N	188 / 189	187 / 187		
Baseline Mean (SD)	76.64 (17.46)	76.81 (14.59)		
Week 52 Mean (SD)	85.03 (13.91)	85.15 (12.27)		
Week 100 Mean (SD)	83.05 (14.95)	83.33 (14.40)		
Week 28: Adjusted Mean Change (SE)	5.76 (0.79)	7.73 (0.80)		
Week 52: Adjusted Mean Change (SE)	7.02 (0.84)	8.20 (0.82)	-1.19 [-3.50; 1.12]	0.313
Week 100: Adjusted Mean Change (SE)	6.13 (0.93)	6.56 (0.93)	-0.43 [-3.02; 2.16]	0.743
KITE: Composite Score				
N'/ N	178 / 179	181 / 181		
Baseline Mean (SD)	77.82 (14.99)	76.46 (17.67)		
Week 52 Mean (SD)	86.48 (12.89)	83.54 (15.65)		
Week 100 Mean (SD)	88.08 (12.13)	84.05 (15.32)		
Week 28: Adjusted Mean Change (SE)	5.69 (0.76)	5.88 (0.76)		
Week 52: Adjusted Mean Change (SE)	8.79 (0.83)	6.33 (0.81)	2.46 [0.18; 4.73]	0.035 *
Week 100: Adjusted Mean Change (SE)	8.95 (0.96)	6.20 (0.92)	2.76 [0.13; 5.39]	0.040 *
Pooled Analysis: Composite Score p_H=0.049 *				
N'/ N	366 / 368	368 / 368		
Baseline Mean (SD)	77.21 (16.29)	76.64 (16.16)		
Week 52 Mean (SD)	85.75 (13.41)	84.37 (14.02)		
Week 100 Mean (SD)	85.45 (13.89)	83.69 (14.85)		
Week 28: Adjusted Mean Change (SE)	5.76 (0.56)	6.79 (0.56)		
Week 52: Adjusted Mean Change (SE)	7.91 (0.59)	7.28 (0.58)	0.63 [-1.00; 2.26]	0.445
Week 100: Adjusted Mean Change (SE)	7.55 (0.67)	6.35 (0.65)	1.20 [-0.64; 3.03]	0.201
KESTREL: General Vision				
N'/ N	188 / 189	187 / 187		
Baseline Mean (SD)	61.28 (17.26)	60.21 (14.66)		
Week 52 Mean (SD)	73.02 (14.13)	71.14 (12.87)		
Week 100 Mean (SD)	73.61 (14.89)	72.33 (12.04)		
Week 28: Adjusted Mean Change (SE)	11.36 (0.97)	10.74 (0.98)		
Week 52: Adjusted Mean Change (SE)	11.76 (1.02)	10.65 (1.00)	1.11 [-1.70; 3.93]	0.437
Week 100: Adjusted Mean Change (SE)	13.01 (1.02)	11.83 (1.02)	1.18 [-1.66; 4.01]	0.415

	Treatment Groups		Comparison	
VFQ (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Vision				
N'/ N	178 / 179	181 / 181		
Baseline Mean (SD)	61.80 (16.09)	59.89 (18.32)		
Week 52 Mean (SD)	72.78 (14.51)	70.53 (17.14)		
Week 100 Mean (SD)	73.74 (13.83)	70.55 (16.47)		
Week 28: Adjusted Mean Change (SE)	9.35 (1.03)	9.53 (1.02)		
Week 52: Adjusted Mean Change (SE)	11.71 (1.14)	10.24 (1.12)	1.47 [-1.68; 4.62]	0.358
Week 100: Adjusted Mean Change (SE)	12.21 (1.18)	9.53 (1.13)	2.68 [-0.53; 5.90]	0.102
Pooled Analysis: General Vision p_H=0.762				
N'/ N	366 / 368	368 / 368		
Baseline Mean (SD)	61.53 (16.68)	60.05 (16.54)		
Week 52 Mean (SD)	72.90 (14.29)	70.84 (15.08)		
Week 100 Mean (SD)	73.67 (14.37)	71.44 (14.43)		
Week 28: Adjusted Mean Change (SE)	10.37 (0.71)	10.13 (0.71)		
Week 52: Adjusted Mean Change (SE)	11.73 (0.77)	10.44 (0.75)	1.29 [-0.82; 3.40]	0.231
Week 100: Adjusted Mean Change (SE)	12.66 (0.78)	10.69 (0.76)	1.96 [-0.17; 4.09]	0.071
KESTREL: Ocular Pain				
N'/ N	188 / 189	187 / 187		
Baseline Mean (SD)	83.38 (19.93)	82.15 (20.49)		
Week 52 Mean (SD)	88.59 (15.85)	86.71 (16.19)		
Week 100 Mean (SD)	86.02 (17.46)	83.99 (20.28)		
Week 28: Adjusted Mean Change (SE)	2.77 (1.32)	4.48 (1.33)		
Week 52: Adjusted Mean Change (SE)	4.98 (1.22)	4.47 (1.19)	0.52 [-2.83; 3.87]	0.762
Week 100: Adjusted Mean Change (SE)	3.01 (1.34)	1.88 (1.33)	1.13 [-2.57; 4.84]	0.549
KITE: Ocular Pain				
N'/ N	178 / 179	181 / 181		
Baseline Mean (SD)	84.27 (17.98)	82.46 (20.57)		
Week 52 Mean (SD)	88.80 (16.58)	87.33 (17.80)		
Week 100 Mean (SD)	90.36 (15.39)	89.21 (16.32)		
Week 28: Adjusted Mean Change (SE)	4.39 (1.18)	3.79 (1.17)		
Week 52: Adjusted Mean Change (SE)	4.76 (1.23)	3.76 (1.21)	1.00 [-2.39; 4.40]	0.561
Week 100: Adjusted Mean Change (SE)	6.01 (1.26)	5.40 (1.20)	0.62 [-2.80; 4.04]	0.723

	Treatment Groups		Comparison	
VFQ (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Ocular Pain p_H=0.664				
N'/ N	366 / 368	368 / 368		
Baseline Mean (SD)	83.81 (18.99)	82.30 (20.50)		
Week 52 Mean (SD)	88.69 (16.18)	87.01 (16.97)		
Week 100 Mean (SD)	88.09 (16.62)	86.60 (18.56)		
Week 28: Adjusted Mean Change (SE)	3.57 (0.89)	4.11 (0.89)		
Week 52: Adjusted Mean Change (SE)	4.89 (0.87)	4.11 (0.85)	0.78 [-1.61; 3.17]	0.522
Week 100: Adjusted Mean Change (SE)	4.50 (0.92)	3.61 (0.89)	0.89 [-1.62; 3.41]	0.486
KESTREL: Near Activities				
N'/ N	188 / 189	187 / 187		
Baseline Mean (SD)	63.50 (26.15)	65.64 (21.82)		
Week 52 Mean (SD)	79.22 (21.32)	78.69 (20.11)		
Week 100 Mean (SD)	79.51 (20.76)	77.00 (21.12)		
Week 28: Adjusted Mean Change (SE)	12.27 (1.36)	14.31 (1.37)		
Week 52: Adjusted Mean Change (SE)	13.28 (1.50)	13.55 (1.46)	-0.27 [-4.39; 3.85]	0.897
Week 100: Adjusted Mean Change (SE)	14.42 (1.46)	11.70 (1.45)	2.72 [-1.33; 6.76]	0.188
KITE: Near Activities				
N'/ N	177 / 179	181 / 181		
Baseline Mean (SD)	70.15 (22.39)	69.41 (23.88)		
Week 52 Mean (SD)	80.09 (20.65)	78.64 (22.08)		
Week 100 Mean (SD)	83.87 (18.68)	78.03 (23.07)		
Week 28: Adjusted Mean Change (SE)	6.32 (1.38)	5.91 (1.36)		
Week 52: Adjusted Mean Change (SE)	10.22 (1.39)	9.02 (1.37)	1.21 [-2.63; 5.04]	0.537
Week 100: Adjusted Mean Change (SE)	12.06 (1.51)	7.58 (1.44)	4.48 [0.37; 8.58]	0.033 *
Pooled Analysis: Near Activities p_H=0.450				
N'/ N	365 / 368	368 / 368		
Baseline Mean (SD)	66.72 (24.59)	67.49 (22.91)		
Week 52 Mean (SD)	79.65 (20.96)	78.67 (21.06)		
Week 100 Mean (SD)	81.59 (19.88)	77.51 (22.09)		
Week 28: Adjusted Mean Change (SE)	9.47 (0.98)	10.08 (0.98)		
Week 52: Adjusted Mean Change (SE)	11.82 (1.03)	11.28 (1.01)	0.54 [-2.30; 3.38]	0.710
Week 100: Adjusted Mean Change (SE)	13.33 (1.05)	9.64 (1.02)	3.69 [0.81; 6.56]	0.012 *

	Treatment Groups		Comparison	
VFQ (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KESTREL: Distance Activities				
N'/ N	188 / 189	187 / 187		
Baseline Mean (SD)	75.27 (23.84)	75.36 (21.14)		
Week 52 Mean (SD)	85.40 (17.21)	85.07 (17.06)		
Week 100 Mean (SD)	81.80 (19.93)	83.19 (18.67)		
Week 28: Adjusted Mean Change (SE)	7.36 (1.19)	8.94 (1.21)		
Week 52: Adjusted Mean Change (SE)	8.96 (1.14)	9.46 (1.12)	-0.50 [-3.64; 2.64]	0.755
Week 100: Adjusted Mean Change (SE)	6.55 (1.25)	7.58 (1.25)	-1.02 [-4.51; 2.46]	0.564
KITE: Distance Activities				
N'/ N	178 / 179	181 / 181		
Baseline Mean (SD)	76.90 (21.47)	76.20 (22.44)		
Week 52 Mean (SD)	87.93 (17.49)	84.39 (18.72)		
Week 100 Mean (SD)	89.19 (15.91)	83.82 (18.81)		
Week 28: Adjusted Mean Change (SE)	6.12 (1.20)	5.28 (1.19)		
Week 52: Adjusted Mean Change (SE)	11.27 (1.13)	7.99 (1.11)	3.28 [0.16; 6.40]	0.039 *
Week 100: Adjusted Mean Change (SE)	11.28 (1.24)	6.81 (1.19)	4.47 [1.10; 7.85]	0.010 *
Pooled Analysis: Distance Activities p_H=0.046 *				
N'/ N	366 / 368	368 / 368		
Baseline Mean (SD)	76.06 (22.70)	75.77 (21.76)		
Week 52 Mean (SD)	86.65 (17.36)	84.74 (17.86)		
Week 100 Mean (SD)	85.32 (18.47)	83.50 (18.71)		
Week 28: Adjusted Mean Change (SE)	6.79 (0.85)	7.12 (0.85)		
Week 52: Adjusted Mean Change (SE)	10.12 (0.81)	8.74 (0.79)	1.38 [-0.84; 3.60]	0.222
Week 100: Adjusted Mean Change (SE)	8.86 (0.88)	7.19 (0.86)	1.66 [-0.75; 4.08]	0.177
KESTREL: Social Functioning				
N'/ N	188 / 189	187 / 187		
Baseline Mean (SD)	88.83 (18.91)	89.84 (15.62)		
Week 52 Mean (SD)	92.53 (14.95)	93.71 (13.47)		
Week 100 Mean (SD)	90.63 (17.08)	91.87 (14.94)		
Week 28: Adjusted Mean Change (SE)	1.59 (0.91)	4.01 (0.92)		
Week 52: Adjusted Mean Change (SE)	2.37 (1.03)	3.92 (1.01)	-1.55 [-4.39; 1.29]	0.283
Week 100: Adjusted Mean Change (SE)	1.53 (1.23)	2.27 (1.22)	-0.75 [-4.16; 2.67]	0.667

	Treatment Groups		Comparison	
VFQ (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Social Functioning				
N'/ N	178 / 179	181 / 181		
Baseline Mean (SD)	88.41 (17.33)	86.40 (19.95)		
Week 52 Mean (SD)	95.14 (11.93)	91.58 (14.73)		
Week 100 Mean (SD)	95.04 (13.84)	91.18 (16.88)		
Week 28: Adjusted Mean Change (SE)	3.71 (1.06)	3.85 (1.05)		
Week 52: Adjusted Mean Change (SE)	7.38 (0.91)	4.34 (0.89)	3.04 [0.53; 5.55]	0.018 *
Week 100: Adjusted Mean Change (SE)	6.80 (1.16)	3.73 (1.10)	3.07 [-0.07; 6.21]	0.056
Pooled Analysis: Social Functioning p_H=0.023 *				
N'/ N	366 / 368	368 / 368		
Baseline Mean (SD)	88.63 (18.13)	88.15 (17.94)		
Week 52 Mean (SD)	93.81 (13.59)	92.67 (14.12)		
Week 100 Mean (SD)	92.73 (15.75)	91.52 (15.92)		
Week 28: Adjusted Mean Change (SE)	2.67 (0.70)	3.89 (0.70)		
Week 52: Adjusted Mean Change (SE)	4.90 (0.69)	4.10 (0.68)	0.79 [-1.11; 2.70]	0.413
Week 100: Adjusted Mean Change (SE)	4.14 (0.85)	2.93 (0.82)	1.21 [-1.11; 3.53]	0.305
KESTREL: Mental Health				
N'/ N	188 / 189	187 / 187		
Baseline Mean (SD)	65.53 (24.93)	68.25 (23.03)		
Week 52 Mean (SD)	78.36 (19.97)	78.68 (17.88)		
Week 100 Mean (SD)	74.87 (21.47)	77.61 (21.41)		
Week 28: Adjusted Mean Change (SE)	7.44 (1.28)	9.30 (1.29)		
Week 52: Adjusted Mean Change (SE)	10.50 (1.33)	11.12 (1.30)	-0.62 [-4.27; 3.03]	0.738
Week 100: Adjusted Mean Change (SE)	8.72 (1.51)	10.69 (1.50)	-1.96 [-6.14; 2.22]	0.356
KITE: Mental Health				
N'/ N	178 / 179	181 / 181		
Baseline Mean (SD)	68.93 (21.56)	65.78 (26.01)		
Week 52 Mean (SD)	81.38 (20.72)	76.71 (23.59)		
Week 100 Mean (SD)	84.21 (16.10)	79.62 (22.25)		
Week 28: Adjusted Mean Change (SE)	8.37 (1.29)	8.92 (1.28)		
Week 52: Adjusted Mean Change (SE)	12.66 (1.55)	9.14 (1.52)	3.52 [-0.76; 7.81]	0.106
Week 100: Adjusted Mean Change (SE)	13.71 (1.57)	11.35 (1.50)	2.36 [-1.91; 6.63]	0.278

	Treatment Groups		Comparison	
VFQ (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Mental Health p_H=0.200				
N'/ N	366 / 368	368 / 368		
Baseline Mean (SD)	67.18 (23.38)	67.03 (24.54)		
Week 52 Mean (SD)	79.84 (20.36)	77.72 (20.84)		
Week 100 Mean (SD)	79.32 (19.63)	78.62 (21.82)		
Week 28: Adjusted Mean Change (SE)	7.94 (0.91)	9.08 (0.91)		
Week 52: Adjusted Mean Change (SE)	11.60 (1.02)	10.11 (1.00)	1.48 [-1.32; 4.28]	0.300
Week 100: Adjusted Mean Change (SE)	11.23 (1.09)	10.99 (1.06)	0.24 [-2.74; 3.22]	0.874
KESTREL: Role Difficulties				
N'/ N	188 / 189	187 / 187		
Baseline Mean (SD)	72.01 (28.62)	71.79 (26.65)		
Week 52 Mean (SD)	80.70 (25.31)	83.15 (22.83)		
Week 100 Mean (SD)	81.51 (25.73)	79.71 (25.31)		
Week 28: Adjusted Mean Change (SE)	5.80 (1.60)	9.02 (1.62)		
Week 52: Adjusted Mean Change (SE)	6.52 (1.77)	10.87 (1.73)	-4.35 [-9.21; 0.52]	0.080
Week 100: Adjusted Mean Change (SE)	9.04 (1.81)	7.67 (1.81)	1.37 [-3.66; 6.41]	0.592
KITE: Role Difficulties				
N'/ N	178 / 179	181 / 181		
Baseline Mean (SD)	71.07 (27.27)	67.20 (29.32)		
Week 52 Mean (SD)	82.90 (21.96)	78.17 (25.26)		
Week 100 Mean (SD)	85.02 (22.86)	80.31 (25.29)		
Week 28: Adjusted Mean Change (SE)	7.36 (1.58)	8.14 (1.57)		
Week 52: Adjusted Mean Change (SE)	12.31 (1.69)	8.43 (1.65)	3.88 [-0.77; 8.52]	0.101
Week 100: Adjusted Mean Change (SE)	11.86 (1.86)	9.77 (1.78)	2.09 [-2.99; 7.16]	0.419
Pooled Analysis: Role Difficulties p_H=0.132				
N'/ N	366 / 368	368 / 368		
Baseline Mean (SD)	71.55 (27.94)	69.53 (28.05)		
Week 52 Mean (SD)	81.78 (23.71)	80.72 (24.13)		
Week 100 Mean (SD)	83.18 (24.43)	80.01 (25.26)		
Week 28: Adjusted Mean Change (SE)	6.59 (1.13)	8.56 (1.13)		
Week 52: Adjusted Mean Change (SE)	9.38 (1.22)	9.68 (1.20)	-0.30 [-3.66; 3.06]	0.860
Week 100: Adjusted Mean Change (SE)	10.49 (1.30)	8.72 (1.27)	1.78 [-1.78; 5.33]	0.327

	Treatment Groups		Comparison	
VFQ (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KESTREL: Dependency				
N'/ N	188 / 189	187 / 187		
Baseline Mean (SD)	81.52 (26.38)	82.75 (23.79)		
Week 52 Mean (SD)	88.98 (21.88)	92.04 (17.02)		
Week 100 Mean (SD)	86.17 (22.48)	88.41 (20.98)		
Week 28: Adjusted Mean Change (SE)	5.62 (1.37)	6.83 (1.39)		
Week 52: Adjusted Mean Change (SE)	5.49 (1.44)	8.75 (1.41)	-3.27 [-7.22; 0.69]	0.105
Week 100: Adjusted Mean Change (SE)	3.66 (1.60)	5.57 (1.59)	-1.91 [-6.35; 2.53]	0.397
KITE: Dependency				
N'/ N	178 / 179	181 / 181		
Baseline Mean (SD)	83.43 (23.55)	81.91 (26.99)		
Week 52 Mean (SD)	91.09 (19.20)	86.72 (22.71)		
Week 100 Mean (SD)	93.07 (14.55)	87.39 (22.96)		
Week 28: Adjusted Mean Change (SE)	5.25 (1.29)	3.04 (1.28)		
Week 52: Adjusted Mean Change (SE)	7.25 (1.40)	3.02 (1.37)	4.22 [0.37; 8.07]	0.032 *
Week 100: Adjusted Mean Change (SE)	6.61 (1.53)	2.90 (1.47)	3.71 [-0.46; 7.88]	0.081
Pooled Analysis: Dependency p_H=0.019 *				
N'/ N	366 / 368	368 / 368		
Baseline Mean (SD)	82.45 (25.03)	82.34 (25.38)		
Week 52 Mean (SD)	90.02 (20.60)	89.45 (20.13)		
Week 100 Mean (SD)	89.45 (19.39)	87.90 (21.96)		
Week 28: Adjusted Mean Change (SE)	5.49 (0.95)	4.93 (0.95)		
Week 52: Adjusted Mean Change (SE)	6.38 (1.01)	5.92 (0.99)	0.46 [-2.31; 3.24]	0.744
Week 100: Adjusted Mean Change (SE)	5.23 (1.11)	4.25 (1.08)	0.98 [-2.06; 4.02]	0.528
KESTREL: Driving				
N'/ N	120 / 189	120 / 187		
Baseline Mean (SD)	79.93 (18.60)	77.15 (19.69)		
Week 52 Mean (SD)	84.26 (20.09)	84.33 (18.02)		
Week 100 Mean (SD)	82.96 (19.30)	79.97 (21.54)		
Week 28: Adjusted Mean Change (SE)	1.97 (1.38)	5.51 (1.43)		
Week 52: Adjusted Mean Change (SE)	3.49 (1.59)	5.88 (1.65)	-2.39 [-6.90; 2.12]	0.297
Week 100: Adjusted Mean Change (SE)	2.28 (1.78)	1.64 (1.84)	0.64 [-4.41; 5.69]	0.804

	Treatment Groups		Comparison	
VFQ (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Driving				
N'/ N	103 / 179	96 / 181		
Baseline Mean (SD)	79.00 (20.35)	82.07 (21.76)		
Week 52 Mean (SD)	86.90 (17.22)	87.83 (15.76)		
Week 100 Mean (SD)	86.27 (15.03)	87.11 (14.52)		
Week 28: Adjusted Mean Change (SE)	0.75 (1.45)	5.34 (1.50)		
Week 52: Adjusted Mean Change (SE)	5.84 (1.27)	4.76 (1.32)	1.08 [-2.55; 4.71]	0.559
Week 100: Adjusted Mean Change (SE)	4.22 (1.42)	2.79 (1.45)	1.42 [-2.59; 5.44]	0.484
Pooled Analysis: Driving p_H=0.792				
N'/ N	223 / 368	216 / 368		
Baseline Mean (SD)	79.50 (19.39)	79.34 (20.73)		
Week 52 Mean (SD)	85.47 (18.83)	85.91 (17.08)		
Week 100 Mean (SD)	84.51 (17.46)	83.36 (18.83)		
Week 28: Adjusted Mean Change (SE)	1.40 (1.00)	5.40 (1.04)		
Week 52: Adjusted Mean Change (SE)	4.68 (1.03)	5.40 (1.07)	-0.72 [-3.65; 2.21]	0.628
Week 100: Adjusted Mean Change (SE)	3.20 (1.17)	2.20 (1.20)	0.99 [-2.29; 4.28]	0.552
KESTREL: Color Vision				
N'/ N	186 / 189	184 / 187		
Baseline Mean (SD)	93.01 (16.59)	94.02 (14.95)		
Week 52 Mean (SD)	96.62 (11.16)	95.92 (11.98)		
Week 100 Mean (SD)	94.68 (12.96)	95.07 (12.36)		
Week 28: Adjusted Mean Change (SE)	2.06 (0.84)	1.78 (0.85)		
Week 52: Adjusted Mean Change (SE)	2.17 (0.86)	1.80 (0.85)	0.37 [-2.02; 2.76]	0.759
Week 100: Adjusted Mean Change (SE)	0.67 (1.02)	0.85 (1.02)	-0.18 [-3.01; 2.65]	0.902
KITE: Color Vision				
N'/ N	178 / 179	179 / 181		
Baseline Mean (SD)	92.13 (16.85)	91.76 (16.07)		
Week 52 Mean (SD)	97.55 (8.56)	94.90 (12.39)		
Week 100 Mean (SD)	97.31 (8.94)	95.07 (13.40)		
Week 28: Adjusted Mean Change (SE)	3.44 (0.83)	4.04 (0.83)		
Week 52: Adjusted Mean Change (SE)	5.60 (0.75)	3.26 (0.74)	2.34 [0.28; 4.41]	0.026 *
Week 100: Adjusted Mean Change (SE)	4.95 (0.91)	3.28 (0.87)	1.67 [-0.80; 4.14]	0.185

	Treatment Groups		Comparison	
VFQ (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Color Vision p_H=0.477				
N'/ N	364 / 368	363 / 368		
Baseline Mean (SD)	92.58 (16.70)	92.91 (15.53)		
Week 52 Mean (SD)	97.08 (9.96)	95.42 (12.18)		
Week 100 Mean (SD)	95.94 (11.27)	95.07 (12.87)		
Week 28: Adjusted Mean Change (SE)	2.79 (0.60)	2.88 (0.60)		
Week 52: Adjusted Mean Change (SE)	3.87 (0.57)	2.49 (0.56)	1.38 [-0.19; 2.95]	0.086
Week 100: Adjusted Mean Change (SE)	2.83 (0.69)	1.94 (0.67)	0.89 [-0.99; 2.78]	0.353
KESTREL: Peripheral Vision				
N'/ N	187 / 189	186 / 187		
Baseline Mean (SD)	83.96 (21.77)	80.11 (23.27)		
Week 52 Mean (SD)	89.26 (19.55)	88.54 (17.79)		
Week 100 Mean (SD)	84.27 (22.14)	87.50 (20.81)		
Week 28: Adjusted Mean Change (SE)	2.63 (1.35)	7.64 (1.36)		
Week 52: Adjusted Mean Change (SE)	5.55 (1.38)	7.09 (1.35)	-1.53 [-5.35; 2.28]	0.430
Week 100: Adjusted Mean Change (SE)	1.03 (1.64)	5.83 (1.62)	-4.80 [-9.35; -0.26]	0.038 *
KITE: Peripheral Vision				
N'/ N	178 / 179	180 / 181		
Baseline Mean (SD)	83.15 (20.16)	84.72 (21.37)		
Week 52 Mean (SD)	89.76 (17.09)	87.75 (19.41)		
Week 100 Mean (SD)	92.37 (15.16)	87.76 (18.66)		
Week 28: Adjusted Mean Change (SE)	4.56 (1.20)	4.46 (1.19)		
Week 52: Adjusted Mean Change (SE)	6.32 (1.28)	3.48 (1.26)	2.84 [-0.70; 6.38]	0.116
Week 100: Adjusted Mean Change (SE)	7.58 (1.29)	2.90 (1.24)	4.68 [1.15; 8.21]	0.009 *
Pooled Analysis: Peripheral Vision p_H=0.003 *				
N'/ N	365 / 368	366 / 368		
Baseline Mean (SD)	83.56 (20.97)	82.38 (22.44)		
Week 52 Mean (SD)	89.51 (18.35)	88.15 (18.57)		
Week 100 Mean (SD)	88.14 (19.51)	87.63 (19.74)		
Week 28: Adjusted Mean Change (SE)	3.50 (0.91)	6.16 (0.91)		
Week 52: Adjusted Mean Change (SE)	5.85 (0.95)	5.44 (0.93)	0.40 [-2.21; 3.02]	0.761
Week 100: Adjusted Mean Change (SE)	4.10 (1.05)	4.42 (1.03)	-0.32 [-3.21; 2.57]	0.827

	Treatment Groups		Comparison	
VFQ (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KESTREL: General Health				
N'/ N	188 / 189	187 / 187		
Baseline Mean (SD)	44.15 (21.14)	38.50 (20.12)		
Week 52 Mean (SD)	51.85 (24.16)	45.73 (21.52)		
Week 100 Mean (SD)	49.83 (23.19)	48.29 (21.31)		
Week 28: Adjusted Mean Change (SE)	4.46 (1.38)	4.82 (1.39)		
Week 52: Adjusted Mean Change (SE)	8.37 (1.68)	5.32 (1.64)	3.06 [-1.58; 7.69]	0.196
Week 100: Adjusted Mean Change (SE)	7.78 (1.67)	7.55 (1.66)	0.23 [-4.40; 4.87]	0.922
KITE: General Health				
N'/ N	178 / 179	181 / 181		
Baseline Mean (SD)	43.96 (20.29)	44.61 (22.87)		
Week 52 Mean (SD)	49.48 (21.82)	50.17 (23.44)		
Week 100 Mean (SD)	50.76 (19.84)	51.20 (22.42)		
Week 28: Adjusted Mean Change (SE)	3.50 (1.39)	4.34 (1.38)		
Week 52: Adjusted Mean Change (SE)	5.55 (1.65)	5.06 (1.62)	0.50 [-4.05; 5.04]	0.830
Week 100: Adjusted Mean Change (SE)	6.16 (1.54)	5.60 (1.47)	0.56 [-3.62; 4.74]	0.793
Pooled Analysis: General Health p_H=0.834				
N'/ N	366 / 368	368 / 368		
Baseline Mean (SD)	44.06 (20.70)	41.51 (21.70)		
Week 52 Mean (SD)	50.68 (23.03)	47.89 (22.55)		
Week 100 Mean (SD)	50.27 (21.62)	49.74 (21.88)		
Week 28: Adjusted Mean Change (SE)	3.88 (0.98)	4.66 (0.98)		
Week 52: Adjusted Mean Change (SE)	6.87 (1.18)	5.25 (1.15)	1.63 [-1.61; 4.86]	0.324
Week 100: Adjusted Mean Change (SE)	6.89 (1.14)	6.68 (1.11)	0.22 [-2.90; 3.33]	0.892

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline value.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + study + treatment * study.

Table 8.2 VFQ by age (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Composite Score				
Test of heterogeneity in main analysis: **p_H=0.049 ***				
KESTREL: Composite Score				
Interaction test	p=0.471			
< 65 years				
N'/ N	103 / 104	93 / 93		
Baseline Mean (SD)	76.65 (17.57)	74.75 (15.84)		
Week 52 Mean (SD)	86.30 (14.42)	87.09 (11.99)		
Week 100 Mean (SD)	84.44 (16.06)	85.24 (13.96)		
Week 28: Adjusted Mean Change (SE)	7.27 (1.06)	9.06 (1.13)		
Week 52: Adjusted Mean Change (SE)	8.20 (1.13)	10.68 (1.14)	-2.48 [-5.64; 0.68]	0.124
Week 100: Adjusted Mean Change (SE)	7.58 (1.26)	8.91 (1.29)	-1.33 [-4.89; 2.22]	0.461
≥ 65 years				
N'/ N	85 / 85	94 / 94		
Baseline Mean (SD)	76.63 (17.43)	78.85 (12.99)		
Week 52 Mean (SD)	83.48 (13.19)	83.01 (12.30)		
Week 100 Mean (SD)	81.41 (13.47)	81.25 (14.67)		
Week 28: Adjusted Mean Change (SE)	4.04 (1.19)	6.17 (1.15)		
Week 52: Adjusted Mean Change (SE)	5.71 (1.25)	5.41 (1.19)	0.30 [-3.10; 3.69]	0.864
Week 100: Adjusted Mean Change (SE)	4.50 (1.38)	3.93 (1.34)	0.58 [-3.21; 4.37]	0.765
KITE: Composite Score				
Interaction test	p=0.905			
< 65 years				
N'/ N	100 / 100	102 / 102		
Baseline Mean (SD)	78.93 (13.64)	76.91 (17.45)		
Week 52 Mean (SD)	87.32 (11.79)	83.45 (15.91)		
Week 100 Mean (SD)	89.45 (10.54)	85.40 (14.17)		
Week 28: Adjusted Mean Change (SE)	6.68 (1.02)	6.48 (1.01)		
Week 52: Adjusted Mean Change (SE)	8.76 (1.12)	6.27 (1.08)	2.49 [-0.57; 5.55]	0.111
Week 100: Adjusted Mean Change (SE)	10.07 (1.30)	7.38 (1.21)	2.69 [-0.81; 6.19]	0.131

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 65 years				
N'/ N	78 / 79	79 / 79		
Baseline Mean (SD)	76.40 (16.54)	75.89 (18.05)		
Week 52 Mean (SD)	85.49 (14.10)	83.66 (15.45)		
Week 100 Mean (SD)	86.42 (13.74)	82.06 (16.81)		
Week 28: Adjusted Mean Change (SE)	4.40 (1.16)	5.10 (1.16)		
Week 52: Adjusted Mean Change (SE)	8.75 (1.22)	6.36 (1.22)	2.39 [-1.01; 5.79]	0.167
Week 100: Adjusted Mean Change (SE)	7.52 (1.44)	4.53 (1.45)	2.99 [-1.03; 7.01]	0.144
Pooled Analysis: Composite Score				
Interaction test	p=0.590			
< 65 years				
N'/ N	203 / 204	195 / 195		
Baseline Mean (SD)	77.77 (15.76)	75.88 (16.69)		
Week 52 Mean (SD)	86.80 (13.17)	85.27 (14.16)		
Week 100 Mean (SD)	86.84 (13.88)	85.33 (14.03)		
Week 28: Adjusted Mean Change (SE)	7.02 (0.75)	7.82 (0.76)		
Week 52: Adjusted Mean Change (SE)	8.49 (0.80)	8.52 (0.79)	-0.03 [-2.24; 2.18]	0.979
Week 100: Adjusted Mean Change (SE)	8.83 (0.90)	8.21 (0.88)	0.62 [-1.85; 3.09]	0.623

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 65 years				
N'/ N	163 / 164	173 / 173		
Baseline Mean (SD)	76.52 (16.96)	77.50 (15.53)		
Week 52 Mean (SD)	84.48 (13.64)	83.32 (13.83)		
Week 100 Mean (SD)	83.77 (13.77)	81.62 (15.63)		
Week 28: Adjusted Mean Change (SE)	4.23 (0.84)	5.53 (0.82)		
Week 52: Adjusted Mean Change (SE)	7.20 (0.88)	5.76 (0.86)	1.43 [-0.98; 3.85]	0.244
Week 100: Adjusted Mean Change (SE)	5.99 (0.99)	4.06 (0.98)	1.93 [-0.80; 4.67]	0.166
General Vision				
Test of heterogeneity in main analysis: **p_H=0.762**				
KESTREL: General Vision				
Interaction test	p=0.563			
< 65 years				
N'/ N	103 / 104	93 / 93		
Baseline Mean (SD)	60.97 (18.87)	60.22 (13.99)		
Week 52 Mean (SD)	74.15 (14.57)	73.49 (11.73)		
Week 100 Mean (SD)	74.87 (15.93)	75.26 (11.25)		
Week 28: Adjusted Mean Change (SE)	12.37 (1.30)	11.63 (1.37)		
Week 52: Adjusted Mean Change (SE)	13.06 (1.38)	12.64 (1.38)	0.42 [-3.42; 4.27]	0.828
Week 100: Adjusted Mean Change (SE)	14.43 (1.39)	14.36 (1.41)	0.07 [-3.82; 3.96]	0.971
≥ 65 years				
N'/ N	85 / 85	94 / 94		
Baseline Mean (SD)	61.65 (15.19)	60.21 (15.38)		
Week 52 Mean (SD)	71.64 (13.55)	68.53 (13.63)		
Week 100 Mean (SD)	72.12 (13.53)	69.14 (12.13)		
Week 28: Adjusted Mean Change (SE)	10.26 (1.45)	9.65 (1.40)		
Week 52: Adjusted Mean Change (SE)	10.30 (1.53)	8.39 (1.45)	1.91 [-2.24; 6.06]	0.366
Week 100: Adjusted Mean Change (SE)	11.39 (1.51)	8.99 (1.47)	2.39 [-1.75; 6.54]	0.257

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Vision				
Interaction test	p=0.688			
< 65 years				
N'/ N	100 / 100	102 / 102		
Baseline Mean (SD)	62.20 (16.79)	60.98 (19.58)		
Week 52 Mean (SD)	73.59 (14.23)	70.60 (18.83)		
Week 100 Mean (SD)	75.00 (13.74)	71.49 (16.60)		
Week 28: Adjusted Mean Change (SE)	11.01 (1.37)	11.28 (1.36)		
Week 52: Adjusted Mean Change (SE)	12.26 (1.55)	10.08 (1.50)	2.19 [-2.05; 6.42]	0.311
Week 100: Adjusted Mean Change (SE)	13.66 (1.60)	10.35 (1.47)	3.31 [-0.97; 7.58]	0.129
≥ 65 years				
N'/ N	78 / 79	79 / 79		
Baseline Mean (SD)	61.28 (15.23)	58.48 (16.57)		
Week 52 Mean (SD)	71.82 (14.87)	70.45 (14.92)		
Week 100 Mean (SD)	72.20 (13.90)	69.15 (16.33)		
Week 28: Adjusted Mean Change (SE)	7.20 (1.56)	7.28 (1.56)		
Week 52: Adjusted Mean Change (SE)	10.92 (1.69)	10.38 (1.69)	0.54 [-4.15; 5.24]	0.820
Week 100: Adjusted Mean Change (SE)	10.34 (1.77)	8.50 (1.77)	1.85 [-3.08; 6.77]	0.462
Pooled Analysis: General Vision				
Interaction test	p=0.935			
< 65 years				
N'/ N	203 / 204	195 / 195		
Baseline Mean (SD)	61.58 (17.84)	60.62 (17.10)		
Week 52 Mean (SD)	73.88 (14.36)	72.05 (15.71)		
Week 100 Mean (SD)	74.93 (14.87)	73.25 (14.44)		
Week 28: Adjusted Mean Change (SE)	11.73 (0.95)	11.53 (0.97)		
Week 52: Adjusted Mean Change (SE)	12.68 (1.04)	11.36 (1.03)	1.32 [-1.55; 4.19]	0.366
Week 100: Adjusted Mean Change (SE)	14.10 (1.05)	12.29 (1.02)	1.80 [-1.07; 4.68]	0.218
≥ 65 years				
N'/ N	163 / 164	173 / 173		
Baseline Mean (SD)	61.47 (15.16)	59.42 (15.91)		
Week 52 Mean (SD)	71.73 (14.17)	69.44 (14.23)		
Week 100 Mean (SD)	72.16 (13.65)	69.15 (14.14)		
Week 28: Adjusted Mean Change (SE)	8.73 (1.07)	8.45 (1.05)		
Week 52: Adjusted Mean Change (SE)	10.57 (1.14)	9.31 (1.11)	1.27 [-1.87; 4.40]	0.428
Week 100: Adjusted Mean Change (SE)	10.91 (1.16)	8.73 (1.14)	2.18 [-1.01; 5.36]	0.180

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Ocular Pain				
Test of heterogeneity in main analysis: **p_H=0.664**				
KESTREL: Ocular Pain				
Interaction test	p=0.800			
< 65 years				
N'/ N	103 / 104	93 / 93		
Baseline Mean (SD)	84.83 (19.62)	81.99 (21.37)		
Week 52 Mean (SD)	89.18 (16.64)	88.40 (15.22)		
Week 100 Mean (SD)	88.14 (17.89)	85.20 (19.12)		
Week 28: Adjusted Mean Change (SE)	4.06 (1.77)	4.18 (1.87)		
Week 52: Adjusted Mean Change (SE)	5.27 (1.64)	6.00 (1.65)	-0.72 [-5.30; 3.86]	0.757
Week 100: Adjusted Mean Change (SE)	4.85 (1.82)	3.00 (1.85)	1.85 [-3.24; 6.95]	0.475
≥ 65 years				
N'/ N	85 / 85	94 / 94		
Baseline Mean (SD)	81.62 (20.28)	82.31 (19.69)		
Week 52 Mean (SD)	87.87 (14.91)	84.83 (17.11)		
Week 100 Mean (SD)	83.52 (16.72)	82.68 (21.52)		
Week 28: Adjusted Mean Change (SE)	1.28 (1.98)	4.67 (1.90)		
Week 52: Adjusted Mean Change (SE)	4.69 (1.82)	2.71 (1.72)	1.98 [-2.95; 6.91]	0.430
Week 100: Adjusted Mean Change (SE)	0.89 (1.98)	0.60 (1.92)	0.29 [-5.13; 5.72]	0.916
KITE: Ocular Pain				
Interaction test	p=0.606			
< 65 years				
N'/ N	100 / 100	102 / 102		
Baseline Mean (SD)	85.13 (17.83)	83.82 (19.63)		
Week 52 Mean (SD)	87.98 (17.96)	88.40 (16.77)		
Week 100 Mean (SD)	91.32 (15.37)	90.52 (15.13)		
Week 28: Adjusted Mean Change (SE)	4.39 (1.57)	3.97 (1.56)		
Week 52: Adjusted Mean Change (SE)	3.59 (1.67)	4.09 (1.62)	-0.50 [-5.08; 4.09]	0.831
Week 100: Adjusted Mean Change (SE)	6.53 (1.71)	5.94 (1.56)	0.59 [-3.96; 5.13]	0.800

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 65 years				
N'/ N	78 / 79	79 / 79		
Baseline Mean (SD)	83.17 (18.22)	80.70 (21.72)		
Week 52 Mean (SD)	89.77 (14.86)	86.01 (19.03)		
Week 100 Mean (SD)	89.19 (15.48)	87.29 (17.90)		
Week 28: Adjusted Mean Change (SE)	4.38 (1.79)	3.54 (1.79)		
Week 52: Adjusted Mean Change (SE)	6.14 (1.82)	3.32 (1.82)	2.82 [-2.25; 7.88]	0.275
Week 100: Adjusted Mean Change (SE)	5.37 (1.88)	4.63 (1.88)	0.74 [-4.49; 5.98]	0.781
Pooled Analysis: Ocular Pain				
Interaction test	p=0.838			
< 65 years				
N'/ N	203 / 204	195 / 195		
Baseline Mean (SD)	84.98 (18.71)	82.95 (20.45)		
Week 52 Mean (SD)	88.59 (17.25)	88.40 (15.96)		
Week 100 Mean (SD)	89.67 (16.75)	88.04 (17.26)		
Week 28: Adjusted Mean Change (SE)	4.19 (1.19)	4.07 (1.22)		
Week 52: Adjusted Mean Change (SE)	4.46 (1.18)	5.08 (1.16)	-0.62 [-3.87; 2.62]	0.706
Week 100: Adjusted Mean Change (SE)	5.70 (1.24)	4.58 (1.20)	1.13 [-2.26; 4.52]	0.514
≥ 65 years				
N'/ N	163 / 164	173 / 173		
Baseline Mean (SD)	82.36 (19.28)	81.58 (20.60)		
Week 52 Mean (SD)	88.82 (14.86)	85.39 (17.99)		
Week 100 Mean (SD)	86.20 (16.33)	84.79 (20.01)		
Week 28: Adjusted Mean Change (SE)	2.80 (1.34)	4.12 (1.31)		
Week 52: Adjusted Mean Change (SE)	5.41 (1.29)	2.95 (1.26)	2.46 [-1.08; 6.00]	0.173
Week 100: Adjusted Mean Change (SE)	3.06 (1.36)	2.42 (1.34)	0.64 [-3.11; 4.39]	0.738

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.450**				
KESTREL: Near Activities				
Interaction test	p=0.752			
< 65 years				
N'/ N	103 / 104	93 / 93		
Baseline Mean (SD)	63.63 (26.21)	64.20 (20.86)		
Week 52 Mean (SD)	81.20 (21.27)	82.98 (18.34)		
Week 100 Mean (SD)	83.12 (21.01)	79.39 (20.21)		
Week 28: Adjusted Mean Change (SE)	14.10 (1.82)	15.52 (1.92)		
Week 52: Adjusted Mean Change (SE)	14.78 (2.01)	17.80 (2.03)	-3.02 [-8.63; 2.59]	0.291
Week 100: Adjusted Mean Change (SE)	17.56 (1.97)	14.07 (2.02)	3.49 [-2.06; 9.03]	0.217
≥ 65 years				
N'/ N	85 / 85	94 / 94		
Baseline Mean (SD)	63.33 (26.23)	67.07 (22.75)		
Week 52 Mean (SD)	76.80 (21.30)	73.94 (21.02)		
Week 100 Mean (SD)	75.25 (19.77)	74.40 (21.91)		
Week 28: Adjusted Mean Change (SE)	10.23 (2.03)	12.80 (1.96)		
Week 52: Adjusted Mean Change (SE)	11.60 (2.23)	8.73 (2.12)	2.86 [-3.18; 8.91]	0.352
Week 100: Adjusted Mean Change (SE)	10.82 (2.16)	9.01 (2.09)	1.81 [-4.11; 7.72]	0.549
KITE: Near Activities				
Interaction test	p=0.903			
< 65 years				
N'/ N	99 / 100	102 / 102		
Baseline Mean (SD)	71.21 (22.21)	69.49 (23.32)		
Week 52 Mean (SD)	80.13 (20.55)	77.96 (22.85)		
Week 100 Mean (SD)	85.30 (16.81)	79.21 (24.11)		
Week 28: Adjusted Mean Change (SE)	8.03 (1.84)	6.49 (1.81)		
Week 52: Adjusted Mean Change (SE)	9.07 (1.88)	8.74 (1.82)	0.34 [-4.82; 5.49]	0.898
Week 100: Adjusted Mean Change (SE)	13.75 (2.03)	9.01 (1.88)	4.74 [-0.71; 10.19]	0.088

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 65 years				
N'/ N	78 / 79	79 / 79		
Baseline Mean (SD)	68.80 (22.69)	69.30 (24.74)		
Week 52 Mean (SD)	80.05 (20.92)	79.48 (21.23)		
Week 100 Mean (SD)	82.13 (20.75)	76.27 (21.54)		
Week 28: Adjusted Mean Change (SE)	4.08 (2.08)	5.16 (2.07)		
Week 52: Adjusted Mean Change (SE)	11.48 (2.06)	9.31 (2.05)	2.18 [-3.54; 7.90]	0.454
Week 100: Adjusted Mean Change (SE)	9.89 (2.25)	5.56 (2.25)	4.33 [-1.93; 10.59]	0.175
Pooled Analysis: Near Activities				
Interaction test	p=0.880			
< 65 years				
N'/ N	202 / 204	195 / 195		
Baseline Mean (SD)	67.35 (24.57)	66.97 (22.28)		
Week 52 Mean (SD)	80.68 (20.86)	80.47 (20.81)		
Week 100 Mean (SD)	84.17 (19.08)	79.29 (22.31)		
Week 28: Adjusted Mean Change (SE)	11.24 (1.31)	10.96 (1.34)		
Week 52: Adjusted Mean Change (SE)	12.01 (1.39)	13.27 (1.38)	-1.26 [-5.11; 2.59]	0.521
Week 100: Adjusted Mean Change (SE)	15.78 (1.41)	11.65 (1.38)	4.13 [0.26; 8.01]	0.037 *
≥ 65 years				
N'/ N	163 / 164	173 / 173		
Baseline Mean (SD)	65.95 (24.68)	68.09 (23.64)		
Week 52 Mean (SD)	78.41 (21.10)	76.56 (21.23)		
Week 100 Mean (SD)	78.50 (20.45)	75.26 (21.68)		
Week 28: Adjusted Mean Change (SE)	7.30 (1.47)	8.97 (1.44)		
Week 52: Adjusted Mean Change (SE)	11.56 (1.54)	8.88 (1.49)	2.68 [-1.52; 6.89]	0.211
Week 100: Adjusted Mean Change (SE)	10.37 (1.56)	7.18 (1.53)	3.19 [-1.10; 7.48]	0.144

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Distance Activities				
Test of heterogeneity in main analysis: **p_H=0.046 ***				
KESTREL: Distance Activities				
Interaction test	p=0.979			
< 65 years				
N'/ N	103 / 104	93 / 93		
Baseline Mean (SD)	74.68 (24.58)	74.46 (21.54)		
Week 52 Mean (SD)	87.55 (16.15)	88.65 (14.08)		
Week 100 Mean (SD)	84.29 (19.73)	86.07 (17.18)		
Week 28: Adjusted Mean Change (SE)	9.52 (1.60)	10.53 (1.69)		
Week 52: Adjusted Mean Change (SE)	11.52 (1.54)	12.91 (1.55)	-1.39 [-5.69; 2.91]	0.525
Week 100: Adjusted Mean Change (SE)	9.31 (1.70)	9.85 (1.74)	-0.53 [-5.32; 4.25]	0.827
≥ 65 years				
N'/ N	85 / 85	94 / 94		
Baseline Mean (SD)	75.98 (23.03)	76.24 (20.82)		
Week 52 Mean (SD)	82.77 (18.20)	81.11 (19.17)		
Week 100 Mean (SD)	78.85 (19.91)	80.06 (19.81)		
Week 28: Adjusted Mean Change (SE)	4.93 (1.79)	7.01 (1.72)		
Week 52: Adjusted Mean Change (SE)	6.03 (1.71)	5.52 (1.62)	0.51 [-4.11; 5.13]	0.828
Week 100: Adjusted Mean Change (SE)	3.39 (1.86)	4.97 (1.80)	-1.58 [-6.68; 3.51]	0.542
KITE: Distance Activities				
Interaction test	p=0.845			
< 65 years				
N'/ N	100 / 100	102 / 102		
Baseline Mean (SD)	78.54 (20.99)	76.88 (22.14)		
Week 52 Mean (SD)	89.37 (15.51)	85.34 (18.13)		
Week 100 Mean (SD)	90.91 (13.16)	85.73 (17.57)		
Week 28: Adjusted Mean Change (SE)	8.15 (1.60)	6.32 (1.58)		
Week 52: Adjusted Mean Change (SE)	11.89 (1.54)	8.88 (1.49)	3.01 [-1.19; 7.22]	0.160
Week 100: Adjusted Mean Change (SE)	12.91 (1.67)	8.48 (1.55)	4.43 [-0.06; 8.92]	0.053

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 65 years				
N'/ N	78 / 79	79 / 79		
Baseline Mean (SD)	74.79 (22.02)	75.32 (22.93)		
Week 52 Mean (SD)	86.24 (19.56)	83.21 (19.49)		
Week 100 Mean (SD)	87.08 (18.63)	81.00 (20.33)		
Week 28: Adjusted Mean Change (SE)	3.49 (1.82)	3.95 (1.81)		
Week 52: Adjusted Mean Change (SE)	10.38 (1.68)	6.83 (1.67)	3.56 [-1.10; 8.22]	0.134
Week 100: Adjusted Mean Change (SE)	9.16 (1.85)	4.55 (1.86)	4.61 [-0.55; 9.77]	0.080
Pooled Analysis: Distance Activities				
Interaction test	p=0.866			
< 65 years				
N'/ N	203 / 204	195 / 195		
Baseline Mean (SD)	76.58 (22.91)	75.73 (21.83)		
Week 52 Mean (SD)	88.44 (15.82)	87.00 (16.27)		
Week 100 Mean (SD)	87.47 (17.17)	85.89 (17.34)		
Week 28: Adjusted Mean Change (SE)	8.90 (1.14)	8.44 (1.17)		
Week 52: Adjusted Mean Change (SE)	11.77 (1.09)	10.93 (1.08)	0.84 [-2.17; 3.86]	0.583
Week 100: Adjusted Mean Change (SE)	11.09 (1.19)	9.23 (1.16)	1.86 [-1.40; 5.12]	0.263
≥ 65 years				
N'/ N	163 / 164	173 / 173		
Baseline Mean (SD)	75.41 (22.49)	75.82 (21.75)		
Week 52 Mean (SD)	84.49 (18.90)	82.10 (19.28)		
Week 100 Mean (SD)	82.73 (19.68)	80.49 (19.98)		
Week 28: Adjusted Mean Change (SE)	4.21 (1.29)	5.48 (1.26)		
Week 52: Adjusted Mean Change (SE)	8.11 (1.20)	6.09 (1.17)	2.02 [-1.27; 5.31]	0.229
Week 100: Adjusted Mean Change (SE)	6.14 (1.31)	4.70 (1.29)	1.44 [-2.17; 5.05]	0.434

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.023 ***				
KESTREL: Social Functioning				
Interaction test	p=0.247			
< 65 years				
N'/ N	103 / 104	93 / 93		
Baseline Mean (SD)	88.35 (20.13)	88.71 (17.78)		
Week 52 Mean (SD)	93.75 (15.12)	95.58 (11.18)		
Week 100 Mean (SD)	90.54 (18.15)	93.09 (14.05)		
Week 28: Adjusted Mean Change (SE)	2.06 (1.22)	6.42 (1.29)		
Week 52: Adjusted Mean Change (SE)	3.88 (1.39)	6.01 (1.40)	-2.13 [-6.02; 1.75]	0.281
Week 100: Adjusted Mean Change (SE)	1.85 (1.67)	3.68 (1.70)	-1.82 [-6.51; 2.86]	0.444
≥ 65 years				
N'/ N	85 / 85	94 / 94		
Baseline Mean (SD)	89.41 (17.41)	90.96 (13.14)		
Week 52 Mean (SD)	91.04 (14.73)	91.67 (15.42)		
Week 100 Mean (SD)	90.72 (15.86)	90.54 (15.85)		
Week 28: Adjusted Mean Change (SE)	1.14 (1.36)	1.37 (1.31)		
Week 52: Adjusted Mean Change (SE)	0.66 (1.54)	1.58 (1.46)	-0.93 [-5.10; 3.25]	0.663
Week 100: Adjusted Mean Change (SE)	1.20 (1.82)	0.68 (1.77)	0.52 [-4.47; 5.52]	0.837
KITE: Social Functioning				
Interaction test	p=0.731			
< 65 years				
N'/ N	100 / 100	102 / 102		
Baseline Mean (SD)	89.63 (16.09)	88.36 (18.30)		
Week 52 Mean (SD)	94.87 (11.99)	91.42 (14.60)		
Week 100 Mean (SD)	97.05 (9.02)	93.10 (15.46)		
Week 28: Adjusted Mean Change (SE)	4.15 (1.41)	3.15 (1.40)		
Week 52: Adjusted Mean Change (SE)	6.35 (1.24)	3.65 (1.20)	2.70 [-0.69; 6.08]	0.118
Week 100: Adjusted Mean Change (SE)	8.34 (1.56)	4.95 (1.43)	3.39 [-0.77; 7.54]	0.110

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 65 years				
N'/ N	78 / 79	79 / 79		
Baseline Mean (SD)	86.86 (18.78)	83.86 (21.76)		
Week 52 Mean (SD)	95.45 (11.94)	91.79 (15.01)		
Week 100 Mean (SD)	92.58 (17.85)	88.35 (18.55)		
Week 28: Adjusted Mean Change (SE)	3.12 (1.60)	4.75 (1.60)		
Week 52: Adjusted Mean Change (SE)	8.61 (1.35)	5.17 (1.34)	3.44 [-0.30; 7.17]	0.071
Week 100: Adjusted Mean Change (SE)	4.90 (1.72)	1.85 (1.72)	3.05 [-1.73; 7.84]	0.210
Pooled Analysis: Social Functioning				
Interaction test	p=0.492			
< 65 years				
N'/ N	203 / 204	195 / 195		
Baseline Mean (SD)	88.98 (18.22)	88.53 (18.01)		
Week 52 Mean (SD)	94.30 (13.65)	93.48 (13.14)		
Week 100 Mean (SD)	93.67 (14.82)	93.10 (14.77)		
Week 28: Adjusted Mean Change (SE)	3.13 (0.93)	4.73 (0.96)		
Week 52: Adjusted Mean Change (SE)	5.14 (0.94)	4.84 (0.92)	0.30 [-2.29; 2.88]	0.821
Week 100: Adjusted Mean Change (SE)	5.05 (1.15)	4.38 (1.11)	0.67 [-2.46; 3.79]	0.675
≥ 65 years				
N'/ N	163 / 164	173 / 173		
Baseline Mean (SD)	88.19 (18.07)	87.72 (17.91)		
Week 52 Mean (SD)	93.23 (13.55)	91.73 (15.17)		
Week 100 Mean (SD)	91.60 (16.78)	89.53 (17.10)		
Week 28: Adjusted Mean Change (SE)	2.13 (1.05)	2.88 (1.03)		
Week 52: Adjusted Mean Change (SE)	4.60 (1.03)	3.20 (1.00)	1.40 [-1.41; 4.21]	0.329
Week 100: Adjusted Mean Change (SE)	3.04 (1.26)	1.13 (1.24)	1.91 [-1.55; 5.37]	0.279

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Mental Health				
Test of heterogeneity in main analysis: **p_H=0.200**				
KESTREL: Mental Health				
Interaction test	p=0.417			
< 65 years				
N'/ N	103 / 104	93 / 93		
Baseline Mean (SD)	64.26 (25.22)	62.23 (25.96)		
Week 52 Mean (SD)	78.66 (20.25)	78.61 (18.70)		
Week 100 Mean (SD)	75.56 (20.99)	78.95 (19.76)		
Week 28: Adjusted Mean Change (SE)	8.37 (1.72)	10.38 (1.82)		
Week 52: Adjusted Mean Change (SE)	11.30 (1.79)	13.42 (1.80)	-2.12 [-7.11; 2.87]	0.403
Week 100: Adjusted Mean Change (SE)	10.41 (2.04)	14.09 (2.08)	-3.68 [-9.41; 2.05]	0.207
≥ 65 years				
N'/ N	85 / 85	94 / 94		
Baseline Mean (SD)	67.06 (24.63)	74.20 (17.94)		
Week 52 Mean (SD)	77.99 (19.77)	78.75 (17.04)		
Week 100 Mean (SD)	74.05 (22.15)	76.16 (23.12)		
Week 28: Adjusted Mean Change (SE)	6.46 (1.92)	8.00 (1.86)		
Week 52: Adjusted Mean Change (SE)	9.64 (1.98)	8.53 (1.89)	1.11 [-4.27; 6.49]	0.685
Week 100: Adjusted Mean Change (SE)	6.82 (2.23)	6.90 (2.17)	-0.09 [-6.20; 6.03]	0.978
KITE: Mental Health				
Interaction test	p=0.968			
< 65 years				
N'/ N	100 / 100	102 / 102		
Baseline Mean (SD)	70.00 (19.56)	64.15 (26.95)		
Week 52 Mean (SD)	80.93 (19.61)	75.00 (25.36)		
Week 100 Mean (SD)	85.24 (14.55)	79.60 (21.99)		
Week 28: Adjusted Mean Change (SE)	9.32 (1.72)	9.62 (1.71)		
Week 52: Adjusted Mean Change (SE)	11.61 (2.10)	8.78 (2.04)	2.84 [-2.93; 8.61]	0.334
Week 100: Adjusted Mean Change (SE)	14.94 (2.12)	12.01 (1.97)	2.93 [-2.76; 8.61]	0.312

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 65 years				
N'/ N	78 / 79	79 / 79		
Baseline Mean (SD)	67.55 (23.94)	67.88 (24.75)		
Week 52 Mean (SD)	81.91 (22.09)	78.82 (21.18)		
Week 100 Mean (SD)	82.94 (17.86)	79.66 (22.82)		
Week 28: Adjusted Mean Change (SE)	7.12 (1.95)	8.01 (1.95)		
Week 52: Adjusted Mean Change (SE)	13.83 (2.30)	9.55 (2.29)	4.28 [-2.11; 10.67]	0.189
Week 100: Adjusted Mean Change (SE)	12.12 (2.34)	10.44 (2.35)	1.68 [-4.84; 8.20]	0.612
Pooled Analysis: Mental Health				
Interaction test	p=0.589			
< 65 years				
N'/ N	203 / 204	195 / 195		
Baseline Mean (SD)	67.09 (22.74)	63.24 (26.43)		
Week 52 Mean (SD)	79.77 (19.91)	76.81 (22.29)		
Week 100 Mean (SD)	80.21 (18.76)	79.29 (20.92)		
Week 28: Adjusted Mean Change (SE)	8.88 (1.21)	10.03 (1.25)		
Week 52: Adjusted Mean Change (SE)	11.49 (1.38)	11.07 (1.37)	0.42 [-3.39; 4.23]	0.829
Week 100: Adjusted Mean Change (SE)	12.70 (1.47)	13.00 (1.43)	-0.30 [-4.32; 3.73]	0.885
≥ 65 years				
N'/ N	163 / 164	173 / 173		
Baseline Mean (SD)	67.29 (24.23)	71.32 (21.49)		
Week 52 Mean (SD)	79.93 (20.97)	78.79 (19.04)		
Week 100 Mean (SD)	78.25 (20.65)	77.76 (22.96)		
Week 28: Adjusted Mean Change (SE)	6.80 (1.37)	7.92 (1.34)		
Week 52: Adjusted Mean Change (SE)	11.72 (1.52)	8.94 (1.48)	2.77 [-1.38; 6.93]	0.190
Week 100: Adjusted Mean Change (SE)	9.46 (1.62)	8.49 (1.59)	0.96 [-3.49; 5.41]	0.672

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.132**				
KESTREL: Role Difficulties				
Interaction test	p=0.163			
< 65 years				
N'/ N	103 / 104	93 / 93		
Baseline Mean (SD)	72.09 (28.72)	67.07 (27.57)		
Week 52 Mean (SD)	81.86 (24.78)	84.64 (23.13)		
Week 100 Mean (SD)	82.37 (26.91)	83.88 (22.71)		
Week 28: Adjusted Mean Change (SE)	7.20 (2.14)	11.53 (2.27)		
Week 52: Adjusted Mean Change (SE)	7.56 (2.38)	13.71 (2.40)	-6.16 [-12.82; 0.50]	0.070
Week 100: Adjusted Mean Change (SE)	9.67 (2.45)	13.00 (2.50)	-3.33 [-10.21; 3.55]	0.342
≥ 65 years				
N'/ N	85 / 85	94 / 94		
Baseline Mean (SD)	71.91 (28.67)	76.46 (24.99)		
Week 52 Mean (SD)	79.29 (26.07)	81.50 (22.55)		
Week 100 Mean (SD)	80.49 (24.43)	75.18 (27.29)		
Week 28: Adjusted Mean Change (SE)	4.27 (2.40)	6.17 (2.32)		
Week 52: Adjusted Mean Change (SE)	5.44 (2.64)	7.70 (2.51)	-2.27 [-9.43; 4.90]	0.534
Week 100: Adjusted Mean Change (SE)	8.44 (2.68)	1.77 (2.59)	6.67 [-0.67; 14.00]	0.075
KITE: Role Difficulties				
Interaction test	p=0.908			
< 65 years				
N'/ N	100 / 100	102 / 102		
Baseline Mean (SD)	72.00 (25.45)	65.20 (30.85)		
Week 52 Mean (SD)	85.74 (19.92)	77.86 (26.50)		
Week 100 Mean (SD)	86.28 (22.12)	82.18 (23.78)		
Week 28: Adjusted Mean Change (SE)	9.27 (2.11)	10.47 (2.10)		
Week 52: Adjusted Mean Change (SE)	14.67 (2.29)	9.33 (2.21)	5.34 [-0.93; 11.60]	0.095
Week 100: Adjusted Mean Change (SE)	13.28 (2.51)	12.67 (2.33)	0.61 [-6.14; 7.36]	0.859

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 65 years				
N'/ N	78 / 79	79 / 79		
Baseline Mean (SD)	69.87 (29.57)	69.78 (27.20)		
Week 52 Mean (SD)	79.55 (23.88)	78.54 (23.82)		
Week 100 Mean (SD)	83.47 (23.83)	77.54 (27.34)		
Week 28: Adjusted Mean Change (SE)	4.90 (2.40)	5.13 (2.39)		
Week 52: Adjusted Mean Change (SE)	9.31 (2.50)	7.18 (2.49)	2.14 [-4.79; 9.07]	0.545
Week 100: Adjusted Mean Change (SE)	10.01 (2.78)	5.84 (2.79)	4.17 [-3.58; 11.91]	0.291
Pooled Analysis: Role Difficulties				
Interaction test	p=0.247			
< 65 years				
N'/ N	203 / 204	195 / 195		
Baseline Mean (SD)	72.04 (27.09)	66.09 (29.27)		
Week 52 Mean (SD)	83.75 (22.55)	81.25 (25.03)		
Week 100 Mean (SD)	84.25 (24.72)	82.98 (23.23)		
Week 28: Adjusted Mean Change (SE)	8.22 (1.51)	11.00 (1.55)		
Week 52: Adjusted Mean Change (SE)	11.03 (1.65)	11.56 (1.63)	-0.52 [-5.08; 4.04]	0.822
Week 100: Adjusted Mean Change (SE)	11.48 (1.75)	12.87 (1.70)	-1.40 [-6.19; 3.39]	0.567
≥ 65 years				
N'/ N	163 / 164	173 / 173		
Baseline Mean (SD)	70.94 (29.03)	73.41 (26.16)		
Week 52 Mean (SD)	79.42 (24.91)	80.11 (23.12)		
Week 100 Mean (SD)	81.90 (24.10)	76.26 (27.24)		
Week 28: Adjusted Mean Change (SE)	4.64 (1.70)	5.60 (1.67)		
Week 52: Adjusted Mean Change (SE)	7.37 (1.82)	7.38 (1.77)	-0.01 [-4.98; 4.97]	0.998
Week 100: Adjusted Mean Change (SE)	9.31 (1.92)	3.58 (1.89)	5.73 [0.44; 11.03]	0.034 *

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Dependency				
Test of heterogeneity in main analysis: **p_H=0.019 ***				
KESTREL: Dependency				
Interaction test	p=0.458			
< 65 years				
N'/ N	103 / 104	93 / 93		
Baseline Mean (SD)	82.28 (25.80)	78.67 (26.59)		
Week 52 Mean (SD)	90.04 (20.09)	91.77 (18.93)		
Week 100 Mean (SD)	86.54 (22.60)	90.46 (19.71)		
Week 28: Adjusted Mean Change (SE)	6.55 (1.84)	8.59 (1.95)		
Week 52: Adjusted Mean Change (SE)	6.19 (1.94)	9.34 (1.96)	-3.15 [-8.57; 2.26]	0.253
Week 100: Adjusted Mean Change (SE)	4.07 (2.17)	8.65 (2.21)	-4.58 [-10.67; 1.51]	0.140
≥ 65 years				
N'/ N	85 / 85	94 / 94		
Baseline Mean (SD)	80.59 (27.20)	86.79 (19.98)		
Week 52 Mean (SD)	87.69 (23.98)	92.33 (14.74)		
Week 100 Mean (SD)	85.73 (22.49)	86.19 (22.20)		
Week 28: Adjusted Mean Change (SE)	4.58 (2.06)	4.87 (1.99)		
Week 52: Adjusted Mean Change (SE)	4.73 (2.15)	8.10 (2.04)	-3.37 [-9.20; 2.46]	0.256
Week 100: Adjusted Mean Change (SE)	3.22 (2.37)	2.15 (2.30)	1.07 [-5.42; 7.56]	0.745
KITE: Dependency				
Interaction test	p=0.273			
< 65 years				
N'/ N	100 / 100	102 / 102		
Baseline Mean (SD)	85.08 (21.75)	82.52 (26.93)		
Week 52 Mean (SD)	92.95 (16.40)	85.34 (23.70)		
Week 100 Mean (SD)	94.21 (13.24)	88.51 (22.95)		
Week 28: Adjusted Mean Change (SE)	6.76 (1.72)	2.27 (1.70)		
Week 52: Adjusted Mean Change (SE)	8.07 (1.89)	1.77 (1.83)	6.30 [1.12; 11.48]	0.017 *
Week 100: Adjusted Mean Change (SE)	7.73 (2.07)	3.68 (1.92)	4.05 [-1.49; 9.60]	0.151

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 65 years				
N'/ N	78 / 79	79 / 79		
Baseline Mean (SD)	81.30 (25.67)	81.12 (27.21)		
Week 52 Mean (SD)	88.89 (21.99)	88.43 (21.47)		
Week 100 Mean (SD)	91.67 (16.01)	85.73 (23.06)		
Week 28: Adjusted Mean Change (SE)	3.29 (1.95)	4.04 (1.95)		
Week 52: Adjusted Mean Change (SE)	6.20 (2.07)	4.57 (2.06)	1.63 [-4.11; 7.38]	0.577
Week 100: Adjusted Mean Change (SE)	5.17 (2.29)	1.69 (2.29)	3.48 [-2.89; 9.85]	0.283
Pooled Analysis: Dependency				
Interaction test	p=0.935			
< 65 years				
N'/ N	203 / 204	195 / 195		
Baseline Mean (SD)	83.66 (23.87)	80.68 (26.77)		
Week 52 Mean (SD)	91.46 (18.38)	88.55 (21.62)		
Week 100 Mean (SD)	90.22 (19.04)	89.42 (21.46)		
Week 28: Adjusted Mean Change (SE)	6.68 (1.27)	5.51 (1.30)		
Week 52: Adjusted Mean Change (SE)	7.13 (1.36)	5.65 (1.35)	1.49 [-2.28; 5.25]	0.439
Week 100: Adjusted Mean Change (SE)	5.95 (1.50)	6.30 (1.45)	-0.35 [-4.44; 3.75]	0.869
≥ 65 years				
N'/ N	163 / 164	173 / 173		
Baseline Mean (SD)	80.93 (26.40)	84.20 (23.66)		
Week 52 Mean (SD)	88.28 (22.94)	90.49 (18.26)		
Week 100 Mean (SD)	88.53 (19.85)	85.98 (22.51)		
Week 28: Adjusted Mean Change (SE)	4.02 (1.43)	4.21 (1.40)		
Week 52: Adjusted Mean Change (SE)	5.46 (1.50)	6.19 (1.46)	-0.73 [-4.84; 3.38]	0.726
Week 100: Adjusted Mean Change (SE)	4.35 (1.65)	1.68 (1.62)	2.67 [-1.86; 7.21]	0.247

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Driving				
Test of heterogeneity in main analysis: **p_H=0.792**				
KESTREL: Driving				
Interaction test	p=0.934			
< 65 years				
N'/ N	68 / 104	64 / 93		
Baseline Mean (SD)	79.29 (19.24)	75.91 (20.47)		
Week 52 Mean (SD)	87.21 (18.68)	88.30 (15.01)		
Week 100 Mean (SD)	86.48 (18.51)	83.18 (19.58)		
Week 28: Adjusted Mean Change (SE)	5.25 (1.79)	7.73 (1.85)		
Week 52: Adjusted Mean Change (SE)	6.04 (2.07)	9.81 (2.11)	-3.78 [-9.62; 2.06]	0.203
Week 100: Adjusted Mean Change (SE)	6.87 (2.32)	5.40 (2.34)	1.47 [-5.02; 7.96]	0.655
≥ 65 years				
N'/ N	52 / 85	56 / 94		
Baseline Mean (SD)	80.77 (17.89)	78.57 (18.84)		
Week 52 Mean (SD)	80.08 (21.48)	77.86 (20.70)		
Week 100 Mean (SD)	77.78 (19.52)	74.31 (23.93)		
Week 28: Adjusted Mean Change (SE)	-2.47 (2.16)	2.61 (2.24)		
Week 52: Adjusted Mean Change (SE)	0.09 (2.47)	0.26 (2.63)	-0.17 [-7.29; 6.95]	0.962
Week 100: Adjusted Mean Change (SE)	-4.15 (2.79)	-3.67 (3.02)	-0.49 [-8.59; 7.62]	0.906
KITE: Driving				
Interaction test	p=0.931			
< 65 years				
N'/ N	66 / 100	58 / 102		
Baseline Mean (SD)	78.66 (19.94)	81.90 (23.85)		
Week 52 Mean (SD)	90.12 (11.68)	90.12 (14.20)		
Week 100 Mean (SD)	87.41 (13.68)	89.13 (13.13)		
Week 28: Adjusted Mean Change (SE)	0.41 (1.78)	5.88 (1.91)		
Week 52: Adjusted Mean Change (SE)	8.42 (1.57)	5.87 (1.72)	2.55 [-2.05; 7.15]	0.275
Week 100: Adjusted Mean Change (SE)	5.01 (1.81)	3.75 (1.86)	1.25 [-3.87; 6.38]	0.630

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 65 years				
N'/ N	37 / 79	38 / 79		
Baseline Mean (SD)	79.62 (21.33)	82.35 (18.42)		
Week 52 Mean (SD)	81.11 (23.36)	84.85 (17.36)		
Week 100 Mean (SD)	84.44 (17.05)	83.91 (16.20)		
Week 28: Adjusted Mean Change (SE)	1.88 (2.49)	4.41 (2.43)		
Week 52: Adjusted Mean Change (SE)	1.31 (2.10)	3.00 (2.02)	-1.69 [-7.44; 4.05]	0.562
Week 100: Adjusted Mean Change (SE)	2.89 (2.32)	1.18 (2.33)	1.70 [-4.78; 8.19]	0.605
Pooled Analysis: Driving				
Interaction test	p=0.912			
< 65 years				
N'/ N	134 / 204	122 / 195		
Baseline Mean (SD)	78.98 (19.52)	78.76 (22.25)		
Week 52 Mean (SD)	88.62 (15.70)	89.08 (14.62)		
Week 100 Mean (SD)	86.92 (16.32)	85.94 (17.07)		
Week 28: Adjusted Mean Change (SE)	2.89 (1.27)	6.82 (1.34)		
Week 52: Adjusted Mean Change (SE)	7.27 (1.32)	8.05 (1.38)	-0.78 [-4.54; 2.98]	0.684
Week 100: Adjusted Mean Change (SE)	5.94 (1.50)	4.57 (1.53)	1.37 [-2.83; 5.58]	0.521
≥ 65 years				
N'/ N	89 / 164	94 / 173		
Baseline Mean (SD)	80.29 (19.29)	80.10 (18.67)		
Week 52 Mean (SD)	80.52 (22.14)	81.25 (19.34)		
Week 100 Mean (SD)	80.81 (18.60)	79.03 (20.89)		
Week 28: Adjusted Mean Change (SE)	-0.69 (1.64)	3.33 (1.65)		
Week 52: Adjusted Mean Change (SE)	0.80 (1.66)	1.46 (1.69)	-0.66 [-5.30; 3.99]	0.782
Week 100: Adjusted Mean Change (SE)	-0.90 (1.86)	-1.38 (1.94)	0.48 [-4.81; 5.77]	0.858

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Color Vision				
Test of heterogeneity in main analysis: **p_H=0.477**				
KESTREL: Color Vision				
Interaction test	p=0.962			
< 65 years				
N'/ N	103 / 104	92 / 93		
Baseline Mean (SD)	93.20 (15.73)	93.75 (16.42)		
Week 52 Mean (SD)	97.56 (10.10)	97.19 (9.74)		
Week 100 Mean (SD)	94.55 (13.15)	94.67 (14.41)		
Week 28: Adjusted Mean Change (SE)	2.11 (1.11)	1.76 (1.19)		
Week 52: Adjusted Mean Change (SE)	2.93 (1.16)	2.69 (1.18)	0.24 [-3.01; 3.49]	0.883
Week 100: Adjusted Mean Change (SE)	0.45 (1.37)	0.44 (1.40)	0.01 [-3.84; 3.87]	0.994
≥ 65 years				
N'/ N	83 / 85	92 / 94		
Baseline Mean (SD)	92.77 (17.69)	94.29 (13.42)		
Week 52 Mean (SD)	95.45 (12.33)	94.52 (13.97)		
Week 100 Mean (SD)	94.84 (12.83)	95.52 (9.66)		
Week 28: Adjusted Mean Change (SE)	2.02 (1.27)	1.77 (1.22)		
Week 52: Adjusted Mean Change (SE)	1.26 (1.29)	0.81 (1.23)	0.45 [-3.06; 3.97]	0.801
Week 100: Adjusted Mean Change (SE)	0.94 (1.53)	1.30 (1.48)	-0.36 [-4.55; 3.82]	0.865
KITE: Color Vision				
Interaction test	p=0.238			
< 65 years				
N'/ N	100 / 100	102 / 102		
Baseline Mean (SD)	92.75 (16.40)	93.38 (14.47)		
Week 52 Mean (SD)	97.44 (8.63)	95.12 (10.71)		
Week 100 Mean (SD)	97.18 (9.95)	96.47 (11.01)		
Week 28: Adjusted Mean Change (SE)	2.65 (1.10)	3.98 (1.09)		
Week 52: Adjusted Mean Change (SE)	4.98 (1.01)	3.00 (0.99)	1.98 [-0.81; 4.76]	0.164
Week 100: Adjusted Mean Change (SE)	4.33 (1.22)	4.01 (1.12)	0.32 [-2.94; 3.59]	0.845

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 65 years				
N'/ N	78 / 79	77 / 79		
Baseline Mean (SD)	91.35 (17.48)	89.61 (17.84)		
Week 52 Mean (SD)	97.69 (8.53)	94.62 (14.32)		
Week 100 Mean (SD)	97.46 (7.62)	92.98 (16.20)		
Week 28: Adjusted Mean Change (SE)	4.47 (1.26)	4.11 (1.27)		
Week 52: Adjusted Mean Change (SE)	6.39 (1.11)	3.59 (1.12)	2.80 [-0.29; 5.90]	0.076
Week 100: Adjusted Mean Change (SE)	5.74 (1.35)	2.16 (1.37)	3.58 [-0.20; 7.35]	0.063
Pooled Analysis: Color Vision				
Interaction test	p=0.427			
< 65 years				
N'/ N	203 / 204	194 / 195		
Baseline Mean (SD)	92.98 (16.02)	93.56 (15.39)		
Week 52 Mean (SD)	97.50 (9.38)	96.14 (10.26)		
Week 100 Mean (SD)	95.81 (11.77)	95.63 (12.71)		
Week 28: Adjusted Mean Change (SE)	2.40 (0.79)	2.87 (0.82)		
Week 52: Adjusted Mean Change (SE)	3.95 (0.77)	2.84 (0.77)	1.10 [-1.03; 3.23]	0.309
Week 100: Adjusted Mean Change (SE)	2.40 (0.93)	2.20 (0.90)	0.20 [-2.33; 2.73]	0.876
≥ 65 years				
N'/ N	161 / 164	169 / 173		
Baseline Mean (SD)	92.08 (17.55)	92.16 (15.71)		
Week 52 Mean (SD)	96.56 (10.64)	94.57 (14.08)		
Week 100 Mean (SD)	96.11 (10.67)	94.35 (13.08)		
Week 28: Adjusted Mean Change (SE)	3.29 (0.90)	2.88 (0.89)		
Week 52: Adjusted Mean Change (SE)	3.79 (0.85)	2.08 (0.83)	1.71 [-0.63; 4.05]	0.151
Week 100: Adjusted Mean Change (SE)	3.36 (1.02)	1.60 (1.02)	1.75 [-1.08; 4.59]	0.225

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.003 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.694			
< 65 years				
N'/ N	103 / 104	92 / 93		
Baseline Mean (SD)	83.50 (22.84)	78.80 (25.12)		
Week 52 Mean (SD)	90.55 (19.10)	91.87 (17.07)		
Week 100 Mean (SD)	85.90 (23.35)	89.14 (19.29)		
Week 28: Adjusted Mean Change (SE)	6.51 (1.79)	8.34 (1.89)		
Week 52: Adjusted Mean Change (SE)	7.24 (1.86)	10.73 (1.87)	-3.49 [-8.68; 1.70]	0.187
Week 100: Adjusted Mean Change (SE)	2.92 (2.22)	7.23 (2.26)	-4.31 [-10.55; 1.92]	0.174
≥ 65 years				
N'/ N	84 / 85	94 / 94		
Baseline Mean (SD)	84.52 (20.50)	81.38 (21.36)		
Week 52 Mean (SD)	87.69 (20.12)	84.80 (17.95)		
Week 100 Mean (SD)	82.31 (20.60)	85.71 (22.35)		
Week 28: Adjusted Mean Change (SE)	-2.01 (2.02)	6.65 (1.93)		
Week 52: Adjusted Mean Change (SE)	3.65 (2.07)	2.89 (1.96)	0.75 [-4.86; 6.36]	0.792
Week 100: Adjusted Mean Change (SE)	-1.12 (2.44)	4.17 (2.35)	-5.29 [-11.95; 1.37]	0.119
KITE: Peripheral Vision				
Interaction test	p=0.943			
< 65 years				
N'/ N	100 / 100	101 / 102		
Baseline Mean (SD)	85.00 (18.46)	85.15 (21.27)		
Week 52 Mean (SD)	90.38 (16.23)	87.80 (20.50)		
Week 100 Mean (SD)	94.79 (13.23)	88.95 (17.41)		
Week 28: Adjusted Mean Change (SE)	5.97 (1.60)	5.83 (1.59)		
Week 52: Adjusted Mean Change (SE)	5.67 (1.74)	3.68 (1.70)	2.00 [-2.77; 6.77]	0.411
Week 100: Adjusted Mean Change (SE)	9.17 (1.75)	3.99 (1.62)	5.18 [0.50; 9.87]	0.030 *

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 65 years				
N'/ N	78 / 79	79 / 79		
Baseline Mean (SD)	80.77 (22.04)	84.18 (21.62)		
Week 52 Mean (SD)	89.02 (18.15)	87.69 (18.14)		
Week 100 Mean (SD)	89.41 (16.87)	86.02 (20.38)		
Week 28: Adjusted Mean Change (SE)	2.72 (1.82)	2.71 (1.81)		
Week 52: Adjusted Mean Change (SE)	6.98 (1.90)	3.18 (1.89)	3.80 [-1.46; 9.06]	0.156
Week 100: Adjusted Mean Change (SE)	5.57 (1.94)	1.48 (1.94)	4.08 [-1.31; 9.47]	0.137
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.806			
< 65 years				
N'/ N	203 / 204	193 / 195		
Baseline Mean (SD)	84.24 (20.76)	82.12 (23.34)		
Week 52 Mean (SD)	90.47 (17.70)	89.85 (18.91)		
Week 100 Mean (SD)	90.17 (19.62)	89.04 (18.26)		
Week 28: Adjusted Mean Change (SE)	6.20 (1.21)	7.30 (1.24)		
Week 52: Adjusted Mean Change (SE)	6.46 (1.28)	7.40 (1.27)	-0.94 [-4.49; 2.60]	0.601
Week 100: Adjusted Mean Change (SE)	5.87 (1.43)	5.79 (1.38)	0.08 [-3.82; 3.98]	0.966
≥ 65 years				
N'/ N	162 / 164	173 / 173		
Baseline Mean (SD)	82.72 (21.27)	82.66 (21.46)		
Week 52 Mean (SD)	88.35 (19.11)	86.17 (18.03)		
Week 100 Mean (SD)	85.69 (19.17)	85.85 (21.39)		
Week 28: Adjusted Mean Change (SE)	0.16 (1.37)	4.76 (1.33)		
Week 52: Adjusted Mean Change (SE)	5.08 (1.41)	3.09 (1.37)	1.99 [-1.87; 5.86]	0.312
Week 100: Adjusted Mean Change (SE)	1.93 (1.57)	2.77 (1.54)	-0.84 [-5.16; 3.48]	0.703

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
General Health				
Test of heterogeneity in main analysis: **p_H=0.834**				
KESTREL: General Health				
Interaction test	p=0.266			
< 65 years				
N'/ N	103 / 104	93 / 93		
Baseline Mean (SD)	45.87 (21.61)	40.86 (19.78)		
Week 52 Mean (SD)	53.66 (25.50)	48.49 (21.86)		
Week 100 Mean (SD)	51.92 (24.43)	48.36 (20.14)		
Week 28: Adjusted Mean Change (SE)	6.54 (1.84)	3.91 (1.94)		
Week 52: Adjusted Mean Change (SE)	9.14 (2.27)	6.36 (2.27)	2.77 [-3.55; 9.10]	0.389
Week 100: Adjusted Mean Change (SE)	9.39 (2.26)	6.69 (2.30)	2.70 [-3.64; 9.05]	0.403
≥ 65 years				
N'/ N	85 / 85	94 / 94		
Baseline Mean (SD)	42.06 (20.49)	36.17 (20.29)		
Week 52 Mean (SD)	49.63 (22.40)	42.67 (20.87)		
Week 100 Mean (SD)	47.35 (21.54)	48.21 (22.65)		
Week 28: Adjusted Mean Change (SE)	1.92 (2.06)	5.69 (1.99)		
Week 52: Adjusted Mean Change (SE)	7.46 (2.51)	4.08 (2.39)	3.38 [-3.45; 10.20]	0.331
Week 100: Adjusted Mean Change (SE)	5.89 (2.47)	8.45 (2.40)	-2.55 [-9.32; 4.22]	0.459
KITE: General Health				
Interaction test	p=0.186			
< 65 years				
N'/ N	100 / 100	102 / 102		
Baseline Mean (SD)	45.25 (20.63)	45.59 (23.71)		
Week 52 Mean (SD)	49.36 (21.69)	50.90 (23.89)		
Week 100 Mean (SD)	51.39 (18.71)	52.87 (23.63)		
Week 28: Adjusted Mean Change (SE)	2.78 (1.84)	5.72 (1.83)		
Week 52: Adjusted Mean Change (SE)	4.17 (2.24)	5.39 (2.17)	-1.22 [-7.35; 4.92]	0.696
Week 100: Adjusted Mean Change (SE)	6.67 (2.07)	7.77 (1.91)	-1.10 [-6.65; 4.45]	0.697

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 65 years				
N'/ N	78 / 79	79 / 79		
Baseline Mean (SD)	42.31 (19.86)	43.35 (21.82)		
Week 52 Mean (SD)	49.62 (22.14)	49.25 (23.02)		
Week 100 Mean (SD)	50.00 (21.27)	48.73 (20.46)		
Week 28: Adjusted Mean Change (SE)	4.45 (2.10)	2.55 (2.09)		
Week 52: Adjusted Mean Change (SE)	7.19 (2.44)	4.55 (2.43)	2.64 [-4.14; 9.41]	0.445
Week 100: Adjusted Mean Change (SE)	5.47 (2.29)	2.52 (2.29)	2.95 [-3.43; 9.33]	0.364
Pooled Analysis: General Health				
Interaction test	p=0.961			
< 65 years				
N'/ N	203 / 204	195 / 195		
Baseline Mean (SD)	45.57 (21.08)	43.33 (21.99)		
Week 52 Mean (SD)	51.56 (23.74)	49.70 (22.86)		
Week 100 Mean (SD)	51.67 (21.80)	50.77 (22.12)		
Week 28: Adjusted Mean Change (SE)	4.59 (1.31)	4.93 (1.34)		
Week 52: Adjusted Mean Change (SE)	6.56 (1.59)	5.93 (1.57)	0.63 [-3.76; 5.02]	0.778
Week 100: Adjusted Mean Change (SE)	7.95 (1.54)	7.34 (1.49)	0.62 [-3.58; 4.82]	0.772
≥ 65 years				
N'/ N	163 / 164	173 / 173		
Baseline Mean (SD)	42.18 (20.13)	39.45 (21.24)		
Week 52 Mean (SD)	49.62 (22.19)	45.77 (22.08)		
Week 100 Mean (SD)	48.60 (21.37)	48.45 (21.59)		
Week 28: Adjusted Mean Change (SE)	3.01 (1.48)	4.31 (1.45)		
Week 52: Adjusted Mean Change (SE)	7.24 (1.75)	4.43 (1.70)	2.81 [-1.98; 7.60]	0.249
Week 100: Adjusted Mean Change (SE)	5.60 (1.69)	5.87 (1.66)	-0.26 [-4.91; 4.39]	0.911

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + baseline value + age + treatment * age + visit * age + treatment * age * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + baseline value + study + treatment * study + age + treatment * age + visit * age + treatment * age * visit.

Table 8.3 VFQ by gender (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Composite Score				
Test of heterogeneity in main analysis: **p_H=0.049 ***				
KESTREL: Composite Score				
Interaction test	p=0.535			
Male				
N'/ N	110 / 110	126 / 126		
Baseline Mean (SD)	78.32 (16.74)	78.50 (13.72)		
Week 52 Mean (SD)	86.46 (13.07)	85.45 (12.18)		
Week 100 Mean (SD)	84.98 (13.54)	84.77 (13.84)		
Week 28: Adjusted Mean Change (SE)	6.72 (1.04)	8.49 (0.98)		
Week 52: Adjusted Mean Change (SE)	7.82 (1.10)	7.90 (1.02)	-0.09 [-3.04; 2.86]	0.954
Week 100: Adjusted Mean Change (SE)	7.16 (1.23)	6.98 (1.15)	0.18 [-3.14; 3.50]	0.915
Female				
N'/ N	78 / 79	61 / 61		
Baseline Mean (SD)	74.26 (18.27)	73.34 (15.78)		
Week 52 Mean (SD)	83.03 (14.88)	84.62 (12.52)		
Week 100 Mean (SD)	80.42 (16.44)	80.71 (15.14)		
Week 28: Adjusted Mean Change (SE)	4.45 (1.22)	6.21 (1.39)		
Week 52: Adjusted Mean Change (SE)	5.95 (1.29)	8.67 (1.40)	-2.73 [-6.47; 1.02]	0.153
Week 100: Adjusted Mean Change (SE)	4.76 (1.43)	5.78 (1.57)	-1.02 [-5.20; 3.16]	0.633
KITE: Composite Score				
Interaction test	p=0.617			
Male				
N'/ N	119 / 120	115 / 115		
Baseline Mean (SD)	79.75 (13.27)	79.00 (16.18)		
Week 52 Mean (SD)	88.17 (12.06)	85.73 (13.85)		
Week 100 Mean (SD)	90.21 (10.76)	85.44 (15.58)		
Week 28: Adjusted Mean Change (SE)	5.61 (0.93)	6.04 (0.96)		
Week 52: Adjusted Mean Change (SE)	8.69 (1.00)	7.61 (1.02)	1.08 [-1.73; 3.89]	0.451
Week 100: Adjusted Mean Change (SE)	9.75 (1.17)	6.56 (1.16)	3.19 [-0.06; 6.43]	0.054

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Female				
N'/ N	59 / 59	66 / 66		
Baseline Mean (SD)	73.92 (17.44)	72.03 (19.34)		
Week 52 Mean (SD)	82.90 (13.96)	79.88 (17.82)		
Week 100 Mean (SD)	83.59 (13.70)	81.61 (14.69)		
Week 28: Adjusted Mean Change (SE)	5.90 (1.37)	5.59 (1.26)		
Week 52: Adjusted Mean Change (SE)	9.03 (1.47)	4.17 (1.34)	4.87 [0.98; 8.76]	0.014 *
Week 100: Adjusted Mean Change (SE)	7.28 (1.71)	5.53 (1.54)	1.75 [-2.77; 6.26]	0.447
Pooled Analysis: Composite Score				
Interaction test	p=0.926			
Male				
N'/ N	229 / 230	241 / 241		
Baseline Mean (SD)	79.07 (15.02)	78.74 (14.92)		
Week 52 Mean (SD)	87.36 (12.54)	85.58 (12.97)		
Week 100 Mean (SD)	87.69 (12.42)	85.10 (14.69)		
Week 28: Adjusted Mean Change (SE)	6.12 (0.71)	7.30 (0.70)		
Week 52: Adjusted Mean Change (SE)	8.27 (0.75)	7.78 (0.73)	0.49 [-1.56; 2.54]	0.638
Week 100: Adjusted Mean Change (SE)	8.52 (0.85)	6.77 (0.81)	1.75 [-0.55; 4.05]	0.135

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Female				
N'/ N	137 / 138	127 / 127		
Baseline Mean (SD)	74.12 (17.86)	72.66 (17.66)		
Week 52 Mean (SD)	82.97 (14.43)	82.25 (15.51)		
Week 100 Mean (SD)	81.71 (15.39)	81.16 (14.85)		
Week 28: Adjusted Mean Change (SE)	5.17 (0.92)	5.83 (0.95)		
Week 52: Adjusted Mean Change (SE)	7.34 (0.98)	6.36 (0.98)	0.98 [-1.72; 3.68]	0.477
Week 100: Adjusted Mean Change (SE)	5.93 (1.09)	5.57 (1.09)	0.35 [-2.68; 3.38]	0.818
General Vision				
Test of heterogeneity in main analysis: **p_H=0.762**				
KESTREL: General Vision				
Interaction test	p=0.692			
Male				
N'/ N	110 / 110	126 / 126		
Baseline Mean (SD)	60.55 (16.80)	60.16 (15.49)		
Week 52 Mean (SD)	73.56 (14.14)	71.57 (12.72)		
Week 100 Mean (SD)	73.98 (13.52)	72.34 (12.13)		
Week 28: Adjusted Mean Change (SE)	11.65 (1.27)	11.87 (1.20)		
Week 52: Adjusted Mean Change (SE)	12.25 (1.34)	11.35 (1.24)	0.90 [-2.70; 4.50]	0.622
Week 100: Adjusted Mean Change (SE)	13.34 (1.35)	11.73 (1.27)	1.61 [-2.04; 5.25]	0.387
Female				
N'/ N	78 / 79	61 / 61		
Baseline Mean (SD)	62.31 (17.94)	60.33 (12.91)		
Week 52 Mean (SD)	72.26 (14.19)	70.36 (13.21)		
Week 100 Mean (SD)	73.11 (16.69)	72.31 (11.98)		
Week 28: Adjusted Mean Change (SE)	10.97 (1.49)	8.48 (1.70)		
Week 52: Adjusted Mean Change (SE)	11.09 (1.59)	9.31 (1.69)	1.78 [-2.78; 6.33]	0.444
Week 100: Adjusted Mean Change (SE)	12.57 (1.57)	11.96 (1.72)	0.61 [-3.96; 5.19]	0.792

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Vision				
Interaction test	p=0.411			
Male				
N'/ N	119 / 120	115 / 115		
Baseline Mean (SD)	62.69 (16.66)	61.39 (17.52)		
Week 52 Mean (SD)	73.88 (15.03)	72.34 (15.55)		
Week 100 Mean (SD)	75.73 (13.97)	72.90 (16.06)		
Week 28: Adjusted Mean Change (SE)	9.27 (1.25)	10.49 (1.29)		
Week 52: Adjusted Mean Change (SE)	12.01 (1.39)	11.56 (1.41)	0.44 [-3.45; 4.34]	0.823
Week 100: Adjusted Mean Change (SE)	13.65 (1.42)	11.34 (1.40)	2.31 [-1.62; 6.23]	0.249
Female				
N'/ N	59 / 59	66 / 66		
Baseline Mean (SD)	60.00 (14.86)	57.27 (19.50)		
Week 52 Mean (SD)	70.43 (13.16)	67.50 (19.28)		
Week 100 Mean (SD)	69.52 (12.68)	66.42 (16.54)		
Week 28: Adjusted Mean Change (SE)	9.57 (1.84)	7.87 (1.69)		
Week 52: Adjusted Mean Change (SE)	11.13 (2.03)	7.92 (1.84)	3.21 [-2.17; 8.60]	0.241
Week 100: Adjusted Mean Change (SE)	9.22 (2.07)	6.37 (1.86)	2.85 [-2.63; 8.33]	0.306
Pooled Analysis: General Vision				
Interaction test	p=0.356			
Male				
N'/ N	229 / 230	241 / 241		
Baseline Mean (SD)	61.66 (16.72)	60.75 (16.47)		
Week 52 Mean (SD)	73.73 (14.58)	71.94 (14.12)		
Week 100 Mean (SD)	74.88 (13.74)	72.62 (14.18)		
Week 28: Adjusted Mean Change (SE)	10.48 (0.89)	11.23 (0.88)		
Week 52: Adjusted Mean Change (SE)	12.21 (0.97)	11.51 (0.94)	0.70 [-1.95; 3.35]	0.603
Week 100: Adjusted Mean Change (SE)	13.61 (0.98)	11.59 (0.94)	2.02 [-0.65; 4.69]	0.138
Female				
N'/ N	137 / 138	127 / 127		
Baseline Mean (SD)	61.31 (16.66)	58.74 (16.67)		
Week 52 Mean (SD)	71.48 (13.73)	68.93 (16.51)		
Week 100 Mean (SD)	71.65 (15.22)	69.33 (14.69)		
Week 28: Adjusted Mean Change (SE)	10.21 (1.17)	8.09 (1.20)		
Week 52: Adjusted Mean Change (SE)	10.95 (1.26)	8.51 (1.25)	2.44 [-1.06; 5.93]	0.171
Week 100: Adjusted Mean Change (SE)	11.07 (1.27)	9.06 (1.26)	2.02 [-1.50; 5.53]	0.261

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Ocular Pain				
Test of heterogeneity in main analysis: **p_H=0.664**				
KESTREL: Ocular Pain				
Interaction test	p=0.517			
Male				
N'/ N	110 / 110	126 / 126		
Baseline Mean (SD)	86.36 (17.80)	85.22 (17.64)		
Week 52 Mean (SD)	90.52 (13.61)	86.89 (16.72)		
Week 100 Mean (SD)	90.21 (13.67)	86.97 (17.57)		
Week 28: Adjusted Mean Change (SE)	3.99 (1.73)	5.24 (1.63)		
Week 52: Adjusted Mean Change (SE)	5.91 (1.60)	3.90 (1.48)	2.01 [-2.26; 6.28]	0.356
Week 100: Adjusted Mean Change (SE)	5.82 (1.75)	3.69 (1.64)	2.13 [-2.57; 6.84]	0.374
Female				
N'/ N	78 / 79	61 / 61		
Baseline Mean (SD)	79.17 (22.04)	75.82 (24.35)		
Week 52 Mean (SD)	85.89 (18.32)	86.38 (15.31)		
Week 100 Mean (SD)	80.33 (20.34)	78.61 (23.66)		
Week 28: Adjusted Mean Change (SE)	1.16 (2.03)	2.93 (2.32)		
Week 52: Adjusted Mean Change (SE)	3.79 (1.88)	5.38 (2.03)	-1.60 [-7.01; 3.82]	0.562
Week 100: Adjusted Mean Change (SE)	-0.76 (2.04)	-1.43 (2.23)	0.68 [-5.23; 6.59]	0.822
KITE: Ocular Pain				
Interaction test	p=0.685			
Male				
N'/ N	119 / 120	115 / 115		
Baseline Mean (SD)	87.08 (16.75)	84.89 (18.10)		
Week 52 Mean (SD)	90.31 (16.11)	88.70 (16.50)		
Week 100 Mean (SD)	93.26 (11.93)	90.59 (15.16)		
Week 28: Adjusted Mean Change (SE)	4.05 (1.43)	5.52 (1.47)		
Week 52: Adjusted Mean Change (SE)	5.08 (1.51)	4.58 (1.53)	0.49 [-3.73; 4.71]	0.819
Week 100: Adjusted Mean Change (SE)	7.89 (1.53)	6.04 (1.49)	1.86 [-2.34; 6.05]	0.384

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Female				
N'/ N	59 / 59	66 / 66		
Baseline Mean (SD)	78.60 (19.15)	78.22 (23.85)		
Week 52 Mean (SD)	85.60 (17.27)	85.04 (19.72)		
Week 100 Mean (SD)	84.23 (19.73)	86.79 (18.08)		
Week 28: Adjusted Mean Change (SE)	5.19 (2.11)	0.78 (1.93)		
Week 52: Adjusted Mean Change (SE)	4.16 (2.20)	2.31 (1.99)	1.85 [-3.97; 7.68]	0.532
Week 100: Adjusted Mean Change (SE)	2.09 (2.22)	4.27 (1.98)	-2.18 [-8.03; 3.67]	0.464
Pooled Analysis: Ocular Pain				
Interaction test	p=0.827			
Male				
N'/ N	229 / 230	241 / 241		
Baseline Mean (SD)	86.74 (17.23)	85.06 (17.82)		
Week 52 Mean (SD)	90.41 (14.94)	87.76 (16.60)		
Week 100 Mean (SD)	91.79 (12.85)	88.77 (16.47)		
Week 28: Adjusted Mean Change (SE)	3.96 (1.12)	5.33 (1.10)		
Week 52: Adjusted Mean Change (SE)	5.41 (1.10)	4.22 (1.07)	1.19 [-1.82; 4.20]	0.438
Week 100: Adjusted Mean Change (SE)	6.87 (1.16)	4.81 (1.11)	2.05 [-1.08; 5.19]	0.199
Female				
N'/ N	137 / 138	127 / 127		
Baseline Mean (SD)	78.92 (20.77)	77.07 (24.03)		
Week 52 Mean (SD)	85.76 (17.80)	85.71 (17.59)		
Week 100 Mean (SD)	81.92 (20.09)	82.74 (21.33)		
Week 28: Adjusted Mean Change (SE)	2.97 (1.46)	1.81 (1.51)		
Week 52: Adjusted Mean Change (SE)	4.10 (1.44)	3.83 (1.43)	0.28 [-3.69; 4.24]	0.891
Week 100: Adjusted Mean Change (SE)	0.58 (1.49)	1.43 (1.48)	-0.85 [-4.97; 3.27]	0.686

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.450**				
KESTREL: Near Activities				
Interaction test	p=0.989			
Male				
N'/ N	110 / 110	126 / 126		
Baseline Mean (SD)	63.94 (25.19)	66.40 (21.84)		
Week 52 Mean (SD)	79.93 (21.32)	78.76 (20.97)		
Week 100 Mean (SD)	81.73 (19.10)	78.99 (19.86)		
Week 28: Adjusted Mean Change (SE)	12.71 (1.79)	15.45 (1.68)		
Week 52: Adjusted Mean Change (SE)	13.98 (1.97)	13.75 (1.82)	0.23 [-5.04; 5.50]	0.932
Week 100: Adjusted Mean Change (SE)	16.73 (1.91)	13.12 (1.79)	3.61 [-1.55; 8.77]	0.170
Female				
N'/ N	78 / 79	61 / 61		
Baseline Mean (SD)	62.87 (27.60)	64.07 (21.87)		
Week 52 Mean (SD)	78.23 (21.46)	78.57 (18.64)		
Week 100 Mean (SD)	76.50 (22.63)	73.40 (22.99)		
Week 28: Adjusted Mean Change (SE)	11.72 (2.09)	12.01 (2.38)		
Week 52: Adjusted Mean Change (SE)	12.35 (2.32)	13.06 (2.48)	-0.71 [-7.39; 5.97]	0.835
Week 100: Adjusted Mean Change (SE)	11.29 (2.22)	9.06 (2.44)	2.23 [-4.26; 8.72]	0.500
KITE: Near Activities				
Interaction test	p=0.658			
Male				
N'/ N	118 / 120	115 / 115		
Baseline Mean (SD)	71.79 (21.91)	72.86 (22.06)		
Week 52 Mean (SD)	82.14 (20.97)	81.07 (21.01)		
Week 100 Mean (SD)	87.27 (17.36)	79.93 (22.76)		
Week 28: Adjusted Mean Change (SE)	6.62 (1.68)	6.09 (1.73)		
Week 52: Adjusted Mean Change (SE)	10.81 (1.69)	10.22 (1.73)	0.59 [-4.16; 5.35]	0.806
Week 100: Adjusted Mean Change (SE)	14.72 (1.82)	8.56 (1.80)	6.16 [1.14; 11.18]	0.016 *

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Female				
N'/ N	59 / 59	66 / 66		
Baseline Mean (SD)	66.88 (23.17)	63.38 (25.85)		
Week 52 Mean (SD)	75.72 (19.47)	74.55 (23.39)		
Week 100 Mean (SD)	76.69 (19.54)	74.69 (23.45)		
Week 28: Adjusted Mean Change (SE)	5.75 (2.46)	5.59 (2.27)		
Week 52: Adjusted Mean Change (SE)	9.05 (2.47)	6.95 (2.25)	2.10 [-4.48; 8.67]	0.531
Week 100: Adjusted Mean Change (SE)	6.39 (2.65)	5.87 (2.38)	0.52 [-6.48; 7.52]	0.884
Pooled Analysis: Near Activities				
Interaction test	p=0.880			
Male				
N'/ N	228 / 230	241 / 241		
Baseline Mean (SD)	68.00 (23.82)	69.48 (22.14)		
Week 52 Mean (SD)	81.10 (21.10)	79.87 (20.97)		
Week 100 Mean (SD)	84.59 (18.38)	79.46 (21.30)		
Week 28: Adjusted Mean Change (SE)	9.76 (1.24)	10.94 (1.22)		
Week 52: Adjusted Mean Change (SE)	12.56 (1.31)	12.10 (1.27)	0.45 [-3.12; 4.02]	0.804
Week 100: Adjusted Mean Change (SE)	15.92 (1.32)	10.95 (1.27)	4.97 [1.38; 8.56]	0.007 *
Female				
N'/ N	137 / 138	127 / 127		
Baseline Mean (SD)	64.60 (25.77)	63.71 (23.92)		
Week 52 Mean (SD)	77.16 (20.58)	76.56 (21.15)		
Week 100 Mean (SD)	76.58 (21.33)	74.05 (23.12)		
Week 28: Adjusted Mean Change (SE)	9.04 (1.61)	8.48 (1.66)		
Week 52: Adjusted Mean Change (SE)	10.65 (1.70)	9.77 (1.69)	0.88 [-3.83; 5.58]	0.714
Week 100: Adjusted Mean Change (SE)	8.99 (1.70)	7.27 (1.70)	1.73 [-2.99; 6.45]	0.473

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Distance Activities				
Test of heterogeneity in main analysis: **p_H=0.046 ***				
KESTREL: Distance Activities				
Interaction test	p=0.177			
Male				
N'/ N	110 / 110	126 / 126		
Baseline Mean (SD)	79.20 (22.12)	77.94 (20.80)		
Week 52 Mean (SD)	87.84 (15.90)	86.72 (16.32)		
Week 100 Mean (SD)	86.35 (17.27)	84.57 (18.53)		
Week 28: Adjusted Mean Change (SE)	9.75 (1.56)	9.86 (1.47)		
Week 52: Adjusted Mean Change (SE)	10.17 (1.50)	10.16 (1.39)	0.01 [-4.00; 4.03]	0.995
Week 100: Adjusted Mean Change (SE)	9.68 (1.65)	7.42 (1.54)	2.26 [-2.17; 6.69]	0.317
Female				
N'/ N	78 / 79	61 / 61		
Baseline Mean (SD)	69.71 (25.18)	70.01 (21.00)		
Week 52 Mean (SD)	81.99 (18.49)	82.07 (18.10)		
Week 100 Mean (SD)	75.61 (21.72)	80.69 (18.83)		
Week 28: Adjusted Mean Change (SE)	4.12 (1.83)	7.08 (2.08)		
Week 52: Adjusted Mean Change (SE)	7.39 (1.76)	8.11 (1.90)	-0.72 [-5.81; 4.36]	0.780
Week 100: Adjusted Mean Change (SE)	2.33 (1.92)	7.78 (2.10)	-5.45 [-11.02; 0.13]	0.056
KITE: Distance Activities				
Interaction test	p=0.635			
Male				
N'/ N	119 / 120	115 / 115		
Baseline Mean (SD)	78.68 (20.06)	79.71 (21.28)		
Week 52 Mean (SD)	89.46 (16.28)	87.37 (16.62)		
Week 100 Mean (SD)	90.78 (14.86)	85.17 (19.39)		
Week 28: Adjusted Mean Change (SE)	6.39 (1.46)	5.93 (1.51)		
Week 52: Adjusted Mean Change (SE)	11.43 (1.37)	9.87 (1.40)	1.56 [-2.29; 5.40]	0.427
Week 100: Adjusted Mean Change (SE)	12.01 (1.51)	7.08 (1.49)	4.93 [0.77; 9.10]	0.020 *

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Female				
N'/ N	59 / 59	66 / 66		
Baseline Mean (SD)	73.31 (23.84)	70.08 (23.24)		
Week 52 Mean (SD)	84.69 (19.62)	79.39 (21.01)		
Week 100 Mean (SD)	85.81 (17.66)	81.45 (17.67)		
Week 28: Adjusted Mean Change (SE)	5.57 (2.15)	4.18 (1.98)		
Week 52: Adjusted Mean Change (SE)	10.97 (2.01)	4.83 (1.82)	6.14 [0.82; 11.46]	0.024 *
Week 100: Adjusted Mean Change (SE)	9.72 (2.20)	6.32 (1.98)	3.41 [-2.40; 9.22]	0.250
Pooled Analysis: Distance Activities				
Interaction test	p=0.568			
Male				
N'/ N	229 / 230	241 / 241		
Baseline Mean (SD)	78.93 (21.03)	78.79 (21.01)		
Week 52 Mean (SD)	88.69 (16.08)	87.03 (16.42)		
Week 100 Mean (SD)	88.64 (16.17)	84.87 (18.92)		
Week 28: Adjusted Mean Change (SE)	7.86 (1.08)	7.94 (1.06)		
Week 52: Adjusted Mean Change (SE)	10.70 (1.02)	10.03 (0.99)	0.67 [-2.12; 3.45]	0.638
Week 100: Adjusted Mean Change (SE)	10.80 (1.11)	7.25 (1.07)	3.55 [0.52; 6.58]	0.022 *
Female				
N'/ N	137 / 138	127 / 127		
Baseline Mean (SD)	71.26 (24.58)	70.05 (22.10)		
Week 52 Mean (SD)	83.14 (18.94)	80.73 (19.57)		
Week 100 Mean (SD)	79.77 (20.69)	81.07 (18.17)		
Week 28: Adjusted Mean Change (SE)	5.00 (1.41)	5.58 (1.45)		
Week 52: Adjusted Mean Change (SE)	9.20 (1.33)	6.44 (1.32)	2.76 [-0.91; 6.43]	0.140
Week 100: Adjusted Mean Change (SE)	5.61 (1.44)	7.04 (1.44)	-1.42 [-5.41; 2.56]	0.484

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.023 ***				
KESTREL: Social Functioning				
Interaction test	p=0.303			
Male				
N'/ N	110 / 110	126 / 126		
Baseline Mean (SD)	89.20 (18.43)	89.98 (15.57)		
Week 52 Mean (SD)	93.10 (14.23)	93.38 (13.59)		
Week 100 Mean (SD)	92.47 (15.85)	92.55 (13.88)		
Week 28: Adjusted Mean Change (SE)	3.96 (1.18)	4.90 (1.11)		
Week 52: Adjusted Mean Change (SE)	2.78 (1.36)	3.71 (1.25)	-0.93 [-4.56; 2.70]	0.615
Week 100: Adjusted Mean Change (SE)	3.16 (1.62)	2.70 (1.52)	0.46 [-3.91; 4.83]	0.837
Female				
N'/ N	78 / 79	61 / 61		
Baseline Mean (SD)	88.30 (19.67)	89.55 (15.84)		
Week 52 Mean (SD)	91.73 (16.00)	94.32 (13.35)		
Week 100 Mean (SD)	88.11 (18.46)	90.63 (16.77)		
Week 28: Adjusted Mean Change (SE)	-1.67 (1.38)	2.22 (1.58)		
Week 52: Adjusted Mean Change (SE)	1.85 (1.60)	4.26 (1.72)	-2.41 [-7.03; 2.20]	0.305
Week 100: Adjusted Mean Change (SE)	-0.65 (1.89)	1.46 (2.06)	-2.11 [-7.60; 3.38]	0.449
KITE: Social Functioning				
Interaction test	p=0.683			
Male				
N'/ N	119 / 120	115 / 115		
Baseline Mean (SD)	90.44 (15.67)	87.93 (19.44)		
Week 52 Mean (SD)	96.17 (10.06)	92.95 (13.29)		
Week 100 Mean (SD)	96.35 (11.95)	90.46 (18.65)		
Week 28: Adjusted Mean Change (SE)	4.21 (1.28)	3.68 (1.32)		
Week 52: Adjusted Mean Change (SE)	7.43 (1.11)	5.66 (1.13)	1.77 [-1.34; 4.88]	0.263
Week 100: Adjusted Mean Change (SE)	7.54 (1.41)	3.04 (1.38)	4.50 [0.62; 8.38]	0.023 *

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Female				
N'/ N	59 / 59	66 / 66		
Baseline Mean (SD)	84.32 (19.78)	83.71 (20.68)		
Week 52 Mean (SD)	92.93 (15.06)	89.29 (16.76)		
Week 100 Mean (SD)	92.26 (17.01)	92.45 (13.28)		
Week 28: Adjusted Mean Change (SE)	2.64 (1.89)	4.14 (1.73)		
Week 52: Adjusted Mean Change (SE)	7.29 (1.62)	2.14 (1.47)	5.15 [0.85; 9.45]	0.019 *
Week 100: Adjusted Mean Change (SE)	5.25 (2.05)	4.89 (1.83)	0.36 [-5.04; 5.77]	0.895
Pooled Analysis: Social Functioning				
Interaction test	p=0.315			
Male				
N'/ N	229 / 230	241 / 241		
Baseline Mean (SD)	89.85 (17.02)	89.00 (17.52)		
Week 52 Mean (SD)	94.73 (12.26)	93.18 (13.41)		
Week 100 Mean (SD)	94.48 (14.06)	91.51 (16.41)		
Week 28: Adjusted Mean Change (SE)	3.97 (0.88)	4.29 (0.87)		
Week 52: Adjusted Mean Change (SE)	5.13 (0.87)	4.67 (0.85)	0.46 [-1.93; 2.85]	0.707
Week 100: Adjusted Mean Change (SE)	5.35 (1.07)	2.83 (1.03)	2.52 [-0.39; 5.44]	0.089
Female				
N'/ N	137 / 138	127 / 127		
Baseline Mean (SD)	86.59 (19.74)	86.52 (18.67)		
Week 52 Mean (SD)	92.25 (15.54)	91.78 (15.31)		
Week 100 Mean (SD)	89.81 (17.91)	91.55 (15.06)		
Week 28: Adjusted Mean Change (SE)	0.46 (1.15)	3.14 (1.18)		
Week 52: Adjusted Mean Change (SE)	4.54 (1.14)	3.09 (1.13)	1.45 [-1.71; 4.61]	0.367
Week 100: Adjusted Mean Change (SE)	2.12 (1.38)	3.08 (1.37)	-0.96 [-4.78; 2.87]	0.624

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Mental Health				
Test of heterogeneity in main analysis: **p_H=0.200**				
KESTREL: Mental Health				
Interaction test	p=0.312			
Male				
N'/ N	110 / 110	126 / 126		
Baseline Mean (SD)	67.44 (22.78)	71.28 (21.30)		
Week 52 Mean (SD)	80.96 (16.97)	79.17 (17.53)		
Week 100 Mean (SD)	76.13 (18.70)	78.79 (21.65)		
Week 28: Adjusted Mean Change (SE)	8.33 (1.68)	9.97 (1.59)		
Week 52: Adjusted Mean Change (SE)	12.39 (1.73)	10.18 (1.61)	2.21 [-2.43; 6.85]	0.350
Week 100: Adjusted Mean Change (SE)	8.93 (1.99)	10.09 (1.87)	-1.17 [-6.54; 4.21]	0.670
Female				
N'/ N	78 / 79	61 / 61		
Baseline Mean (SD)	62.82 (27.60)	61.99 (25.29)		
Week 52 Mean (SD)	74.70 (23.20)	77.79 (18.61)		
Week 100 Mean (SD)	73.16 (24.80)	75.48 (21.00)		
Week 28: Adjusted Mean Change (SE)	6.23 (1.97)	7.93 (2.26)		
Week 52: Adjusted Mean Change (SE)	7.85 (2.04)	12.81 (2.19)	-4.95 [-10.83; 0.93]	0.099
Week 100: Adjusted Mean Change (SE)	8.48 (2.32)	11.77 (2.54)	-3.29 [-10.04; 3.46]	0.338
KITE: Mental Health				
Interaction test	p=0.696			
Male				
N'/ N	119 / 120	115 / 115		
Baseline Mean (SD)	71.90 (19.81)	69.24 (23.31)		
Week 52 Mean (SD)	84.25 (19.08)	80.25 (20.54)		
Week 100 Mean (SD)	87.22 (13.36)	81.25 (20.54)		
Week 28: Adjusted Mean Change (SE)	8.52 (1.57)	10.11 (1.62)		
Week 52: Adjusted Mean Change (SE)	13.73 (1.88)	11.68 (1.91)	2.05 [-3.22; 7.32]	0.444
Week 100: Adjusted Mean Change (SE)	14.98 (1.91)	11.87 (1.88)	3.11 [-2.14; 8.37]	0.245

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Female				
N'/ N	59 / 59	66 / 66		
Baseline Mean (SD)	62.92 (23.78)	59.75 (29.36)		
Week 52 Mean (SD)	75.27 (22.86)	70.76 (27.13)		
Week 100 Mean (SD)	77.83 (19.43)	76.77 (24.92)		
Week 28: Adjusted Mean Change (SE)	8.12 (2.32)	6.82 (2.13)		
Week 52: Adjusted Mean Change (SE)	10.48 (2.75)	4.82 (2.50)	5.66 [-1.62; 12.94]	0.127
Week 100: Adjusted Mean Change (SE)	11.11 (2.77)	10.40 (2.50)	0.71 [-6.61; 8.03]	0.848
Pooled Analysis: Mental Health				
Interaction test	p=0.712			
Male				
N'/ N	229 / 230	241 / 241		
Baseline Mean (SD)	69.76 (21.36)	70.31 (22.26)		
Week 52 Mean (SD)	82.70 (18.15)	79.69 (18.99)		
Week 100 Mean (SD)	81.87 (17.04)	80.01 (21.09)		
Week 28: Adjusted Mean Change (SE)	8.37 (1.15)	10.01 (1.13)		
Week 52: Adjusted Mean Change (SE)	13.03 (1.29)	10.86 (1.25)	2.17 [-1.34; 5.69]	0.226
Week 100: Adjusted Mean Change (SE)	12.07 (1.38)	10.93 (1.33)	1.15 [-2.61; 4.90]	0.549
Female				
N'/ N	137 / 138	127 / 127		
Baseline Mean (SD)	62.86 (25.93)	60.83 (27.40)		
Week 52 Mean (SD)	74.94 (22.95)	74.27 (23.43)		
Week 100 Mean (SD)	75.06 (22.78)	76.13 (22.96)		
Week 28: Adjusted Mean Change (SE)	7.24 (1.50)	7.34 (1.55)		
Week 52: Adjusted Mean Change (SE)	9.17 (1.68)	8.77 (1.67)	0.40 [-4.24; 5.03]	0.866
Week 100: Adjusted Mean Change (SE)	9.84 (1.78)	11.05 (1.78)	-1.20 [-6.14; 3.73]	0.632

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.132**				
KESTREL: Role Difficulties				
Interaction test	p=0.739			
Male				
N'/ N	110 / 110	126 / 126		
Baseline Mean (SD)	74.77 (26.72)	73.41 (25.98)		
Week 52 Mean (SD)	82.76 (23.98)	81.13 (24.04)		
Week 100 Mean (SD)	81.78 (26.07)	82.58 (23.77)		
Week 28: Adjusted Mean Change (SE)	6.80 (2.11)	9.89 (1.98)		
Week 52: Adjusted Mean Change (SE)	8.35 (2.31)	8.51 (2.14)	-0.16 [-6.35; 6.03]	0.960
Week 100: Adjusted Mean Change (SE)	8.73 (2.39)	9.80 (2.23)	-1.07 [-7.49; 5.36]	0.744
Female				
N'/ N	78 / 79	61 / 61		
Baseline Mean (SD)	68.11 (30.86)	68.44 (27.91)		
Week 52 Mean (SD)	77.82 (27.01)	86.83 (20.14)		
Week 100 Mean (SD)	81.15 (25.48)	74.52 (27.34)		
Week 28: Adjusted Mean Change (SE)	4.41 (2.47)	7.30 (2.81)		
Week 52: Adjusted Mean Change (SE)	3.92 (2.72)	15.01 (2.92)	-11.09 [-18.92; -3.25]	0.006 *
Week 100: Adjusted Mean Change (SE)	9.56 (2.77)	3.90 (3.04)	5.66 [-2.43; 13.75]	0.170
KITE: Role Difficulties				
Interaction test	p=0.931			
Male				
N'/ N	119 / 120	115 / 115		
Baseline Mean (SD)	72.16 (26.21)	71.63 (26.51)		
Week 52 Mean (SD)	85.59 (20.65)	81.12 (23.60)		
Week 100 Mean (SD)	89.47 (19.57)	84.14 (23.25)		
Week 28: Adjusted Mean Change (SE)	7.86 (1.92)	8.60 (1.98)		
Week 52: Adjusted Mean Change (SE)	13.13 (2.05)	10.24 (2.08)	2.89 [-2.85; 8.64]	0.323
Week 100: Adjusted Mean Change (SE)	15.10 (2.23)	12.14 (2.21)	2.96 [-3.21; 9.12]	0.346

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Female				
N'/ N	59 / 59	66 / 66		
Baseline Mean (SD)	68.86 (29.40)	59.47 (32.45)		
Week 52 Mean (SD)	77.17 (23.76)	73.21 (27.33)		
Week 100 Mean (SD)	75.60 (26.47)	73.58 (27.48)		
Week 28: Adjusted Mean Change (SE)	6.40 (2.84)	7.29 (2.62)		
Week 52: Adjusted Mean Change (SE)	10.70 (2.99)	5.24 (2.73)	5.46 [-2.49; 13.41]	0.178
Week 100: Adjusted Mean Change (SE)	5.09 (3.25)	5.59 (2.93)	-0.50 [-9.10; 8.10]	0.909
Pooled Analysis: Role Difficulties				
Interaction test	p=0.852			
Male				
N'/ N	229 / 230	241 / 241		
Baseline Mean (SD)	73.42 (26.43)	72.56 (26.19)		
Week 52 Mean (SD)	84.26 (22.26)	81.12 (23.77)		
Week 100 Mean (SD)	85.76 (23.19)	83.36 (23.47)		
Week 28: Adjusted Mean Change (SE)	7.25 (1.43)	9.28 (1.40)		
Week 52: Adjusted Mean Change (SE)	10.74 (1.54)	9.39 (1.50)	1.35 [-2.87; 5.57]	0.529
Week 100: Adjusted Mean Change (SE)	12.00 (1.63)	10.98 (1.57)	1.01 [-3.43; 5.46]	0.654
Female				
N'/ N	137 / 138	127 / 127		
Baseline Mean (SD)	68.43 (30.13)	63.78 (30.57)		
Week 52 Mean (SD)	77.55 (25.56)	80.02 (24.86)		
Week 100 Mean (SD)	78.88 (25.90)	74.05 (27.28)		
Week 28: Adjusted Mean Change (SE)	5.53 (1.86)	7.20 (1.92)		
Week 52: Adjusted Mean Change (SE)	7.11 (2.01)	10.06 (2.00)	-2.96 [-8.51; 2.60]	0.297
Week 100: Adjusted Mean Change (SE)	8.04 (2.11)	4.66 (2.11)	3.38 [-2.48; 9.24]	0.258

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Dependency				
Test of heterogeneity in main analysis: **p_H=0.019 ***				
KESTREL: Dependency				
Interaction test	p=0.578			
Male				
N'/ N	110 / 110	126 / 126		
Baseline Mean (SD)	83.48 (25.11)	85.65 (21.23)		
Week 52 Mean (SD)	90.71 (19.21)	92.48 (15.89)		
Week 100 Mean (SD)	87.05 (21.00)	88.30 (20.46)		
Week 28: Adjusted Mean Change (SE)	5.77 (1.81)	7.36 (1.71)		
Week 52: Adjusted Mean Change (SE)	6.35 (1.89)	8.27 (1.75)	-1.91 [-6.97; 3.15]	0.458
Week 100: Adjusted Mean Change (SE)	3.50 (2.11)	4.25 (1.98)	-0.75 [-6.45; 4.95]	0.796
Female				
N'/ N	78 / 79	61 / 61		
Baseline Mean (SD)	78.74 (28.00)	76.78 (27.60)		
Week 52 Mean (SD)	86.56 (25.13)	91.22 (19.03)		
Week 100 Mean (SD)	84.97 (24.48)	88.62 (22.08)		
Week 28: Adjusted Mean Change (SE)	5.41 (2.12)	5.75 (2.42)		
Week 52: Adjusted Mean Change (SE)	4.27 (2.22)	9.64 (2.39)	-5.37 [-11.78; 1.04]	0.100
Week 100: Adjusted Mean Change (SE)	3.88 (2.46)	7.95 (2.69)	-4.08 [-11.24; 3.09]	0.264
KITE: Dependency				
Interaction test	p=0.148			
Male				
N'/ N	119 / 120	115 / 115		
Baseline Mean (SD)	86.62 (20.22)	84.71 (24.90)		
Week 52 Mean (SD)	93.45 (17.06)	90.25 (17.95)		
Week 100 Mean (SD)	94.85 (12.59)	90.23 (20.10)		
Week 28: Adjusted Mean Change (SE)	4.83 (1.57)	3.57 (1.62)		
Week 52: Adjusted Mean Change (SE)	7.10 (1.69)	5.47 (1.72)	1.63 [-3.12; 6.38]	0.499
Week 100: Adjusted Mean Change (SE)	6.76 (1.86)	4.73 (1.84)	2.03 [-3.11; 7.16]	0.438

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Female				
N'/ N	59 / 59	66 / 66		
Baseline Mean (SD)	76.98 (28.25)	77.02 (29.85)		
Week 52 Mean (SD)	86.05 (22.50)	80.80 (28.20)		
Week 100 Mean (SD)	89.29 (17.59)	82.39 (26.74)		
Week 28: Adjusted Mean Change (SE)	6.16 (2.33)	2.11 (2.13)		
Week 52: Adjusted Mean Change (SE)	7.57 (2.48)	-1.16 (2.25)	8.73 [2.16; 15.30]	0.009 *
Week 100: Adjusted Mean Change (SE)	6.34 (2.71)	-0.34 (2.44)	6.68 [-0.48; 13.84]	0.067
Pooled Analysis: Dependency				
Interaction test	p=0.581			
Male				
N'/ N	229 / 230	241 / 241		
Baseline Mean (SD)	85.12 (22.70)	85.20 (23.01)		
Week 52 Mean (SD)	92.16 (18.10)	91.41 (16.90)		
Week 100 Mean (SD)	91.09 (17.56)	89.26 (20.25)		
Week 28: Adjusted Mean Change (SE)	5.32 (1.20)	5.48 (1.18)		
Week 52: Adjusted Mean Change (SE)	6.81 (1.28)	6.88 (1.24)	-0.07 [-3.56; 3.42]	0.969
Week 100: Adjusted Mean Change (SE)	5.36 (1.41)	4.50 (1.35)	0.87 [-2.96; 4.69]	0.657
Female				
N'/ N	137 / 138	127 / 127		
Baseline Mean (SD)	77.98 (28.02)	76.90 (28.68)		
Week 52 Mean (SD)	86.34 (23.94)	86.01 (24.51)		
Week 100 Mean (SD)	86.73 (21.94)	85.48 (24.62)		
Week 28: Adjusted Mean Change (SE)	5.78 (1.57)	3.91 (1.62)		
Week 52: Adjusted Mean Change (SE)	5.65 (1.67)	4.21 (1.66)	1.44 [-3.16; 6.03]	0.540
Week 100: Adjusted Mean Change (SE)	5.02 (1.82)	3.78 (1.82)	1.24 [-3.80; 6.28]	0.629

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Driving				
Test of heterogeneity in main analysis: **p_H=0.792**				
KESTREL: Driving				
Interaction test	p=0.538			
Male				
N'/ N	90 / 110	99 / 126		
Baseline Mean (SD)	81.11 (18.05)	78.24 (19.13)		
Week 52 Mean (SD)	87.33 (17.41)	85.36 (17.38)		
Week 100 Mean (SD)	86.67 (16.26)	82.68 (20.23)		
Week 28: Adjusted Mean Change (SE)	4.50 (1.57)	6.30 (1.55)		
Week 52: Adjusted Mean Change (SE)	6.44 (1.82)	6.56 (1.79)	-0.11 [-5.16; 4.93]	0.965
Week 100: Adjusted Mean Change (SE)	5.33 (2.01)	3.93 (1.94)	1.40 [-4.10; 6.91]	0.615
Female				
N'/ N	30 / 79	21 / 61		
Baseline Mean (SD)	76.39 (20.07)	72.02 (21.94)		
Week 52 Mean (SD)	75.64 (24.60)	80.09 (20.44)		
Week 100 Mean (SD)	72.92 (23.34)	65.38 (23.29)		
Week 28: Adjusted Mean Change (SE)	-5.17 (2.69)	1.73 (3.33)		
Week 52: Adjusted Mean Change (SE)	-4.47 (3.03)	2.40 (3.72)	-6.87 [-16.31; 2.58]	0.153
Week 100: Adjusted Mean Change (SE)	-5.57 (3.29)	-10.58 (4.38)	5.01 [-5.77; 15.79]	0.361
KITE: Driving				
Interaction test	p=0.668			
Male				
N'/ N	94 / 120	88 / 115		
Baseline Mean (SD)	79.48 (19.01)	81.82 (22.38)		
Week 52 Mean (SD)	87.29 (16.43)	88.59 (15.39)		
Week 100 Mean (SD)	87.44 (13.59)	87.56 (14.61)		
Week 28: Adjusted Mean Change (SE)	1.46 (1.52)	5.51 (1.58)		
Week 52: Adjusted Mean Change (SE)	6.12 (1.31)	5.67 (1.38)	0.44 [-3.32; 4.20]	0.816
Week 100: Adjusted Mean Change (SE)	5.20 (1.45)	3.20 (1.50)	2.00 [-2.14; 6.14]	0.341

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Female				
N'/ N	9 / 59	8 / 66		
Baseline Mean (SD)	74.07 (32.39)	84.90 (13.72)		
Week 52 Mean (SD)	81.94 (27.09)	80.36 (18.74)		
Week 100 Mean (SD)	72.22 (24.53)	83.33 (14.09)		
Week 28: Adjusted Mean Change (SE)	-6.40 (4.70)	3.53 (4.99)		
Week 52: Adjusted Mean Change (SE)	2.78 (4.62)	-4.15 (4.34)	6.93 [-5.60; 19.46]	0.277
Week 100: Adjusted Mean Change (SE)	-6.94 (5.01)	-1.16 (4.49)	-5.79 [-19.09; 7.52]	0.392
Pooled Analysis: Driving				
Interaction test	p=0.328			
Male				
N'/ N	184 / 230	187 / 241		
Baseline Mean (SD)	80.28 (18.52)	79.92 (20.74)		
Week 52 Mean (SD)	87.31 (16.86)	86.92 (16.47)		
Week 100 Mean (SD)	87.07 (14.86)	85.07 (17.81)		
Week 28: Adjusted Mean Change (SE)	2.97 (1.10)	5.93 (1.11)		
Week 52: Adjusted Mean Change (SE)	6.41 (1.13)	6.17 (1.14)	0.25 [-2.91; 3.41]	0.878
Week 100: Adjusted Mean Change (SE)	5.35 (1.25)	3.62 (1.25)	1.74 [-1.74; 5.22]	0.327
Female				
N'/ N	39 / 138	29 / 127		
Baseline Mean (SD)	75.85 (23.00)	75.57 (20.62)		
Week 52 Mean (SD)	76.82 (24.75)	80.17 (19.59)		
Week 100 Mean (SD)	72.78 (23.15)	72.22 (21.78)		
Week 28: Adjusted Mean Change (SE)	-5.68 (2.37)	2.11 (2.78)		
Week 52: Adjusted Mean Change (SE)	-3.14 (2.45)	0.69 (2.80)	-3.83 [-11.14; 3.48]	0.303
Week 100: Adjusted Mean Change (SE)	-6.24 (2.70)	-6.88 (3.18)	0.64 [-7.55; 8.82]	0.879

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Color Vision				
Test of heterogeneity in main analysis: **p_H=0.477**				
KESTREL: Color Vision				
Interaction test	p=0.412			
Male				
N'/ N	110 / 110	124 / 126		
Baseline Mean (SD)	93.64 (16.39)	94.56 (12.97)		
Week 52 Mean (SD)	95.98 (11.98)	95.92 (11.18)		
Week 100 Mean (SD)	94.88 (13.39)	96.15 (9.81)		
Week 28: Adjusted Mean Change (SE)	2.56 (1.09)	2.32 (1.04)		
Week 52: Adjusted Mean Change (SE)	1.41 (1.13)	1.77 (1.06)	-0.37 [-3.42; 2.69]	0.814
Week 100: Adjusted Mean Change (SE)	0.61 (1.33)	1.72 (1.27)	-1.10 [-4.72; 2.51]	0.548
Female				
N'/ N	76 / 79	60 / 61		
Baseline Mean (SD)	92.11 (16.94)	92.92 (18.46)		
Week 52 Mean (SD)	97.54 (9.90)	95.91 (13.41)		
Week 100 Mean (SD)	94.40 (12.43)	93.14 (15.87)		
Week 28: Adjusted Mean Change (SE)	1.35 (1.30)	0.67 (1.47)		
Week 52: Adjusted Mean Change (SE)	3.26 (1.34)	1.79 (1.43)	1.48 [-2.39; 5.35]	0.452
Week 100: Adjusted Mean Change (SE)	0.74 (1.59)	-0.74 (1.70)	1.48 [-3.11; 6.06]	0.527
KITE: Color Vision				
Interaction test	p=0.405			
Male				
N'/ N	119 / 120	114 / 115		
Baseline Mean (SD)	93.70 (14.63)	92.76 (15.14)		
Week 52 Mean (SD)	98.20 (7.44)	95.38 (11.68)		
Week 100 Mean (SD)	97.73 (9.00)	95.00 (14.12)		
Week 28: Adjusted Mean Change (SE)	4.30 (1.00)	3.82 (1.04)		
Week 52: Adjusted Mean Change (SE)	5.76 (0.91)	3.54 (0.94)	2.22 [-0.35; 4.79]	0.090
Week 100: Adjusted Mean Change (SE)	5.04 (1.11)	2.94 (1.09)	2.10 [-0.96; 5.16]	0.177

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Female				
N'/ N	59 / 59	65 / 66		
Baseline Mean (SD)	88.98 (20.38)	90.00 (17.57)		
Week 52 Mean (SD)	96.20 (10.50)	94.09 (13.58)		
Week 100 Mean (SD)	96.43 (8.85)	95.19 (12.17)		
Week 28: Adjusted Mean Change (SE)	1.59 (1.48)	4.43 (1.36)		
Week 52: Adjusted Mean Change (SE)	5.27 (1.33)	2.81 (1.21)	2.46 [-1.08; 6.01]	0.172
Week 100: Adjusted Mean Change (SE)	4.76 (1.60)	3.88 (1.44)	0.89 [-3.35; 5.13]	0.680
Pooled Analysis: Color Vision				
Interaction test	p=0.870			
Male				
N'/ N	229 / 230	238 / 241		
Baseline Mean (SD)	93.67 (15.47)	93.70 (14.05)		
Week 52 Mean (SD)	97.15 (9.88)	95.66 (11.40)		
Week 100 Mean (SD)	96.35 (11.40)	95.58 (12.13)		
Week 28: Adjusted Mean Change (SE)	3.41 (0.75)	3.07 (0.74)		
Week 52: Adjusted Mean Change (SE)	3.61 (0.72)	2.66 (0.71)	0.95 [-1.03; 2.93]	0.345
Week 100: Adjusted Mean Change (SE)	2.87 (0.87)	2.21 (0.84)	0.66 [-1.71; 3.04]	0.583
Female				
N'/ N	135 / 138	125 / 127		
Baseline Mean (SD)	90.74 (18.51)	91.40 (17.99)		
Week 52 Mean (SD)	96.96 (10.13)	95.00 (13.46)		
Week 100 Mean (SD)	95.25 (11.06)	94.17 (14.09)		
Week 28: Adjusted Mean Change (SE)	1.69 (0.99)	2.52 (1.01)		
Week 52: Adjusted Mean Change (SE)	4.33 (0.94)	2.20 (0.93)	2.13 [-0.47; 4.74]	0.109
Week 100: Adjusted Mean Change (SE)	2.75 (1.13)	1.45 (1.12)	1.30 [-1.82; 4.43]	0.413

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.003 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.688			
Male				
N'/ N	110 / 110	126 / 126		
Baseline Mean (SD)	85.68 (21.00)	82.34 (22.15)		
Week 52 Mean (SD)	90.80 (19.11)	90.10 (16.23)		
Week 100 Mean (SD)	86.45 (21.13)	90.16 (17.28)		
Week 28: Adjusted Mean Change (SE)	4.53 (1.75)	9.66 (1.65)		
Week 52: Adjusted Mean Change (SE)	6.35 (1.82)	7.80 (1.68)	-1.45 [-6.32; 3.42]	0.559
Week 100: Adjusted Mean Change (SE)	2.29 (2.15)	7.43 (2.02)	-5.14 [-10.94; 0.66]	0.082
Female				
N'/ N	77 / 79	60 / 61		
Baseline Mean (SD)	81.49 (22.73)	75.42 (25.00)		
Week 52 Mean (SD)	87.10 (20.11)	85.71 (20.15)		
Week 100 Mean (SD)	81.25 (23.30)	82.69 (25.50)		
Week 28: Adjusted Mean Change (SE)	-0.00 (2.07)	3.52 (2.35)		
Week 52: Adjusted Mean Change (SE)	4.51 (2.14)	5.60 (2.29)	-1.09 [-7.25; 5.07]	0.728
Week 100: Adjusted Mean Change (SE)	-0.64 (2.52)	2.74 (2.73)	-3.38 [-10.70; 3.93]	0.364
KITE: Peripheral Vision				
Interaction test	p=0.783			
Male				
N'/ N	119 / 120	115 / 115		
Baseline Mean (SD)	84.87 (19.59)	86.30 (20.21)		
Week 52 Mean (SD)	91.07 (16.15)	89.10 (17.02)		
Week 100 Mean (SD)	92.98 (14.59)	87.37 (19.72)		
Week 28: Adjusted Mean Change (SE)	5.01 (1.45)	4.43 (1.50)		
Week 52: Adjusted Mean Change (SE)	6.28 (1.56)	5.00 (1.59)	1.27 [-3.10; 5.65]	0.568
Week 100: Adjusted Mean Change (SE)	7.17 (1.58)	2.30 (1.55)	4.88 [0.53; 9.23]	0.028 *

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Female				
N'/ N	59 / 59	65 / 66		
Baseline Mean (SD)	79.66 (21.01)	81.92 (23.18)		
Week 52 Mean (SD)	86.96 (18.81)	85.45 (22.92)		
Week 100 Mean (SD)	91.07 (16.40)	88.46 (16.76)		
Week 28: Adjusted Mean Change (SE)	3.58 (2.15)	4.53 (1.98)		
Week 52: Adjusted Mean Change (SE)	6.40 (2.28)	0.89 (2.08)	5.50 [-0.57; 11.58]	0.076
Week 100: Adjusted Mean Change (SE)	8.44 (2.30)	3.96 (2.07)	4.48 [-1.62; 10.58]	0.149
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.706			
Male				
N'/ N	229 / 230	241 / 241		
Baseline Mean (SD)	85.26 (20.24)	84.23 (21.29)		
Week 52 Mean (SD)	90.95 (17.56)	89.62 (16.58)		
Week 100 Mean (SD)	89.83 (18.29)	88.77 (18.54)		
Week 28: Adjusted Mean Change (SE)	4.57 (1.14)	7.17 (1.12)		
Week 52: Adjusted Mean Change (SE)	6.12 (1.20)	6.51 (1.17)	-0.39 [-3.67; 2.89]	0.816
Week 100: Adjusted Mean Change (SE)	4.63 (1.34)	4.95 (1.28)	-0.32 [-3.95; 3.31]	0.863
Female				
N'/ N	136 / 138	125 / 127		
Baseline Mean (SD)	80.70 (21.94)	78.80 (24.19)		
Week 52 Mean (SD)	87.04 (19.48)	85.59 (21.47)		
Week 100 Mean (SD)	85.29 (21.21)	85.58 (21.67)		
Week 28: Adjusted Mean Change (SE)	1.65 (1.50)	4.26 (1.54)		
Week 52: Adjusted Mean Change (SE)	5.41 (1.57)	3.53 (1.55)	1.89 [-2.44; 6.21]	0.393
Week 100: Adjusted Mean Change (SE)	3.24 (1.74)	3.44 (1.72)	-0.20 [-5.00; 4.60]	0.934

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
General Health				
Test of heterogeneity in main analysis: **p_H=0.834**				
KESTREL: General Health				
Interaction test	p=0.738			
Male				
N'/ N	110 / 110	126 / 126		
Baseline Mean (SD)	45.00 (22.67)	40.28 (19.23)		
Week 52 Mean (SD)	51.72 (23.44)	47.55 (21.26)		
Week 100 Mean (SD)	53.61 (23.14)	49.47 (20.73)		
Week 28: Adjusted Mean Change (SE)	4.90 (1.81)	5.73 (1.70)		
Week 52: Adjusted Mean Change (SE)	8.03 (2.21)	6.14 (2.04)	1.89 [-4.03; 7.81]	0.530
Week 100: Adjusted Mean Change (SE)	11.11 (2.19)	7.24 (2.05)	3.87 [-2.03; 9.77]	0.198
Female				
N'/ N	78 / 79	61 / 61		
Baseline Mean (SD)	42.95 (18.85)	34.84 (21.54)		
Week 52 Mean (SD)	52.02 (25.33)	42.41 (21.80)		
Week 100 Mean (SD)	44.67 (22.41)	46.15 (22.35)		
Week 28: Adjusted Mean Change (SE)	3.93 (2.11)	2.94 (2.42)		
Week 52: Adjusted Mean Change (SE)	8.96 (2.60)	3.74 (2.78)	5.22 [-2.28; 12.72]	0.172
Week 100: Adjusted Mean Change (SE)	3.29 (2.54)	7.99 (2.78)	-4.70 [-12.12; 2.72]	0.214
KITE: General Health				
Interaction test	p=0.288			
Male				
N'/ N	119 / 120	115 / 115		
Baseline Mean (SD)	44.75 (21.80)	45.87 (21.70)		
Week 52 Mean (SD)	50.00 (23.81)	53.72 (21.05)		
Week 100 Mean (SD)	52.53 (20.66)	53.76 (21.16)		
Week 28: Adjusted Mean Change (SE)	5.19 (1.67)	5.79 (1.73)		
Week 52: Adjusted Mean Change (SE)	5.33 (1.99)	8.29 (2.02)	-2.95 [-8.54; 2.63]	0.299
Week 100: Adjusted Mean Change (SE)	7.51 (1.85)	8.10 (1.82)	-0.59 [-5.71; 4.53]	0.821

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Female				
N'/ N	59 / 59	66 / 66		
Baseline Mean (SD)	42.37 (16.90)	42.42 (24.80)		
Week 52 Mean (SD)	48.37 (17.00)	44.20 (26.11)		
Week 100 Mean (SD)	47.02 (17.64)	46.70 (24.04)		
Week 28: Adjusted Mean Change (SE)	-0.17 (2.47)	1.87 (2.26)		
Week 52: Adjusted Mean Change (SE)	6.04 (2.91)	-0.48 (2.63)	6.52 [-1.20; 14.24]	0.098
Week 100: Adjusted Mean Change (SE)	3.28 (2.70)	1.24 (2.42)	2.04 [-5.10; 9.17]	0.575
Pooled Analysis: General Health				
Interaction test	p=0.615			
Male				
N'/ N	229 / 230	241 / 241		
Baseline Mean (SD)	44.87 (22.17)	42.95 (20.59)		
Week 52 Mean (SD)	50.81 (23.59)	50.51 (21.33)		
Week 100 Mean (SD)	53.05 (21.83)	51.60 (21.00)		
Week 28: Adjusted Mean Change (SE)	5.02 (1.23)	5.80 (1.21)		
Week 52: Adjusted Mean Change (SE)	6.54 (1.48)	7.23 (1.44)	-0.69 [-4.74; 3.36]	0.739
Week 100: Adjusted Mean Change (SE)	9.20 (1.43)	7.71 (1.37)	1.48 [-2.41; 5.38]	0.454
Female				
N'/ N	137 / 138	127 / 127		
Baseline Mean (SD)	42.70 (17.98)	38.78 (23.51)		
Week 52 Mean (SD)	50.46 (22.15)	43.30 (23.96)		
Week 100 Mean (SD)	45.63 (20.54)	46.43 (23.11)		
Week 28: Adjusted Mean Change (SE)	1.99 (1.61)	2.51 (1.66)		
Week 52: Adjusted Mean Change (SE)	7.55 (1.93)	1.70 (1.91)	5.85 [0.51; 11.19]	0.032 *
Week 100: Adjusted Mean Change (SE)	3.04 (1.85)	4.76 (1.84)	-1.72 [-6.84; 3.40]	0.510

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + gender + treatment * gender + visit * gender + treatment * gender * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + study + treatment * study + gender + treatment * gender + visit * gender + treatment * gender * visit.

Table 8.4 VFQ by BCVA (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Composite Score				
Test of heterogeneity in main analysis: **p_H=0.049 ***				
KESTREL: Composite Score				
Interaction test	p=0.944			
≤ 65 letters				
N'/ N	74 / 74	64 / 64		
Baseline Mean (SD)	69.97 (18.31)	71.63 (16.50)		
Week 52 Mean (SD)	80.63 (16.96)	81.39 (14.03)		
Week 100 Mean (SD)	80.61 (16.49)	79.27 (17.16)		
Week 28: Adjusted Mean Change (SE)	3.51 (1.28)	7.21 (1.38)		
Week 52: Adjusted Mean Change (SE)	5.18 (1.39)	6.36 (1.44)	-1.18 [-5.08; 2.73]	0.554
Week 100: Adjusted Mean Change (SE)	6.76 (1.55)	4.80 (1.61)	1.96 [-2.42; 6.34]	0.380
> 65 letters				
N'/ N	114 / 115	123 / 123		
Baseline Mean (SD)	80.97 (15.49)	79.51 (12.74)		
Week 52 Mean (SD)	87.53 (11.17)	87.06 (10.86)		
Week 100 Mean (SD)	84.47 (13.88)	85.44 (12.30)		
Week 28: Adjusted Mean Change (SE)	7.22 (1.02)	7.97 (0.99)		
Week 52: Adjusted Mean Change (SE)	8.16 (1.06)	9.13 (1.01)	-0.97 [-3.85; 1.91]	0.508
Week 100: Adjusted Mean Change (SE)	5.84 (1.19)	7.48 (1.15)	-1.64 [-4.89; 1.61]	0.321
KITE: Composite Score				
Interaction test	p=0.448			
≤ 65 letters				
N'/ N	65 / 65	91 / 91		
Baseline Mean (SD)	73.01 (14.42)	69.95 (19.83)		
Week 52 Mean (SD)	82.57 (14.10)	78.32 (17.15)		
Week 100 Mean (SD)	84.33 (13.90)	78.71 (17.24)		
Week 28: Adjusted Mean Change (SE)	5.18 (1.27)	4.48 (1.08)		
Week 52: Adjusted Mean Change (SE)	8.67 (1.38)	5.01 (1.16)	3.66 [0.14; 7.18]	0.042 *
Week 100: Adjusted Mean Change (SE)	8.23 (1.59)	5.61 (1.36)	2.63 [-1.46; 6.71]	0.207

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 65 letters				
N'/ N	113 / 114	90 / 90		
Baseline Mean (SD)	80.59 (14.66)	83.04 (12.11)		
Week 52 Mean (SD)	88.69 (11.65)	88.77 (12.00)		
Week 100 Mean (SD)	90.33 (10.40)	88.71 (11.68)		
Week 28: Adjusted Mean Change (SE)	6.00 (0.97)	7.33 (1.10)		
Week 52: Adjusted Mean Change (SE)	8.86 (1.04)	7.67 (1.16)	1.20 [-1.84; 4.24]	0.439
Week 100: Adjusted Mean Change (SE)	9.40 (1.22)	6.83 (1.29)	2.57 [-0.90; 6.04]	0.146
Pooled Analysis: Composite Score				
Interaction test	p=0.329			
≤ 65 letters				
N'/ N	139 / 139	155 / 155		
Baseline Mean (SD)	71.39 (16.61)	70.65 (18.49)		
Week 52 Mean (SD)	81.58 (15.58)	79.59 (15.95)		
Week 100 Mean (SD)	82.40 (15.34)	78.94 (17.13)		
Week 28: Adjusted Mean Change (SE)	4.55 (0.91)	5.53 (0.87)		
Week 52: Adjusted Mean Change (SE)	7.13 (0.98)	5.47 (0.92)	1.66 [-0.95; 4.27]	0.212
Week 100: Adjusted Mean Change (SE)	7.67 (1.10)	5.16 (1.04)	2.51 [-0.44; 5.46]	0.095

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 65 letters				
N'/ N	227 / 229	213 / 213		
Baseline Mean (SD)	80.78 (15.05)	81.00 (12.57)		
Week 52 Mean (SD)	88.10 (11.39)	87.77 (11.34)		
Week 100 Mean (SD)	87.25 (12.66)	86.91 (12.10)		
Week 28: Adjusted Mean Change (SE)	6.52 (0.71)	7.69 (0.75)		
Week 52: Adjusted Mean Change (SE)	8.39 (0.75)	8.55 (0.77)	-0.16 [-2.25; 1.92]	0.877
Week 100: Adjusted Mean Change (SE)	7.49 (0.85)	7.18 (0.86)	0.30 [-2.05; 2.66]	0.799
General Vision				
Test of heterogeneity in main analysis: **p_H=0.762**				
KESTREL: General Vision				
Interaction test	p=0.602			
≤ 65 letters				
N'/ N	74 / 74	64 / 64		
Baseline Mean (SD)	57.57 (15.86)	57.19 (15.06)		
Week 52 Mean (SD)	69.63 (13.87)	67.92 (12.61)		
Week 100 Mean (SD)	71.32 (14.94)	70.40 (10.87)		
Week 28: Adjusted Mean Change (SE)	8.89 (1.54)	9.48 (1.66)		
Week 52: Adjusted Mean Change (SE)	9.29 (1.68)	8.22 (1.72)	1.08 [-3.67; 5.82]	0.656
Week 100: Adjusted Mean Change (SE)	11.70 (1.69)	11.03 (1.75)	0.67 [-4.12; 5.46]	0.782
> 65 letters				
N'/ N	114 / 115	123 / 123		
Baseline Mean (SD)	63.68 (17.76)	61.79 (14.26)		
Week 52 Mean (SD)	74.95 (13.98)	72.76 (12.75)		
Week 100 Mean (SD)	74.95 (14.79)	73.33 (12.54)		
Week 28: Adjusted Mean Change (SE)	13.00 (1.24)	11.38 (1.21)		
Week 52: Adjusted Mean Change (SE)	13.27 (1.28)	11.86 (1.22)	1.41 [-2.07; 4.89]	0.425
Week 100: Adjusted Mean Change (SE)	13.82 (1.29)	12.23 (1.26)	1.58 [-1.96; 5.13]	0.380

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Vision				
Interaction test	p=0.687			
≤ 65 letters				
N'/ N	65 / 65	91 / 91		
Baseline Mean (SD)	59.08 (15.18)	55.38 (17.91)		
Week 52 Mean (SD)	68.08 (13.29)	66.93 (17.55)		
Week 100 Mean (SD)	70.20 (12.33)	66.18 (18.04)		
Week 28: Adjusted Mean Change (SE)	7.95 (1.69)	7.74 (1.44)		
Week 52: Adjusted Mean Change (SE)	9.52 (1.90)	8.55 (1.59)	0.97 [-3.89; 5.82]	0.695
Week 100: Adjusted Mean Change (SE)	10.66 (1.94)	7.37 (1.64)	3.29 [-1.70; 8.27]	0.196
> 65 letters				
N'/ N	113 / 114	90 / 90		
Baseline Mean (SD)	63.36 (16.45)	64.44 (17.68)		
Week 52 Mean (SD)	75.43 (14.56)	74.13 (16.03)		
Week 100 Mean (SD)	75.85 (14.31)	74.36 (14.01)		
Week 28: Adjusted Mean Change (SE)	10.18 (1.30)	11.38 (1.47)		
Week 52: Adjusted Mean Change (SE)	12.97 (1.43)	11.89 (1.58)	1.08 [-3.10; 5.27]	0.611
Week 100: Adjusted Mean Change (SE)	13.16 (1.49)	11.52 (1.55)	1.63 [-2.58; 5.85]	0.447
Pooled Analysis: General Vision				
Interaction test	p=0.853			
≤ 65 letters				
N'/ N	139 / 139	155 / 155		
Baseline Mean (SD)	58.27 (15.51)	56.13 (16.76)		
Week 52 Mean (SD)	68.87 (13.55)	67.34 (15.65)		
Week 100 Mean (SD)	70.78 (13.69)	67.97 (15.50)		
Week 28: Adjusted Mean Change (SE)	8.54 (1.14)	8.41 (1.09)		
Week 52: Adjusted Mean Change (SE)	9.49 (1.26)	8.35 (1.17)	1.14 [-2.24; 4.51]	0.509
Week 100: Adjusted Mean Change (SE)	11.33 (1.27)	8.86 (1.20)	2.47 [-0.95; 5.89]	0.157
> 65 letters				
N'/ N	227 / 229	213 / 213		
Baseline Mean (SD)	63.52 (17.09)	62.91 (15.81)		
Week 52 Mean (SD)	75.19 (14.23)	73.33 (14.18)		
Week 100 Mean (SD)	75.38 (14.53)	73.79 (13.19)		
Week 28: Adjusted Mean Change (SE)	11.53 (0.90)	11.38 (0.94)		
Week 52: Adjusted Mean Change (SE)	13.07 (0.96)	11.91 (0.98)	1.16 [-1.53; 3.85]	0.398
Week 100: Adjusted Mean Change (SE)	13.47 (0.98)	11.95 (0.98)	1.51 [-1.21; 4.23]	0.276

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Ocular Pain				
Test of heterogeneity in main analysis: **p_H=0.664**				
KESTREL: Ocular Pain				
Interaction test	p=0.737			
≤ 65 letters				
N'/ N	74 / 74	64 / 64		
Baseline Mean (SD)	80.41 (21.01)	79.30 (25.32)		
Week 52 Mean (SD)	87.50 (17.51)	87.26 (15.98)		
Week 100 Mean (SD)	85.38 (18.47)	78.50 (24.49)		
Week 28: Adjusted Mean Change (SE)	2.49 (2.10)	3.62 (2.28)		
Week 52: Adjusted Mean Change (SE)	4.35 (2.01)	5.89 (2.07)	-1.54 [-7.22; 4.15]	0.595
Week 100: Adjusted Mean Change (SE)	2.81 (2.20)	-1.81 (2.28)	4.62 [-1.62; 10.85]	0.146
> 65 letters				
N'/ N	114 / 115	123 / 123		
Baseline Mean (SD)	85.31 (19.05)	83.64 (17.40)		
Week 52 Mean (SD)	89.21 (14.88)	86.43 (16.36)		
Week 100 Mean (SD)	86.40 (16.94)	86.85 (17.15)		
Week 28: Adjusted Mean Change (SE)	2.97 (1.70)	4.94 (1.65)		
Week 52: Adjusted Mean Change (SE)	5.35 (1.53)	3.75 (1.46)	1.60 [-2.57; 5.77]	0.450
Week 100: Adjusted Mean Change (SE)	3.14 (1.68)	3.79 (1.63)	-0.65 [-5.26; 3.96]	0.781
KITE: Ocular Pain				
Interaction test	p=0.115			
≤ 65 letters				
N'/ N	65 / 65	91 / 91		
Baseline Mean (SD)	83.65 (17.67)	79.95 (23.56)		
Week 52 Mean (SD)	88.94 (14.99)	83.83 (19.90)		
Week 100 Mean (SD)	89.29 (14.66)	87.32 (16.66)		
Week 28: Adjusted Mean Change (SE)	6.09 (1.94)	2.68 (1.64)		
Week 52: Adjusted Mean Change (SE)	5.49 (2.05)	0.88 (1.71)	4.61 [-0.63; 9.85]	0.085
Week 100: Adjusted Mean Change (SE)	5.32 (2.07)	4.73 (1.75)	0.58 [-4.76; 5.93]	0.830

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 65 letters				
N'/ N	113 / 114	90 / 90		
Baseline Mean (SD)	84.62 (18.22)	85.00 (16.78)		
Week 52 Mean (SD)	88.72 (17.49)	90.83 (14.72)		
Week 100 Mean (SD)	91.01 (15.87)	90.87 (15.95)		
Week 28: Adjusted Mean Change (SE)	3.38 (1.49)	4.93 (1.69)		
Week 52: Adjusted Mean Change (SE)	4.35 (1.54)	6.63 (1.70)	-2.28 [-6.79; 2.23]	0.321
Week 100: Adjusted Mean Change (SE)	6.47 (1.60)	6.06 (1.65)	0.41 [-4.10; 4.92]	0.858
Pooled Analysis: Ocular Pain				
Interaction test	p=0.143			
≤ 65 letters				
N'/ N	139 / 139	155 / 155		
Baseline Mean (SD)	81.92 (19.51)	79.68 (24.22)		
Week 52 Mean (SD)	88.21 (16.26)	85.25 (18.39)		
Week 100 Mean (SD)	87.25 (16.78)	83.58 (20.72)		
Week 28: Adjusted Mean Change (SE)	4.36 (1.43)	2.89 (1.37)		
Week 52: Adjusted Mean Change (SE)	5.10 (1.44)	2.80 (1.33)	2.30 [-1.55; 6.16]	0.241
Week 100: Adjusted Mean Change (SE)	4.20 (1.50)	1.83 (1.41)	2.37 [-1.68; 6.41]	0.251
> 65 letters				
N'/ N	227 / 229	213 / 213		
Baseline Mean (SD)	84.97 (18.61)	84.21 (17.11)		
Week 52 Mean (SD)	88.97 (16.17)	88.26 (15.81)		
Week 100 Mean (SD)	88.58 (16.56)	88.65 (16.69)		
Week 28: Adjusted Mean Change (SE)	3.08 (1.13)	5.00 (1.18)		
Week 52: Adjusted Mean Change (SE)	4.77 (1.09)	5.04 (1.12)	-0.27 [-3.34; 2.80]	0.862
Week 100: Adjusted Mean Change (SE)	4.68 (1.16)	4.82 (1.16)	-0.14 [-3.36; 3.07]	0.931

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.450**				
KESTREL: Near Activities				
Interaction test	p=0.558			
≤ 65 letters				
N'/ N	74 / 74	64 / 64		
Baseline Mean (SD)	53.10 (25.31)	57.10 (23.07)		
Week 52 Mean (SD)	73.61 (23.72)	74.92 (21.84)		
Week 100 Mean (SD)	76.34 (22.64)	73.00 (20.12)		
Week 28: Adjusted Mean Change (SE)	8.98 (2.20)	13.37 (2.35)		
Week 52: Adjusted Mean Change (SE)	10.37 (2.50)	12.90 (2.55)	-2.52 [-9.51; 4.46]	0.477
Week 100: Adjusted Mean Change (SE)	14.74 (2.43)	10.94 (2.52)	3.80 [-3.05; 10.65]	0.276
> 65 letters				
N'/ N	114 / 115	123 / 123		
Baseline Mean (SD)	70.25 (24.52)	70.09 (19.82)		
Week 52 Mean (SD)	82.41 (19.24)	80.60 (19.00)		
Week 100 Mean (SD)	81.36 (19.47)	79.08 (21.43)		
Week 28: Adjusted Mean Change (SE)	14.38 (1.75)	14.82 (1.70)		
Week 52: Adjusted Mean Change (SE)	15.02 (1.89)	13.88 (1.80)	1.14 [-3.98; 6.26]	0.662
Week 100: Adjusted Mean Change (SE)	14.29 (1.86)	12.13 (1.81)	2.16 [-2.91; 7.24]	0.402
KITE: Near Activities				
Interaction test	p=0.389			
≤ 65 letters				
N'/ N	64 / 65	91 / 91		
Baseline Mean (SD)	61.39 (23.35)	61.45 (25.76)		
Week 52 Mean (SD)	73.08 (21.68)	71.44 (24.71)		
Week 100 Mean (SD)	76.62 (21.58)	70.10 (25.89)		
Week 28: Adjusted Mean Change (SE)	3.02 (2.29)	2.38 (1.91)		
Week 52: Adjusted Mean Change (SE)	8.98 (2.34)	5.94 (1.94)	3.04 [-2.87; 8.95]	0.312
Week 100: Adjusted Mean Change (SE)	10.38 (2.49)	5.14 (2.11)	5.24 [-1.12; 11.61]	0.106

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 65 letters				
N'/ N	113 / 114	90 / 90		
Baseline Mean (SD)	75.11 (20.31)	77.45 (18.77)		
Week 52 Mean (SD)	84.06 (19.05)	85.83 (16.31)		
Week 100 Mean (SD)	88.21 (15.27)	84.94 (17.77)		
Week 28: Adjusted Mean Change (SE)	8.25 (1.73)	9.59 (1.96)		
Week 52: Adjusted Mean Change (SE)	10.92 (1.74)	12.12 (1.94)	-1.20 [-6.30; 3.90]	0.643
Week 100: Adjusted Mean Change (SE)	13.05 (1.91)	10.01 (2.00)	3.05 [-2.35; 8.44]	0.267
Pooled Analysis: Near Activities				
Interaction test	p=0.573			
≤ 65 letters				
N'/ N	138 / 139	155 / 155		
Baseline Mean (SD)	56.94 (24.69)	59.65 (24.70)		
Week 52 Mean (SD)	73.35 (22.64)	72.88 (23.54)		
Week 100 Mean (SD)	76.47 (22.03)	71.33 (23.56)		
Week 28: Adjusted Mean Change (SE)	6.49 (1.60)	7.15 (1.51)		
Week 52: Adjusted Mean Change (SE)	10.01 (1.72)	9.01 (1.59)	1.00 [-3.56; 5.55]	0.667
Week 100: Adjusted Mean Change (SE)	12.94 (1.74)	7.74 (1.62)	5.20 [0.58; 9.83]	0.027 *
> 65 letters				
N'/ N	227 / 229	213 / 213		
Baseline Mean (SD)	72.67 (22.60)	73.20 (19.68)		
Week 52 Mean (SD)	83.22 (19.11)	82.78 (18.07)		
Week 100 Mean (SD)	84.61 (17.88)	81.70 (20.03)		
Week 28: Adjusted Mean Change (SE)	11.29 (1.24)	12.26 (1.30)		
Week 52: Adjusted Mean Change (SE)	12.89 (1.30)	12.91 (1.34)	-0.01 [-3.65; 3.62]	0.994
Week 100: Adjusted Mean Change (SE)	13.56 (1.33)	11.01 (1.34)	2.55 [-1.14; 6.23]	0.175

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Distance Activities				
Test of heterogeneity in main analysis: **p_H=0.046 ***				
KESTREL: Distance Activities				
Interaction test	p=0.887			
≤ 65 letters				
N'/ N	74 / 74	64 / 64		
Baseline Mean (SD)	67.68 (24.54)	69.53 (23.81)		
Week 52 Mean (SD)	80.56 (19.97)	80.82 (19.97)		
Week 100 Mean (SD)	79.48 (20.97)	79.33 (22.06)		
Week 28: Adjusted Mean Change (SE)	5.20 (1.92)	7.38 (2.07)		
Week 52: Adjusted Mean Change (SE)	6.66 (1.89)	7.19 (1.94)	-0.54 [-5.85; 4.78]	0.842
Week 100: Adjusted Mean Change (SE)	7.14 (2.09)	6.34 (2.16)	0.80 [-5.10; 6.69]	0.791
> 65 letters				
N'/ N	114 / 115	123 / 123		
Baseline Mean (SD)	80.19 (22.12)	78.39 (19.01)		
Week 52 Mean (SD)	88.16 (14.84)	87.22 (15.04)		
Week 100 Mean (SD)	83.15 (19.28)	85.20 (16.40)		
Week 28: Adjusted Mean Change (SE)	8.76 (1.54)	9.73 (1.49)		
Week 52: Adjusted Mean Change (SE)	10.36 (1.44)	10.60 (1.37)	-0.24 [-4.15; 3.66]	0.903
Week 100: Adjusted Mean Change (SE)	6.27 (1.60)	8.21 (1.55)	-1.94 [-6.31; 2.43]	0.383
KITE: Distance Activities				
Interaction test	p=0.093			
≤ 65 letters				
N'/ N	65 / 65	91 / 91		
Baseline Mean (SD)	70.13 (19.54)	69.32 (24.20)		
Week 52 Mean (SD)	83.49 (20.13)	77.39 (21.48)		
Week 100 Mean (SD)	85.46 (19.00)	76.53 (21.07)		
Week 28: Adjusted Mean Change (SE)	3.56 (1.98)	2.70 (1.67)		
Week 52: Adjusted Mean Change (SE)	11.30 (1.88)	4.42 (1.57)	6.89 [2.12; 11.66]	0.005 *
Week 100: Adjusted Mean Change (SE)	10.90 (2.03)	3.90 (1.72)	7.01 [1.81; 12.20]	0.008 *

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 65 letters				
N'/ N	113 / 114	90 / 90		
Baseline Mean (SD)	80.79 (21.64)	83.15 (18.13)		
Week 52 Mean (SD)	90.44 (15.36)	91.39 (12.03)		
Week 100 Mean (SD)	91.41 (13.38)	90.17 (13.86)		
Week 28: Adjusted Mean Change (SE)	7.65 (1.51)	7.95 (1.72)		
Week 52: Adjusted Mean Change (SE)	11.26 (1.41)	11.55 (1.56)	-0.30 [-4.41; 3.82]	0.887
Week 100: Adjusted Mean Change (SE)	11.53 (1.55)	9.56 (1.63)	1.97 [-2.44; 6.38]	0.380
Pooled Analysis: Distance Activities				
Interaction test	p=0.117			
≤ 65 letters				
N'/ N	139 / 139	155 / 155		
Baseline Mean (SD)	68.82 (22.29)	69.41 (23.96)		
Week 52 Mean (SD)	82.00 (20.01)	78.81 (20.86)		
Week 100 Mean (SD)	82.35 (20.18)	77.72 (21.45)		
Week 28: Adjusted Mean Change (SE)	4.66 (1.38)	4.61 (1.32)		
Week 52: Adjusted Mean Change (SE)	9.18 (1.33)	5.57 (1.23)	3.61 [0.07; 7.15]	0.046 *
Week 100: Adjusted Mean Change (SE)	9.12 (1.45)	4.88 (1.36)	4.24 [0.36; 8.12]	0.032 *
> 65 letters				
N'/ N	227 / 229	213 / 213		
Baseline Mean (SD)	80.49 (21.84)	80.40 (18.75)		
Week 52 Mean (SD)	89.28 (15.10)	88.96 (13.98)		
Week 100 Mean (SD)	87.07 (17.20)	87.43 (15.47)		
Week 28: Adjusted Mean Change (SE)	8.11 (1.08)	8.94 (1.14)		
Week 52: Adjusted Mean Change (SE)	10.70 (1.01)	10.99 (1.04)	-0.29 [-3.12; 2.54]	0.838
Week 100: Adjusted Mean Change (SE)	8.71 (1.11)	8.81 (1.12)	-0.10 [-3.19; 3.00]	0.951

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.023 ***				
KESTREL: Social Functioning				
Interaction test	p=0.848			
≤ 65 letters				
N'/ N	74 / 74	64 / 64		
Baseline Mean (SD)	84.63 (20.85)	86.91 (15.97)		
Week 52 Mean (SD)	87.96 (19.87)	90.09 (17.22)		
Week 100 Mean (SD)	88.92 (19.09)	87.75 (17.94)		
Week 28: Adjusted Mean Change (SE)	-0.84 (1.45)	2.52 (1.56)		
Week 52: Adjusted Mean Change (SE)	-1.03 (1.70)	1.63 (1.73)	-2.66 [-7.43; 2.12]	0.274
Week 100: Adjusted Mean Change (SE)	1.69 (2.03)	-0.85 (2.10)	2.55 [-3.20; 8.29]	0.384
> 65 letters				
N'/ N	114 / 115	123 / 123		
Baseline Mean (SD)	91.56 (17.08)	91.36 (15.28)		
Week 52 Mean (SD)	95.13 (10.52)	95.55 (10.73)		
Week 100 Mean (SD)	91.62 (15.82)	94.01 (12.69)		
Week 28: Adjusted Mean Change (SE)	3.16 (1.17)	4.79 (1.14)		
Week 52: Adjusted Mean Change (SE)	4.37 (1.29)	5.09 (1.23)	-0.73 [-4.23; 2.77]	0.684
Week 100: Adjusted Mean Change (SE)	1.48 (1.55)	3.91 (1.51)	-2.43 [-6.69; 1.82]	0.261
KITE: Social Functioning				
Interaction test	p=0.359			
≤ 65 letters				
N'/ N	65 / 65	91 / 91		
Baseline Mean (SD)	85.77 (19.75)	80.91 (23.00)		
Week 52 Mean (SD)	93.27 (13.44)	86.83 (17.66)		
Week 100 Mean (SD)	91.84 (19.36)	87.68 (20.66)		
Week 28: Adjusted Mean Change (SE)	2.25 (1.72)	0.95 (1.46)		
Week 52: Adjusted Mean Change (SE)	6.99 (1.50)	1.64 (1.26)	5.35 [1.50; 9.20]	0.007 *
Week 100: Adjusted Mean Change (SE)	4.13 (1.90)	2.81 (1.61)	1.32 [-3.57; 6.22]	0.595

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 65 letters				
N'/ N	113 / 114	90 / 90		
Baseline Mean (SD)	89.93 (15.66)	91.94 (14.43)		
Week 52 Mean (SD)	96.20 (10.92)	96.33 (8.90)		
Week 100 Mean (SD)	96.95 (8.69)	94.23 (12.04)		
Week 28: Adjusted Mean Change (SE)	4.59 (1.33)	6.90 (1.50)		
Week 52: Adjusted Mean Change (SE)	7.61 (1.13)	7.04 (1.25)	0.57 [-2.74; 3.88]	0.734
Week 100: Adjusted Mean Change (SE)	8.42 (1.46)	4.69 (1.52)	3.73 [-0.40; 7.86]	0.076
Pooled Analysis: Social Functioning				
Interaction test	p=0.252			
≤ 65 letters				
N'/ N	139 / 139	155 / 155		
Baseline Mean (SD)	85.16 (20.28)	83.39 (20.55)		
Week 52 Mean (SD)	90.57 (17.15)	88.18 (17.49)		
Week 100 Mean (SD)	90.32 (19.18)	87.71 (19.47)		
Week 28: Adjusted Mean Change (SE)	0.95 (1.12)	1.35 (1.07)		
Week 52: Adjusted Mean Change (SE)	3.27 (1.14)	1.38 (1.05)	1.89 [-1.14; 4.92]	0.222
Week 100: Adjusted Mean Change (SE)	3.15 (1.39)	1.00 (1.30)	2.15 [-1.57; 5.87]	0.258
> 65 letters				
N'/ N	227 / 229	213 / 213		
Baseline Mean (SD)	90.75 (16.37)	91.61 (14.89)		
Week 52 Mean (SD)	95.66 (10.70)	95.88 (9.98)		
Week 100 Mean (SD)	94.15 (13.17)	94.11 (12.37)		
Week 28: Adjusted Mean Change (SE)	3.74 (0.89)	5.78 (0.93)		
Week 52: Adjusted Mean Change (SE)	5.86 (0.86)	6.04 (0.88)	-0.19 [-2.60; 2.23]	0.879
Week 100: Adjusted Mean Change (SE)	4.73 (1.07)	4.27 (1.07)	0.46 [-2.50; 3.42]	0.760

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Mental Health				
Test of heterogeneity in main analysis: **p_H=0.200**				
KESTREL: Mental Health				
Interaction test	p=0.834			
≤ 65 letters				
N'/ N	74 / 74	64 / 64		
Baseline Mean (SD)	56.17 (25.85)	62.21 (25.74)		
Week 52 Mean (SD)	73.73 (22.10)	74.88 (20.34)		
Week 100 Mean (SD)	71.58 (22.29)	72.13 (25.57)		
Week 28: Adjusted Mean Change (SE)	3.24 (2.05)	9.87 (2.20)		
Week 52: Adjusted Mean Change (SE)	9.33 (2.21)	8.87 (2.25)	0.47 [-5.72; 6.66]	0.882
Week 100: Adjusted Mean Change (SE)	9.05 (2.50)	8.09 (2.58)	0.96 [-6.09; 8.01]	0.788
> 65 letters				
N'/ N	114 / 115	123 / 123		
Baseline Mean (SD)	71.60 (22.41)	71.39 (20.91)		
Week 52 Mean (SD)	80.99 (18.25)	80.60 (16.26)		
Week 100 Mean (SD)	76.79 (20.86)	80.47 (18.39)		
Week 28: Adjusted Mean Change (SE)	10.17 (1.64)	8.97 (1.60)		
Week 52: Adjusted Mean Change (SE)	11.29 (1.68)	12.28 (1.60)	-0.99 [-5.53; 3.55]	0.668
Week 100: Adjusted Mean Change (SE)	8.61 (1.91)	12.05 (1.85)	-3.44 [-8.66; 1.78]	0.196
KITE: Mental Health				
Interaction test	p=0.463			
≤ 65 letters				
N'/ N	65 / 65	91 / 91		
Baseline Mean (SD)	63.17 (20.67)	57.83 (28.74)		
Week 52 Mean (SD)	78.25 (21.70)	70.83 (24.90)		
Week 100 Mean (SD)	79.97 (17.16)	73.62 (25.91)		
Week 28: Adjusted Mean Change (SE)	7.77 (2.13)	6.50 (1.82)		
Week 52: Adjusted Mean Change (SE)	12.70 (2.60)	7.21 (2.18)	5.49 [-1.14; 12.13]	0.104
Week 100: Adjusted Mean Change (SE)	11.66 (2.58)	9.84 (2.19)	1.81 [-4.82; 8.44]	0.591

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 65 letters				
N'/ N	113 / 114	90 / 90		
Baseline Mean (SD)	72.23 (21.46)	73.82 (20.07)		
Week 52 Mean (SD)	83.15 (20.04)	82.58 (20.74)		
Week 100 Mean (SD)	86.74 (14.97)	84.86 (16.99)		
Week 28: Adjusted Mean Change (SE)	8.75 (1.64)	11.40 (1.85)		
Week 52: Adjusted Mean Change (SE)	12.66 (1.95)	11.05 (2.17)	1.61 [-4.11; 7.32]	0.580
Week 100: Adjusted Mean Change (SE)	14.99 (1.98)	12.84 (2.08)	2.16 [-3.46; 7.78]	0.451
Pooled Analysis: Mental Health				
Interaction test	p=0.537			
≤ 65 letters				
N'/ N	139 / 139	155 / 155		
Baseline Mean (SD)	59.44 (23.75)	59.64 (27.54)		
Week 52 Mean (SD)	75.94 (21.92)	72.51 (23.13)		
Week 100 Mean (SD)	75.61 (20.33)	72.99 (25.67)		
Week 28: Adjusted Mean Change (SE)	5.63 (1.47)	7.77 (1.41)		
Week 52: Adjusted Mean Change (SE)	11.15 (1.69)	7.68 (1.57)	3.47 [-1.03; 7.97]	0.131
Week 100: Adjusted Mean Change (SE)	10.54 (1.79)	8.92 (1.68)	1.61 [-3.18; 6.40]	0.509
> 65 letters				
N'/ N	227 / 229	213 / 213		
Baseline Mean (SD)	71.92 (21.89)	72.42 (20.55)		
Week 52 Mean (SD)	82.05 (19.13)	81.42 (18.23)		
Week 100 Mean (SD)	81.50 (18.92)	82.44 (17.86)		
Week 28: Adjusted Mean Change (SE)	9.39 (1.16)	10.01 (1.21)		
Week 52: Adjusted Mean Change (SE)	11.91 (1.28)	11.83 (1.31)	0.07 [-3.52; 3.67]	0.967
Week 100: Adjusted Mean Change (SE)	11.66 (1.37)	12.41 (1.38)	-0.75 [-4.56; 3.06]	0.700

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.132**				
KESTREL: Role Difficulties				
Interaction test	p=0.661			
≤ 65 letters				
N'/ N	74 / 74	64 / 64		
Baseline Mean (SD)	62.84 (28.14)	63.09 (28.47)		
Week 52 Mean (SD)	73.61 (30.20)	76.65 (24.27)		
Week 100 Mean (SD)	75.00 (29.52)	73.75 (28.26)		
Week 28: Adjusted Mean Change (SE)	0.71 (2.54)	5.62 (2.75)		
Week 52: Adjusted Mean Change (SE)	1.58 (2.91)	6.79 (2.99)	-5.22 [-13.41; 2.98]	0.211
Week 100: Adjusted Mean Change (SE)	5.97 (3.00)	4.46 (3.12)	1.51 [-6.97; 10.00]	0.726
> 65 letters				
N'/ N	114 / 115	123 / 123		
Baseline Mean (SD)	77.96 (27.44)	76.32 (24.58)		
Week 52 Mean (SD)	84.74 (21.20)	86.43 (21.45)		
Week 100 Mean (SD)	85.30 (22.56)	82.81 (23.17)		
Week 28: Adjusted Mean Change (SE)	9.10 (2.04)	10.77 (1.98)		
Week 52: Adjusted Mean Change (SE)	9.58 (2.22)	12.91 (2.11)	-3.33 [-9.34; 2.68]	0.276
Week 100: Adjusted Mean Change (SE)	10.98 (2.30)	9.29 (2.23)	1.69 [-4.60; 7.98]	0.597
KITE: Role Difficulties				
Interaction test	p=0.217			
≤ 65 letters				
N'/ N	65 / 65	91 / 91		
Baseline Mean (SD)	60.96 (26.75)	59.62 (31.18)		
Week 52 Mean (SD)	75.00 (24.88)	71.33 (25.81)		
Week 100 Mean (SD)	79.08 (25.05)	70.96 (28.52)		
Week 28: Adjusted Mean Change (SE)	6.21 (2.62)	4.72 (2.21)		
Week 52: Adjusted Mean Change (SE)	9.02 (2.80)	4.50 (2.33)	4.52 [-2.60; 11.63]	0.213
Week 100: Adjusted Mean Change (SE)	10.11 (3.03)	4.86 (2.57)	5.25 [-2.53; 13.02]	0.185

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 65 letters				
N'/ N	113 / 114	90 / 90		
Baseline Mean (SD)	76.88 (25.94)	74.86 (25.24)		
Week 52 Mean (SD)	87.36 (18.85)	85.00 (22.88)		
Week 100 Mean (SD)	88.57 (20.81)	88.46 (18.77)		
Week 28: Adjusted Mean Change (SE)	8.05 (2.01)	11.59 (2.26)		
Week 52: Adjusted Mean Change (SE)	14.20 (2.10)	12.24 (2.32)	1.96 [-4.17; 8.09]	0.530
Week 100: Adjusted Mean Change (SE)	13.02 (2.33)	14.33 (2.44)	-1.32 [-7.91; 5.28]	0.695
Pooled Analysis: Role Difficulties				
Interaction test	p=0.552			
≤ 65 letters				
N'/ N	139 / 139	155 / 155		
Baseline Mean (SD)	61.96 (27.41)	61.05 (30.05)		
Week 52 Mean (SD)	74.29 (27.59)	73.54 (25.23)		
Week 100 Mean (SD)	76.96 (27.41)	72.14 (28.33)		
Week 28: Adjusted Mean Change (SE)	3.43 (1.82)	4.97 (1.74)		
Week 52: Adjusted Mean Change (SE)	5.26 (2.01)	5.35 (1.86)	-0.09 [-5.44; 5.26]	0.974
Week 100: Adjusted Mean Change (SE)	8.06 (2.12)	4.56 (1.99)	3.50 [-2.18; 9.18]	0.227
> 65 letters				
N'/ N	227 / 229	213 / 213		
Baseline Mean (SD)	77.42 (26.65)	75.70 (24.81)		
Week 52 Mean (SD)	86.03 (20.07)	85.83 (22.01)		
Week 100 Mean (SD)	86.85 (21.75)	85.34 (21.44)		
Week 28: Adjusted Mean Change (SE)	8.56 (1.43)	11.13 (1.50)		
Week 52: Adjusted Mean Change (SE)	11.83 (1.52)	12.72 (1.56)	-0.89 [-5.16; 3.38]	0.682
Week 100: Adjusted Mean Change (SE)	12.00 (1.63)	11.58 (1.64)	0.42 [-4.11; 4.95]	0.856

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Dependency				
Test of heterogeneity in main analysis: **p_H=0.019 ***				
KESTREL: Dependency				
Interaction test	p=0.783			
≤ 65 letters				
N'/ N	74 / 74	64 / 64		
Baseline Mean (SD)	71.40 (31.00)	74.74 (28.44)		
Week 52 Mean (SD)	83.33 (28.36)	86.16 (22.46)		
Week 100 Mean (SD)	82.55 (23.53)	83.67 (26.08)		
Week 28: Adjusted Mean Change (SE)	2.61 (2.21)	4.37 (2.38)		
Week 52: Adjusted Mean Change (SE)	2.67 (2.37)	4.97 (2.44)	-2.30 [-8.97; 4.37]	0.498
Week 100: Adjusted Mean Change (SE)	3.53 (2.66)	3.48 (2.76)	0.04 [-7.46; 7.55]	0.991
> 65 letters				
N'/ N	114 / 115	123 / 123		
Baseline Mean (SD)	88.08 (20.50)	86.92 (19.85)		
Week 52 Mean (SD)	92.19 (16.48)	95.00 (12.59)		
Week 100 Mean (SD)	88.28 (21.69)	90.89 (17.40)		
Week 28: Adjusted Mean Change (SE)	7.56 (1.77)	8.07 (1.72)		
Week 52: Adjusted Mean Change (SE)	7.19 (1.81)	10.66 (1.72)	-3.47 [-8.36; 1.43]	0.164
Week 100: Adjusted Mean Change (SE)	3.80 (2.03)	6.62 (1.97)	-2.83 [-8.38; 2.73]	0.318
KITE: Dependency				
Interaction test	p=0.664			
≤ 65 letters				
N'/ N	65 / 65	91 / 91		
Baseline Mean (SD)	77.56 (23.93)	71.61 (30.48)		
Week 52 Mean (SD)	86.54 (21.46)	80.67 (25.56)		
Week 100 Mean (SD)	90.48 (15.21)	80.02 (27.70)		
Week 28: Adjusted Mean Change (SE)	4.60 (2.14)	1.13 (1.83)		
Week 52: Adjusted Mean Change (SE)	5.68 (2.34)	2.07 (1.97)	3.60 [-2.37; 9.58]	0.237
Week 100: Adjusted Mean Change (SE)	5.95 (2.52)	1.38 (2.15)	4.57 [-1.92; 11.06]	0.167

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 65 letters				
N'/ N	113 / 114	90 / 90		
Baseline Mean (SD)	86.80 (22.76)	92.31 (17.76)		
Week 52 Mean (SD)	93.66 (17.40)	92.78 (17.62)		
Week 100 Mean (SD)	94.61 (14.00)	93.80 (15.34)		
Week 28: Adjusted Mean Change (SE)	5.62 (1.64)	5.02 (1.87)		
Week 52: Adjusted Mean Change (SE)	8.13 (1.75)	3.97 (1.97)	4.16 [-1.00; 9.32]	0.114
Week 100: Adjusted Mean Change (SE)	7.03 (1.93)	4.37 (2.05)	2.66 [-2.85; 8.17]	0.343
Pooled Analysis: Dependency				
Interaction test	p=0.372			
≤ 65 letters				
N'/ N	139 / 139	155 / 155		
Baseline Mean (SD)	74.28 (27.99)	72.90 (29.60)		
Week 52 Mean (SD)	84.91 (25.15)	82.94 (24.39)		
Week 100 Mean (SD)	86.36 (20.27)	81.57 (26.97)		
Week 28: Adjusted Mean Change (SE)	3.87 (1.54)	2.51 (1.48)		
Week 52: Adjusted Mean Change (SE)	4.41 (1.67)	3.24 (1.56)	1.17 [-3.27; 5.62]	0.605
Week 100: Adjusted Mean Change (SE)	5.06 (1.82)	2.22 (1.72)	2.85 [-2.04; 7.73]	0.253
> 65 letters				
N'/ N	227 / 229	213 / 213		
Baseline Mean (SD)	87.44 (21.62)	89.20 (19.14)		
Week 52 Mean (SD)	92.91 (16.91)	94.07 (14.88)		
Week 100 Mean (SD)	91.28 (18.67)	92.19 (16.53)		
Week 28: Adjusted Mean Change (SE)	6.48 (1.21)	6.69 (1.27)		
Week 52: Adjusted Mean Change (SE)	7.53 (1.27)	7.82 (1.30)	-0.29 [-3.84; 3.26]	0.871
Week 100: Adjusted Mean Change (SE)	5.34 (1.40)	5.68 (1.41)	-0.34 [-4.23; 3.56]	0.866

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Driving				
Test of heterogeneity in main analysis: **p_H=0.792**				
KESTREL: Driving				
Interaction test	p=0.822			
≤ 65 letters				
N'/ N	38 / 74	34 / 64		
Baseline Mean (SD)	72.59 (20.40)	75.00 (20.49)		
Week 52 Mean (SD)	83.00 (18.71)	78.13 (22.50)		
Week 100 Mean (SD)	83.97 (16.32)	77.85 (23.24)		
Week 28: Adjusted Mean Change (SE)	-2.74 (2.55)	6.09 (2.84)		
Week 52: Adjusted Mean Change (SE)	3.95 (3.08)	1.39 (3.25)	2.57 [-6.27; 11.40]	0.568
Week 100: Adjusted Mean Change (SE)	6.00 (3.33)	2.51 (3.78)	3.49 [-6.44; 13.43]	0.489
> 65 letters				
N'/ N	82 / 115	86 / 123		
Baseline Mean (SD)	83.33 (16.77)	78.00 (19.42)		
Week 52 Mean (SD)	84.68 (20.65)	86.52 (15.77)		
Week 100 Mean (SD)	82.54 (20.51)	80.60 (21.16)		
Week 28: Adjusted Mean Change (SE)	4.04 (1.67)	5.22 (1.65)		
Week 52: Adjusted Mean Change (SE)	3.55 (1.88)	7.45 (1.90)	-3.89 [-9.19; 1.40]	0.148
Week 100: Adjusted Mean Change (SE)	0.84 (2.12)	1.49 (2.11)	-0.65 [-6.57; 5.26]	0.828
KITE: Driving				
Interaction test	p=0.102			
≤ 65 letters				
N'/ N	32 / 65	32 / 91		
Baseline Mean (SD)	74.87 (21.80)	73.83 (28.34)		
Week 52 Mean (SD)	79.67 (25.47)	85.67 (17.23)		
Week 100 Mean (SD)	79.35 (19.28)	87.08 (15.87)		
Week 28: Adjusted Mean Change (SE)	-5.05 (2.71)	4.62 (2.57)		
Week 52: Adjusted Mean Change (SE)	2.19 (2.35)	4.91 (2.31)	-2.72 [-9.20; 3.76]	0.409
Week 100: Adjusted Mean Change (SE)	1.32 (2.64)	3.19 (2.73)	-1.87 [-9.35; 5.60]	0.622

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 65 letters				
N'/ N	71 / 114	64 / 90		
Baseline Mean (SD)	80.87 (19.54)	86.20 (16.33)		
Week 52 Mean (SD)	89.97 (11.14)	88.89 (15.06)		
Week 100 Mean (SD)	89.17 (11.91)	87.12 (14.15)		
Week 28: Adjusted Mean Change (SE)	2.96 (1.68)	5.69 (1.82)		
Week 52: Adjusted Mean Change (SE)	7.29 (1.51)	4.69 (1.61)	2.60 [-1.77; 6.97]	0.242
Week 100: Adjusted Mean Change (SE)	5.40 (1.69)	2.68 (1.72)	2.72 [-2.03; 7.47]	0.261
Pooled Analysis: Driving				
Interaction test	p=0.710			
≤ 65 letters				
N'/ N	70 / 139	66 / 155		
Baseline Mean (SD)	73.63 (20.93)	74.43 (24.43)		
Week 52 Mean (SD)	81.33 (22.18)	81.97 (20.13)		
Week 100 Mean (SD)	81.80 (17.73)	82.59 (20.09)		
Week 28: Adjusted Mean Change (SE)	-3.38 (1.85)	5.18 (1.92)		
Week 52: Adjusted Mean Change (SE)	4.00 (1.96)	3.12 (2.00)	0.88 [-4.62; 6.37]	0.754
Week 100: Adjusted Mean Change (SE)	4.39 (2.17)	2.72 (2.37)	1.67 [-4.63; 7.97]	0.602
> 65 letters				
N'/ N	153 / 229	150 / 213		
Baseline Mean (SD)	82.19 (18.09)	81.50 (18.56)		
Week 52 Mean (SD)	87.03 (17.24)	87.54 (15.45)		
Week 100 Mean (SD)	85.63 (17.30)	83.61 (18.47)		
Week 28: Adjusted Mean Change (SE)	3.36 (1.18)	5.48 (1.23)		
Week 52: Adjusted Mean Change (SE)	4.99 (1.22)	6.34 (1.27)	-1.36 [-4.82; 2.11]	0.442
Week 100: Adjusted Mean Change (SE)	2.70 (1.39)	2.11 (1.40)	0.59 [-3.28; 4.46]	0.765

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Color Vision				
Test of heterogeneity in main analysis: **p_H=0.477**				
KESTREL: Color Vision				
Interaction test	p=0.853			
≤ 65 letters				
N'/ N	73 / 74	62 / 64		
Baseline Mean (SD)	90.75 (18.40)	91.53 (17.50)		
Week 52 Mean (SD)	93.40 (15.62)	92.00 (17.08)		
Week 100 Mean (SD)	92.79 (15.92)	93.62 (15.17)		
Week 28: Adjusted Mean Change (SE)	-0.32 (1.32)	-0.70 (1.44)		
Week 52: Adjusted Mean Change (SE)	-0.83 (1.41)	-1.94 (1.47)	1.11 [-2.91; 5.13]	0.587
Week 100: Adjusted Mean Change (SE)	-0.46 (1.68)	-0.69 (1.77)	0.23 [-4.59; 5.04]	0.926
> 65 letters				
N'/ N	113 / 115	122 / 123		
Baseline Mean (SD)	94.47 (15.21)	95.29 (13.38)		
Week 52 Mean (SD)	98.42 (7.12)	97.82 (7.91)		
Week 100 Mean (SD)	95.79 (10.82)	95.79 (10.73)		
Week 28: Adjusted Mean Change (SE)	3.59 (1.06)	3.04 (1.03)		
Week 52: Adjusted Mean Change (SE)	3.93 (1.06)	3.63 (1.02)	0.31 [-2.60; 3.21]	0.836
Week 100: Adjusted Mean Change (SE)	1.35 (1.29)	1.61 (1.24)	-0.25 [-3.77; 3.26]	0.887
KITE: Color Vision				
Interaction test	p=0.972			
≤ 65 letters				
N'/ N	65 / 65	89 / 91		
Baseline Mean (SD)	91.92 (17.18)	86.52 (19.60)		
Week 52 Mean (SD)	96.57 (10.02)	92.71 (14.19)		
Week 100 Mean (SD)	96.35 (8.92)	93.36 (14.94)		
Week 28: Adjusted Mean Change (SE)	3.71 (1.37)	2.96 (1.16)		
Week 52: Adjusted Mean Change (SE)	5.23 (1.26)	3.15 (1.07)	2.08 [-1.17; 5.32]	0.209
Week 100: Adjusted Mean Change (SE)	4.38 (1.50)	4.18 (1.30)	0.19 [-3.72; 4.10]	0.923

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 65 letters				
N'/ N	113 / 114	90 / 90		
Baseline Mean (SD)	92.26 (16.73)	96.94 (9.05)		
Week 52 Mean (SD)	98.10 (7.63)	97.00 (10.03)		
Week 100 Mean (SD)	97.87 (8.96)	96.47 (11.90)		
Week 28: Adjusted Mean Change (SE)	3.28 (1.04)	5.18 (1.19)		
Week 52: Adjusted Mean Change (SE)	5.81 (0.94)	3.39 (1.04)	2.42 [-0.34; 5.17]	0.086
Week 100: Adjusted Mean Change (SE)	5.28 (1.14)	2.60 (1.18)	2.68 [-0.55; 5.92]	0.103
Pooled Analysis: Color Vision				
Interaction test	p=0.674			
≤ 65 letters				
N'/ N	138 / 139	151 / 155		
Baseline Mean (SD)	91.30 (17.78)	88.58 (18.87)		
Week 52 Mean (SD)	94.95 (13.21)	92.42 (15.38)		
Week 100 Mean (SD)	94.50 (13.09)	93.47 (14.97)		
Week 28: Adjusted Mean Change (SE)	1.82 (0.96)	1.09 (0.92)		
Week 52: Adjusted Mean Change (SE)	2.34 (0.94)	0.61 (0.88)	1.73 [-0.80; 4.27]	0.180
Week 100: Adjusted Mean Change (SE)	2.08 (1.13)	1.66 (1.08)	0.43 [-2.64; 3.49]	0.784
> 65 letters				
N'/ N	226 / 229	212 / 213		
Baseline Mean (SD)	93.36 (15.99)	95.99 (11.74)		
Week 52 Mean (SD)	98.26 (7.35)	97.47 (8.85)		
Week 100 Mean (SD)	96.78 (9.99)	96.10 (11.24)		
Week 28: Adjusted Mean Change (SE)	3.37 (0.75)	4.18 (0.79)		
Week 52: Adjusted Mean Change (SE)	4.75 (0.71)	3.80 (0.73)	0.95 [-1.05; 2.94]	0.352
Week 100: Adjusted Mean Change (SE)	3.27 (0.86)	2.16 (0.87)	1.11 [-1.29; 3.51]	0.364

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.003 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.698			
≤ 65 letters				
N'/ N	74 / 74	64 / 64		
Baseline Mean (SD)	77.70 (24.33)	76.17 (23.75)		
Week 52 Mean (SD)	84.72 (21.40)	86.06 (18.80)		
Week 100 Mean (SD)	84.43 (22.59)	83.50 (26.05)		
Week 28: Adjusted Mean Change (SE)	0.24 (2.13)	9.94 (2.31)		
Week 52: Adjusted Mean Change (SE)	2.93 (2.29)	6.35 (2.36)	-3.41 [-9.89; 3.06]	0.301
Week 100: Adjusted Mean Change (SE)	3.20 (2.69)	3.47 (2.80)	-0.27 [-7.92; 7.38]	0.944
> 65 letters				
N'/ N	113 / 115	122 / 123		
Baseline Mean (SD)	88.05 (18.93)	82.17 (22.84)		
Week 52 Mean (SD)	91.84 (18.03)	89.76 (17.23)		
Week 100 Mean (SD)	84.17 (22.00)	89.58 (17.27)		
Week 28: Adjusted Mean Change (SE)	4.24 (1.74)	6.37 (1.67)		
Week 52: Adjusted Mean Change (SE)	7.11 (1.75)	7.43 (1.65)	-0.32 [-5.05; 4.42]	0.895
Week 100: Adjusted Mean Change (SE)	-0.16 (2.08)	7.07 (2.01)	-7.23 [-12.91; -1.54]	0.013 *
KITE: Peripheral Vision				
Interaction test	p=0.288			
≤ 65 letters				
N'/ N	65 / 65	91 / 91		
Baseline Mean (SD)	78.46 (21.14)	79.67 (22.95)		
Week 52 Mean (SD)	87.50 (18.85)	83.00 (22.94)		
Week 100 Mean (SD)	88.78 (16.97)	84.93 (19.38)		
Week 28: Adjusted Mean Change (SE)	4.00 (1.97)	1.98 (1.66)		
Week 52: Adjusted Mean Change (SE)	7.45 (2.14)	1.17 (1.78)	6.28 [0.82; 11.73]	0.024 *
Week 100: Adjusted Mean Change (SE)	6.14 (2.13)	2.96 (1.80)	3.18 [-2.31; 8.67]	0.255

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 65 letters				
N'/ N	113 / 114	89 / 90		
Baseline Mean (SD)	85.84 (19.16)	89.89 (18.36)		
Week 52 Mean (SD)	91.03 (15.98)	92.57 (13.55)		
Week 100 Mean (SD)	94.51 (13.62)	90.26 (17.75)		
Week 28: Adjusted Mean Change (SE)	4.88 (1.51)	7.16 (1.73)		
Week 52: Adjusted Mean Change (SE)	5.67 (1.60)	5.89 (1.80)	-0.22 [-4.95; 4.51]	0.926
Week 100: Adjusted Mean Change (SE)	8.42 (1.64)	3.03 (1.73)	5.39 [0.72; 10.06]	0.024 *
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.492			
≤ 65 letters				
N'/ N	139 / 139	155 / 155		
Baseline Mean (SD)	78.06 (22.81)	78.23 (23.27)		
Week 52 Mean (SD)	86.08 (20.14)	84.25 (21.32)		
Week 100 Mean (SD)	86.52 (20.11)	84.32 (22.36)		
Week 28: Adjusted Mean Change (SE)	2.24 (1.46)	5.46 (1.40)		
Week 52: Adjusted Mean Change (SE)	5.26 (1.58)	3.48 (1.46)	1.79 [-2.41; 5.99]	0.404
Week 100: Adjusted Mean Change (SE)	4.72 (1.73)	3.37 (1.62)	1.36 [-3.29; 6.00]	0.567
> 65 letters				
N'/ N	226 / 229	211 / 213		
Baseline Mean (SD)	86.95 (19.03)	85.43 (21.36)		
Week 52 Mean (SD)	91.44 (17.01)	90.92 (15.83)		
Week 100 Mean (SD)	89.10 (19.15)	89.88 (17.44)		
Week 28: Adjusted Mean Change (SE)	4.31 (1.16)	6.66 (1.21)		
Week 52: Adjusted Mean Change (SE)	6.21 (1.19)	6.83 (1.22)	-0.62 [-3.97; 2.73]	0.715
Week 100: Adjusted Mean Change (SE)	3.75 (1.34)	5.15 (1.34)	-1.41 [-5.12; 2.30]	0.456

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
General Health				
Test of heterogeneity in main analysis: **p_H=0.834**				
KESTREL: General Health				
Interaction test	p=0.960			
≤ 65 letters				
N'/ N	74 / 74	64 / 64		
Baseline Mean (SD)	41.89 (21.54)	38.67 (23.12)		
Week 52 Mean (SD)	47.69 (22.92)	42.45 (20.56)		
Week 100 Mean (SD)	46.23 (23.20)	44.00 (23.45)		
Week 28: Adjusted Mean Change (SE)	4.75 (2.19)	4.73 (2.37)		
Week 52: Adjusted Mean Change (SE)	4.82 (2.77)	1.65 (2.83)	3.17 [-4.63; 10.96]	0.425
Week 100: Adjusted Mean Change (SE)	3.52 (2.72)	3.81 (2.82)	-0.29 [-8.02; 7.44]	0.941
> 65 letters				
N'/ N	114 / 115	123 / 123		
Baseline Mean (SD)	45.61 (20.84)	38.41 (18.47)		
Week 52 Mean (SD)	54.21 (24.64)	47.38 (21.91)		
Week 100 Mean (SD)	51.92 (23.04)	50.52 (19.86)		
Week 28: Adjusted Mean Change (SE)	4.25 (1.78)	4.80 (1.73)		
Week 52: Adjusted Mean Change (SE)	10.42 (2.11)	7.17 (2.01)	3.24 [-2.50; 8.98]	0.267
Week 100: Adjusted Mean Change (SE)	10.24 (2.09)	9.52 (2.03)	0.72 [-5.02; 6.46]	0.805
KITE: General Health				
Interaction test	p=0.601			
≤ 65 letters				
N'/ N	65 / 65	91 / 91		
Baseline Mean (SD)	41.92 (17.74)	41.21 (23.97)		
Week 52 Mean (SD)	48.08 (18.42)	45.33 (23.50)		
Week 100 Mean (SD)	44.90 (16.12)	48.16 (24.93)		
Week 28: Adjusted Mean Change (SE)	3.48 (2.29)	3.24 (1.93)		
Week 52: Adjusted Mean Change (SE)	6.74 (2.75)	2.48 (2.29)	4.26 [-2.77; 11.28]	0.234
Week 100: Adjusted Mean Change (SE)	2.88 (2.52)	5.11 (2.13)	-2.23 [-8.72; 4.26]	0.500

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 65 letters				
N'/ N	113 / 114	90 / 90		
Baseline Mean (SD)	45.13 (21.61)	48.06 (21.28)		
Week 52 Mean (SD)	50.27 (23.58)	55.00 (22.51)		
Week 100 Mean (SD)	54.27 (21.08)	53.85 (19.77)		
Week 28: Adjusted Mean Change (SE)	3.49 (1.76)	5.52 (1.99)		
Week 52: Adjusted Mean Change (SE)	4.88 (2.06)	7.66 (2.28)	-2.77 [-8.82; 3.27]	0.367
Week 100: Adjusted Mean Change (SE)	8.11 (1.94)	6.14 (2.02)	1.97 [-3.53; 7.47]	0.481
Pooled Analysis: General Health				
Interaction test	p=0.731			
≤ 65 letters				
N'/ N	139 / 139	155 / 155		
Baseline Mean (SD)	41.91 (19.79)	40.16 (23.58)		
Week 52 Mean (SD)	47.88 (20.74)	44.14 (22.29)		
Week 100 Mean (SD)	45.59 (20.03)	46.40 (24.30)		
Week 28: Adjusted Mean Change (SE)	4.03 (1.58)	3.87 (1.51)		
Week 52: Adjusted Mean Change (SE)	5.63 (1.94)	2.11 (1.79)	3.52 [-1.67; 8.70]	0.183
Week 100: Adjusted Mean Change (SE)	3.06 (1.85)	4.56 (1.73)	-1.50 [-6.48; 3.48]	0.555
> 65 letters				
N'/ N	227 / 229	213 / 213		
Baseline Mean (SD)	45.37 (21.18)	42.49 (20.23)		
Week 52 Mean (SD)	52.27 (24.14)	50.56 (22.42)		
Week 100 Mean (SD)	53.03 (22.10)	52.01 (19.83)		
Week 28: Adjusted Mean Change (SE)	3.78 (1.25)	5.20 (1.31)		
Week 52: Adjusted Mean Change (SE)	7.60 (1.47)	7.45 (1.50)	0.14 [-3.99; 4.28]	0.945
Week 100: Adjusted Mean Change (SE)	9.16 (1.42)	8.13 (1.43)	1.03 [-2.93; 4.99]	0.610

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + BCVA + treatment * BCVA + visit * BCVA + treatment * BCVA * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + study + treatment * study + BCVA + treatment * BCVA + visit * BCVA + treatment * BCVA * visit.

Table 8.5 VFQ by region (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Composite Score				
Test of heterogeneity in main analysis: **p_H=0.049 ***				
KESTREL: Composite Score				
Interaction test	p=0.716			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	72.65 (18.47)	72.26 (15.95)		
Week 52 Mean (SD)	83.05 (15.30)	84.97 (13.30)		
Week 100 Mean (SD)	80.64 (16.40)	81.78 (16.23)		
Week 28: Adjusted Mean Change (SE)	5.96 (1.17)	7.61 (1.24)		
Week 52: Adjusted Mean Change (SE)	6.26 (1.22)	9.76 (1.25)	-3.50 [-6.90; -0.11]	0.043 *
Week 100: Adjusted Mean Change (SE)	5.71 (1.36)	6.68 (1.40)	-0.98 [-4.79; 2.84]	0.615
European Region				
N'/ N	68 / 69	75 / 75		
Baseline Mean (SD)	83.81 (14.77)	82.06 (12.05)		
Week 52 Mean (SD)	89.98 (8.99)	86.62 (11.68)		
Week 100 Mean (SD)	88.99 (10.27)	87.01 (12.47)		
Week 28: Adjusted Mean Change (SE)	5.18 (1.34)	7.65 (1.29)		
Week 52: Adjusted Mean Change (SE)	8.35 (1.40)	7.01 (1.34)	1.34 [-2.43; 5.11]	0.485
Week 100: Adjusted Mean Change (SE)	7.89 (1.58)	7.65 (1.51)	0.25 [-4.00; 4.50]	0.908
Western Pacific Region				
N'/ N	30 / 30	29 / 29		
Baseline Mean (SD)	72.37 (15.07)	76.27 (12.20)		
Week 52 Mean (SD)	79.47 (15.80)	82.12 (10.24)		
Week 100 Mean (SD)	77.61 (15.48)	78.99 (11.43)		
Week 28: Adjusted Mean Change (SE)	6.57 (2.00)	8.17 (2.08)		
Week 52: Adjusted Mean Change (SE)	6.19 (2.10)	6.68 (2.10)	-0.49 [-6.31; 5.34]	0.869
Week 100: Adjusted Mean Change (SE)	3.73 (2.25)	3.71 (2.33)	0.01 [-6.35; 6.38]	0.996

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Composite Score				
Interaction test	p=0.642			
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	73.10 (12.58)	71.30 (19.28)		
Week 52 Mean (SD)	85.86 (9.60)	77.76 (18.90)		
Week 100 Mean (SD)	86.06 (14.02)	82.48 (17.73)		
Week 28: Adjusted Mean Change (SE)	5.76 (2.04)	4.99 (2.29)		
Week 52: Adjusted Mean Change (SE)	11.44 (2.35)	6.52 (2.59)	4.92 [-1.94; 11.78]	0.159
Week 100: Adjusted Mean Change (SE)	9.95 (2.92)	9.34 (2.84)	0.62 [-7.37; 8.61]	0.879
European Region				
N'/ N	134 / 135	132 / 132		
Baseline Mean (SD)	78.75 (15.44)	77.43 (16.96)		
Week 52 Mean (SD)	86.94 (12.63)	84.16 (14.84)		
Week 100 Mean (SD)	88.48 (12.07)	82.79 (16.01)		
Week 28: Adjusted Mean Change (SE)	5.79 (0.89)	5.75 (0.89)		
Week 52: Adjusted Mean Change (SE)	8.68 (0.95)	6.63 (0.95)	2.05 [-0.58; 4.67]	0.126
Week 100: Adjusted Mean Change (SE)	8.75 (1.07)	4.65 (1.07)	4.10 [1.13; 7.08]	0.007 *
Western Pacific Region				
N'/ N	18 / 18	28 / 28		
Baseline Mean (SD)	77.74 (14.10)	75.77 (19.62)		
Week 52 Mean (SD)	83.74 (17.75)	84.04 (17.31)		
Week 100 Mean (SD)	86.83 (11.30)	90.99 (6.42)		
Week 28: Adjusted Mean Change (SE)	4.89 (2.42)	7.16 (2.02)		
Week 52: Adjusted Mean Change (SE)	6.58 (2.59)	4.79 (2.08)	1.79 [-4.72; 8.29]	0.590
Week 100: Adjusted Mean Change (SE)	9.58 (3.13)	11.40 (2.34)	-1.82 [-9.48; 5.83]	0.640
Pooled Analysis: Composite Score				
Interaction test	p=0.651			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	72.65 (18.47)	72.26 (15.95)		
Week 52 Mean (SD)	83.05 (15.30)	84.97 (13.30)		
Week 100 Mean (SD)	80.64 (16.40)	81.78 (16.23)		
Week 28: Adjusted Mean Change (SE)	6.80 (1.30)	7.81 (1.35)		
Week 52: Adjusted Mean Change (SE)	7.11 (1.35)	9.99 (1.36)	-2.88 [-6.62; 0.86]	0.131
Week 100: Adjusted Mean Change (SE)	6.52 (1.49)	6.85 (1.51)	-0.33 [-4.47; 3.82]	0.877

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	73.10 (12.58)	71.30 (19.28)		
Week 52 Mean (SD)	85.86 (9.60)	77.76 (18.90)		
Week 100 Mean (SD)	86.06 (14.02)	82.48 (17.73)		
Week 28: Adjusted Mean Change (SE)	4.72 (2.21)	4.75 (2.46)		
Week 52: Adjusted Mean Change (SE)	10.48 (2.47)	6.24 (2.69)	4.23 [-2.94; 11.41]	0.247
Week 100: Adjusted Mean Change (SE)	9.09 (3.01)	9.06 (2.92)	0.03 [-8.20; 8.26]	0.995
European Region				
N'/ N	202 / 204	207 / 207		
Baseline Mean (SD)	80.45 (15.37)	79.11 (15.49)		
Week 52 Mean (SD)	87.95 (11.62)	85.03 (13.83)		
Week 100 Mean (SD)	88.64 (11.48)	84.23 (14.99)		
Week 28: Adjusted Mean Change (SE)	5.36 (0.79)	6.39 (0.77)		
Week 52: Adjusted Mean Change (SE)	8.32 (0.82)	6.73 (0.80)	1.59 [-0.65; 3.83]	0.165
Week 100: Adjusted Mean Change (SE)	8.24 (0.92)	5.64 (0.90)	2.60 [0.08; 5.11]	0.043 *
Western Pacific Region				
N'/ N	48 / 48	57 / 57		
Baseline Mean (SD)	74.38 (14.80)	76.02 (16.13)		
Week 52 Mean (SD)	81.12 (16.48)	83.06 (14.04)		
Week 100 Mean (SD)	80.52 (14.79)	84.86 (11.04)		
Week 28: Adjusted Mean Change (SE)	6.14 (1.55)	7.49 (1.45)		
Week 52: Adjusted Mean Change (SE)	6.49 (1.63)	5.54 (1.47)	0.95 [-3.36; 5.26]	0.666
Week 100: Adjusted Mean Change (SE)	5.83 (1.83)	7.24 (1.64)	-1.41 [-6.23; 3.41]	0.567
General Vision				
Test of heterogeneity in main analysis: **p_H=0.762**				
KESTREL: General Vision				
Interaction test	p=0.818			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	60.22 (17.09)	58.55 (14.58)		
Week 52 Mean (SD)	72.57 (14.51)	73.06 (12.63)		
Week 100 Mean (SD)	73.73 (14.02)	73.64 (11.18)		
Week 28: Adjusted Mean Change (SE)	11.67 (1.41)	9.81 (1.49)		
Week 52: Adjusted Mean Change (SE)	11.44 (1.45)	12.62 (1.46)	-1.18 [-5.21; 2.85]	0.565
Week 100: Adjusted Mean Change (SE)	13.27 (1.48)	12.66 (1.51)	0.61 [-3.54; 4.76]	0.774

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
European Region				
N'/ N	68 / 69	75 / 75		
Baseline Mean (SD)	67.06 (15.75)	63.20 (14.35)		
Week 52 Mean (SD)	78.55 (11.45)	71.80 (13.36)		
Week 100 Mean (SD)	77.25 (14.98)	74.29 (12.48)		
Week 28: Adjusted Mean Change (SE)	11.61 (1.61)	12.70 (1.55)		
Week 52: Adjusted Mean Change (SE)	15.30 (1.66)	10.32 (1.57)	4.98 [0.51; 9.45]	0.029 *
Week 100: Adjusted Mean Change (SE)	14.92 (1.71)	13.22 (1.63)	1.70 [-2.93; 6.33]	0.471
Western Pacific Region				
N'/ N	30 / 30	29 / 29		
Baseline Mean (SD)	51.33 (16.34)	57.24 (14.86)		
Week 52 Mean (SD)	61.67 (11.67)	64.00 (10.00)		
Week 100 Mean (SD)	66.15 (14.72)	64.17 (10.18)		
Week 28: Adjusted Mean Change (SE)	10.15 (2.43)	7.81 (2.53)		
Week 52: Adjusted Mean Change (SE)	4.87 (2.51)	5.65 (2.48)	-0.77 [-7.67; 6.12]	0.825
Week 100: Adjusted Mean Change (SE)	8.39 (2.43)	6.05 (2.52)	2.34 [-4.50; 9.18]	0.501
KITE: General Vision				
Interaction test	p=0.668			
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	60.00 (14.97)	58.10 (17.78)		
Week 52 Mean (SD)	67.06 (18.63)	61.43 (14.60)		
Week 100 Mean (SD)	72.31 (15.36)	69.33 (21.20)		
Week 28: Adjusted Mean Change (SE)	8.60 (2.74)	7.87 (3.07)		
Week 52: Adjusted Mean Change (SE)	9.56 (3.26)	6.01 (3.59)	3.56 [-5.96; 13.07]	0.463
Week 100: Adjusted Mean Change (SE)	14.43 (3.70)	11.16 (3.53)	3.26 [-6.78; 13.31]	0.524
European Region				
N'/ N	134 / 135	132 / 132		
Baseline Mean (SD)	61.94 (15.49)	59.39 (17.29)		
Week 52 Mean (SD)	74.11 (13.33)	70.71 (15.87)		
Week 100 Mean (SD)	73.96 (13.85)	69.81 (15.83)		
Week 28: Adjusted Mean Change (SE)	9.50 (1.19)	9.67 (1.20)		
Week 52: Adjusted Mean Change (SE)	12.77 (1.29)	10.72 (1.30)	2.05 [-1.55; 5.65]	0.263
Week 100: Adjusted Mean Change (SE)	12.18 (1.33)	9.22 (1.32)	2.95 [-0.74; 6.64]	0.117

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Western Pacific Region				
N'/ N	18 / 18	28 / 28		
Baseline Mean (SD)	63.33 (21.96)	63.57 (23.13)		
Week 52 Mean (SD)	69.33 (16.68)	75.00 (22.26)		
Week 100 Mean (SD)	73.33 (13.03)	74.78 (16.20)		
Week 28: Adjusted Mean Change (SE)	9.22 (3.25)	10.09 (2.73)		
Week 52: Adjusted Mean Change (SE)	6.30 (3.55)	10.47 (2.84)	-4.17 [-13.06; 4.72]	0.357
Week 100: Adjusted Mean Change (SE)	10.56 (3.91)	9.94 (2.90)	0.62 [-8.92; 10.16]	0.898
Pooled Analysis: General Vision				
Interaction test	p=0.794			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	60.22 (17.09)	58.55 (14.58)		
Week 52 Mean (SD)	72.57 (14.51)	73.06 (12.63)		
Week 100 Mean (SD)	73.73 (14.02)	73.64 (11.18)		
Week 28: Adjusted Mean Change (SE)	11.04 (1.61)	9.65 (1.67)		
Week 52: Adjusted Mean Change (SE)	10.78 (1.70)	12.46 (1.70)	-1.68 [-6.39; 3.03]	0.483
Week 100: Adjusted Mean Change (SE)	12.72 (1.73)	12.42 (1.74)	0.30 [-4.51; 5.11]	0.902
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	60.00 (14.97)	58.10 (17.78)		
Week 52 Mean (SD)	67.06 (18.63)	61.43 (14.60)		
Week 100 Mean (SD)	72.31 (15.36)	69.33 (21.20)		
Week 28: Adjusted Mean Change (SE)	9.10 (2.79)	7.95 (3.10)		
Week 52: Adjusted Mean Change (SE)	9.86 (3.20)	5.87 (3.49)	3.99 [-5.30; 13.28]	0.400
Week 100: Adjusted Mean Change (SE)	14.70 (3.58)	11.12 (3.40)	3.59 [-6.11; 13.28]	0.468
European Region				
N'/ N	202 / 204	207 / 207		
Baseline Mean (SD)	63.66 (15.72)	60.77 (16.35)		
Week 52 Mean (SD)	75.57 (12.88)	71.10 (15.00)		
Week 100 Mean (SD)	75.03 (14.26)	71.34 (14.88)		
Week 28: Adjusted Mean Change (SE)	10.26 (0.99)	10.70 (0.97)		
Week 52: Adjusted Mean Change (SE)	13.66 (1.04)	10.53 (1.02)	3.13 [0.27; 5.99]	0.032 *
Week 100: Adjusted Mean Change (SE)	13.20 (1.07)	10.60 (1.04)	2.59 [-0.33; 5.51]	0.082

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Western Pacific Region				
N'/ N	48 / 48	57 / 57		
Baseline Mean (SD)	55.83 (19.33)	60.35 (19.45)		
Week 52 Mean (SD)	64.62 (14.11)	69.39 (17.84)		
Week 100 Mean (SD)	68.42 (14.43)	69.36 (14.36)		
Week 28: Adjusted Mean Change (SE)	10.29 (1.97)	9.35 (1.85)		
Week 52: Adjusted Mean Change (SE)	6.08 (2.10)	8.47 (1.87)	-2.39 [-7.92; 3.13]	0.395
Week 100: Adjusted Mean Change (SE)	9.66 (2.12)	8.46 (1.90)	1.20 [-4.38; 6.79]	0.673
Ocular Pain				
Test of heterogeneity in main analysis: **p_H=0.664**				
KESTREL: Ocular Pain				
Interaction test	p=0.777			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	79.31 (21.70)	78.46 (23.93)		
Week 52 Mean (SD)	87.32 (16.96)	87.50 (16.39)		
Week 100 Mean (SD)	84.51 (20.99)	81.82 (21.28)		
Week 28: Adjusted Mean Change (SE)	2.89 (1.91)	6.33 (2.02)		
Week 52: Adjusted Mean Change (SE)	4.67 (1.78)	6.37 (1.80)	-1.70 [-6.64; 3.24]	0.498
Week 100: Adjusted Mean Change (SE)	2.95 (1.96)	0.30 (2.00)	2.65 [-2.82; 8.13]	0.341
European Region				
N'/ N	68 / 69	75 / 75		
Baseline Mean (SD)	87.87 (17.14)	86.00 (16.18)		
Week 52 Mean (SD)	89.32 (15.10)	85.45 (17.11)		
Week 100 Mean (SD)	88.24 (12.60)	84.60 (21.32)		
Week 28: Adjusted Mean Change (SE)	1.09 (2.18)	0.93 (2.10)		
Week 52: Adjusted Mean Change (SE)	3.90 (2.02)	2.03 (1.93)	1.87 [-3.61; 7.34]	0.503
Week 100: Adjusted Mean Change (SE)	3.47 (2.25)	1.94 (2.15)	1.53 [-4.58; 7.64]	0.623
Western Pacific Region				
N'/ N	30 / 30	29 / 29		
Baseline Mean (SD)	85.42 (18.30)	82.76 (18.42)		
Week 52 Mean (SD)	90.63 (14.39)	87.50 (13.50)		
Week 100 Mean (SD)	85.58 (15.69)	88.54 (13.75)		
Week 28: Adjusted Mean Change (SE)	6.27 (3.28)	8.53 (3.42)		
Week 52: Adjusted Mean Change (SE)	8.30 (3.04)	5.09 (3.04)	3.21 [-5.23; 11.66]	0.454
Week 100: Adjusted Mean Change (SE)	2.48 (3.19)	6.31 (3.32)	-3.83 [-12.87; 5.21]	0.405

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Ocular Pain				
Interaction test	p=0.890			
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	77.88 (23.27)	75.60 (26.36)		
Week 52 Mean (SD)	82.35 (20.76)	81.25 (25.83)		
Week 100 Mean (SD)	82.69 (22.56)	86.67 (16.68)		
Week 28: Adjusted Mean Change (SE)	5.84 (3.14)	2.59 (3.53)		
Week 52: Adjusted Mean Change (SE)	2.92 (3.58)	2.35 (3.94)	0.57 [-9.85; 10.98]	0.915
Week 100: Adjusted Mean Change (SE)	1.86 (3.94)	6.64 (3.73)	-4.78 [-15.41; 5.86]	0.378
European Region				
N'/ N	134 / 135	132 / 132		
Baseline Mean (SD)	85.35 (17.04)	83.90 (18.82)		
Week 52 Mean (SD)	89.17 (16.14)	87.72 (16.27)		
Week 100 Mean (SD)	90.92 (14.79)	88.66 (17.22)		
Week 28: Adjusted Mean Change (SE)	4.29 (1.37)	3.68 (1.37)		
Week 52: Adjusted Mean Change (SE)	4.57 (1.41)	3.63 (1.41)	0.93 [-2.97; 4.84]	0.638
Week 100: Adjusted Mean Change (SE)	6.17 (1.40)	4.20 (1.39)	1.97 [-1.91; 5.85]	0.318
Western Pacific Region				
N'/ N	18 / 18	28 / 28		
Baseline Mean (SD)	85.42 (15.01)	80.80 (23.19)		
Week 52 Mean (SD)	93.33 (13.25)	89.06 (19.26)		
Week 100 Mean (SD)	93.75 (8.43)	93.48 (10.57)		
Week 28: Adjusted Mean Change (SE)	3.09 (3.72)	5.19 (3.13)		
Week 52: Adjusted Mean Change (SE)	8.17 (3.85)	5.20 (3.07)	2.97 [-6.68; 12.62]	0.545
Week 100: Adjusted Mean Change (SE)	8.93 (4.13)	10.32 (3.04)	-1.39 [-11.45; 8.67]	0.786
Pooled Analysis: Ocular Pain				
Interaction test	p=0.847			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	79.31 (21.70)	78.46 (23.93)		
Week 52 Mean (SD)	87.32 (16.96)	87.50 (16.39)		
Week 100 Mean (SD)	84.51 (20.99)	81.82 (21.28)		
Week 28: Adjusted Mean Change (SE)	4.05 (1.99)	7.65 (2.07)		
Week 52: Adjusted Mean Change (SE)	5.92 (1.96)	7.70 (1.95)	-1.78 [-7.19; 3.63]	0.519
Week 100: Adjusted Mean Change (SE)	4.18 (2.03)	1.61 (2.05)	2.57 [-3.07; 8.22]	0.371

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	77.88 (23.27)	75.60 (26.36)		
Week 52 Mean (SD)	82.35 (20.76)	81.25 (25.83)		
Week 100 Mean (SD)	82.69 (22.56)	86.67 (16.68)		
Week 28: Adjusted Mean Change (SE)	4.37 (3.46)	1.11 (3.85)		
Week 52: Adjusted Mean Change (SE)	1.62 (3.67)	0.85 (4.00)	0.77 [-9.88; 11.42]	0.888
Week 100: Adjusted Mean Change (SE)	0.80 (4.22)	5.17 (4.00)	-4.37 [-15.77; 7.04]	0.452
European Region				
N'/ N	202 / 204	207 / 207		
Baseline Mean (SD)	86.20 (17.07)	84.66 (17.90)		
Week 52 Mean (SD)	89.22 (15.76)	86.92 (16.55)		
Week 100 Mean (SD)	90.05 (14.13)	87.27 (18.75)		
Week 28: Adjusted Mean Change (SE)	2.88 (1.23)	2.38 (1.21)		
Week 52: Adjusted Mean Change (SE)	3.99 (1.20)	2.71 (1.17)	1.28 [-1.99; 4.55]	0.442
Week 100: Adjusted Mean Change (SE)	4.96 (1.25)	3.06 (1.22)	1.90 [-1.53; 5.32]	0.278
Western Pacific Region				
N'/ N	48 / 48	57 / 57		
Baseline Mean (SD)	85.42 (16.97)	81.80 (20.74)		
Week 52 Mean (SD)	91.67 (13.85)	88.27 (16.42)		
Week 100 Mean (SD)	88.16 (14.22)	90.96 (12.42)		
Week 28: Adjusted Mean Change (SE)	5.17 (2.45)	6.58 (2.31)		
Week 52: Adjusted Mean Change (SE)	8.28 (2.40)	4.82 (2.14)	3.46 [-2.85; 9.77]	0.282
Week 100: Adjusted Mean Change (SE)	4.61 (2.48)	7.88 (2.23)	-3.27 [-9.82; 3.28]	0.328
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.450**				
KESTREL: Near Activities				
Interaction test	p=0.930			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	58.24 (26.46)	62.75 (21.47)		
Week 52 Mean (SD)	76.85 (22.70)	80.50 (19.97)		
Week 100 Mean (SD)	77.80 (20.20)	75.00 (23.66)		
Week 28: Adjusted Mean Change (SE)	11.19 (1.98)	12.67 (2.09)		
Week 52: Adjusted Mean Change (SE)	12.42 (2.19)	15.78 (2.20)	-3.36 [-9.43; 2.70]	0.276
Week 100: Adjusted Mean Change (SE)	14.13 (2.14)	10.39 (2.18)	3.74 [-2.24; 9.73]	0.220

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
European Region				
N'/ N	68 / 69	75 / 75		
Baseline Mean (SD)	74.26 (23.34)	70.22 (22.72)		
Week 52 Mean (SD)	85.00 (17.15)	79.44 (21.49)		
Week 100 Mean (SD)	85.46 (20.40)	81.40 (18.75)		
Week 28: Adjusted Mean Change (SE)	13.73 (2.26)	16.94 (2.17)		
Week 52: Adjusted Mean Change (SE)	14.68 (2.50)	12.28 (2.37)	2.40 [-4.33; 9.13]	0.484
Week 100: Adjusted Mean Change (SE)	16.33 (2.47)	14.05 (2.36)	2.28 [-4.38; 8.95]	0.501
Western Pacific Region				
N'/ N	30 / 30	29 / 29		
Baseline Mean (SD)	54.86 (23.82)	62.07 (18.84)		
Week 52 Mean (SD)	72.92 (23.47)	71.67 (15.77)		
Week 100 Mean (SD)	72.28 (20.51)	72.22 (17.49)		
Week 28: Adjusted Mean Change (SE)	12.01 (3.41)	12.06 (3.55)		
Week 52: Adjusted Mean Change (SE)	12.52 (3.76)	10.09 (3.73)	2.43 [-7.95; 12.81]	0.645
Week 100: Adjusted Mean Change (SE)	11.37 (3.53)	9.74 (3.65)	1.63 [-8.33; 11.60]	0.747
KITE: Near Activities				
Interaction test	p=0.087			
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	25 / 26	21 / 21		
Baseline Mean (SD)	66.17 (23.40)	67.26 (22.14)		
Week 52 Mean (SD)	75.49 (14.57)	75.00 (22.41)		
Week 100 Mean (SD)	81.73 (18.13)	82.22 (21.33)		
Week 28: Adjusted Mean Change (SE)	6.18 (3.72)	5.67 (4.09)		
Week 52: Adjusted Mean Change (SE)	5.93 (3.99)	10.09 (4.37)	-4.16 [-15.77; 7.45]	0.481
Week 100: Adjusted Mean Change (SE)	12.36 (4.51)	15.65 (4.36)	-3.29 [-15.60; 9.03]	0.600
European Region				
N'/ N	134 / 135	132 / 132		
Baseline Mean (SD)	70.62 (22.11)	69.63 (23.87)		
Week 52 Mean (SD)	81.40 (19.98)	77.98 (22.64)		
Week 100 Mean (SD)	84.08 (19.08)	74.31 (24.14)		
Week 28: Adjusted Mean Change (SE)	7.30 (1.59)	5.43 (1.59)		
Week 52: Adjusted Mean Change (SE)	11.31 (1.59)	8.48 (1.59)	2.82 [-1.59; 7.24]	0.209
Week 100: Adjusted Mean Change (SE)	11.85 (1.65)	4.11 (1.64)	7.73 [3.17; 12.30]	<.001 *

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Western Pacific Region				
N'/ N	18 / 18	28 / 28		
Baseline Mean (SD)	72.22 (23.74)	69.94 (25.89)		
Week 52 Mean (SD)	75.56 (29.79)	83.85 (19.05)		
Week 100 Mean (SD)	84.38 (16.87)	92.75 (8.81)		
Week 28: Adjusted Mean Change (SE)	-0.75 (4.32)	8.35 (3.61)		
Week 52: Adjusted Mean Change (SE)	7.00 (4.36)	10.67 (3.49)	-3.67 [-14.61; 7.26]	0.509
Week 100: Adjusted Mean Change (SE)	14.57 (4.81)	18.70 (3.60)	-4.13 [-15.90; 7.64]	0.490
Pooled Analysis: Near Activities				
Interaction test	p=0.469			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	58.24 (26.46)	62.75 (21.47)		
Week 52 Mean (SD)	76.85 (22.70)	80.50 (19.97)		
Week 100 Mean (SD)	77.80 (20.20)	75.00 (23.66)		
Week 28: Adjusted Mean Change (SE)	9.74 (2.24)	10.33 (2.32)		
Week 52: Adjusted Mean Change (SE)	10.83 (2.35)	13.56 (2.34)	-2.73 [-9.21; 3.75]	0.408
Week 100: Adjusted Mean Change (SE)	12.54 (2.35)	8.12 (2.37)	4.42 [-2.11; 10.96]	0.184
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	25 / 26	21 / 21		
Baseline Mean (SD)	66.17 (23.40)	67.26 (22.14)		
Week 52 Mean (SD)	75.49 (14.57)	75.00 (22.41)		
Week 100 Mean (SD)	81.73 (18.13)	82.22 (21.33)		
Week 28: Adjusted Mean Change (SE)	7.81 (3.93)	7.86 (4.28)		
Week 52: Adjusted Mean Change (SE)	7.70 (4.36)	12.13 (4.74)	-4.44 [-17.08; 8.21]	0.491
Week 100: Adjusted Mean Change (SE)	14.16 (4.74)	17.66 (4.58)	-3.49 [-16.43; 9.45]	0.596
European Region				
N'/ N	202 / 204	207 / 207		
Baseline Mean (SD)	71.84 (22.54)	69.85 (23.41)		
Week 52 Mean (SD)	82.58 (19.12)	78.49 (22.19)		
Week 100 Mean (SD)	84.53 (19.46)	76.73 (22.64)		
Week 28: Adjusted Mean Change (SE)	10.11 (1.37)	10.18 (1.34)		
Week 52: Adjusted Mean Change (SE)	13.04 (1.43)	10.52 (1.40)	2.52 [-1.39; 6.42]	0.207
Week 100: Adjusted Mean Change (SE)	13.97 (1.44)	8.29 (1.41)	5.68 [1.74; 9.62]	0.005 *

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Western Pacific Region				
N'/ N	48 / 48	57 / 57		
Baseline Mean (SD)	61.37 (25.03)	65.94 (22.73)		
Week 52 Mean (SD)	73.93 (25.73)	77.64 (18.33)		
Week 100 Mean (SD)	76.10 (20.03)	82.27 (17.26)		
Week 28: Adjusted Mean Change (SE)	7.08 (2.72)	10.10 (2.54)		
Week 52: Adjusted Mean Change (SE)	10.22 (2.86)	10.20 (2.56)	0.02 [-7.51; 7.56]	0.995
Week 100: Adjusted Mean Change (SE)	11.86 (2.86)	13.90 (2.56)	-2.04 [-9.57; 5.50]	0.596
Distance Activities				
Test of heterogeneity in main analysis: **p_H=0.046 ***				
KESTREL: Distance Activities				
Interaction test	p=0.653			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	68.19 (25.07)	70.43 (22.17)		
Week 52 Mean (SD)	83.69 (17.44)	84.95 (16.44)		
Week 100 Mean (SD)	79.54 (20.32)	81.06 (21.15)		
Week 28: Adjusted Mean Change (SE)	8.75 (1.75)	7.25 (1.84)		
Week 52: Adjusted Mean Change (SE)	9.32 (1.66)	10.74 (1.68)	-1.42 [-6.02; 3.18]	0.544
Week 100: Adjusted Mean Change (SE)	7.08 (1.81)	6.65 (1.84)	0.43 [-4.60; 5.46]	0.867
European Region				
N'/ N	68 / 69	75 / 75		
Baseline Mean (SD)	86.58 (17.86)	82.67 (19.63)		
Week 52 Mean (SD)	91.97 (11.67)	88.11 (17.08)		
Week 100 Mean (SD)	90.36 (13.88)	90.25 (13.33)		
Week 28: Adjusted Mean Change (SE)	6.40 (2.00)	10.17 (1.92)		
Week 52: Adjusted Mean Change (SE)	10.68 (1.91)	9.40 (1.81)	1.28 [-3.83; 6.39]	0.622
Week 100: Adjusted Mean Change (SE)	9.88 (2.09)	11.36 (1.99)	-1.48 [-7.09; 4.13]	0.604
Western Pacific Region				
N'/ N	30 / 30	29 / 29		
Baseline Mean (SD)	70.83 (22.85)	70.55 (16.51)		
Week 52 Mean (SD)	75.35 (21.35)	78.00 (17.33)		
Week 100 Mean (SD)	70.83 (22.55)	72.57 (16.02)		
Week 28: Adjusted Mean Change (SE)	5.37 (3.00)	10.40 (3.12)		
Week 52: Adjusted Mean Change (SE)	3.88 (2.84)	5.98 (2.85)	-2.10 [-9.98; 5.79]	0.602
Week 100: Adjusted Mean Change (SE)	-1.80 (2.95)	1.25 (3.07)	-3.05 [-11.40; 5.30]	0.472

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Distance Activities				
Interaction test	p=0.929			
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	75.80 (15.90)	75.99 (21.12)		
Week 52 Mean (SD)	89.22 (10.53)	82.14 (22.61)		
Week 100 Mean (SD)	89.42 (14.89)	82.50 (18.38)		
Week 28: Adjusted Mean Change (SE)	4.80 (3.17)	1.85 (3.56)		
Week 52: Adjusted Mean Change (SE)	13.00 (3.26)	8.84 (3.59)	4.17 [-5.35; 13.69]	0.390
Week 100: Adjusted Mean Change (SE)	11.85 (3.81)	7.65 (3.69)	4.20 [-6.21; 14.61]	0.428
European Region				
N'/ N	134 / 135	132 / 132		
Baseline Mean (SD)	77.52 (22.15)	77.02 (22.25)		
Week 52 Mean (SD)	88.32 (17.28)	84.64 (18.18)		
Week 100 Mean (SD)	89.54 (15.98)	82.83 (20.19)		
Week 28: Adjusted Mean Change (SE)	5.86 (1.38)	5.28 (1.39)		
Week 52: Adjusted Mean Change (SE)	11.29 (1.30)	8.18 (1.30)	3.11 [-0.49; 6.71]	0.090
Week 100: Adjusted Mean Change (SE)	11.13 (1.40)	5.79 (1.39)	5.34 [1.48; 9.20]	0.007 *
Western Pacific Region				
N'/ N	18 / 18	28 / 28		
Baseline Mean (SD)	73.84 (23.91)	72.47 (24.62)		
Week 52 Mean (SD)	83.61 (24.62)	84.55 (19.52)		
Week 100 Mean (SD)	85.76 (17.27)	89.31 (9.80)		
Week 28: Adjusted Mean Change (SE)	9.88 (3.77)	7.92 (3.15)		
Week 52: Adjusted Mean Change (SE)	9.26 (3.56)	6.80 (2.84)	2.46 [-6.45; 11.37]	0.588
Week 100: Adjusted Mean Change (SE)	11.92 (4.07)	11.14 (3.04)	0.78 [-9.17; 10.74]	0.877
Pooled Analysis: Distance Activities				
Interaction test	p=0.719			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	68.19 (25.07)	70.43 (22.17)		
Week 52 Mean (SD)	83.69 (17.44)	84.95 (16.44)		
Week 100 Mean (SD)	79.54 (20.32)	81.06 (21.15)		
Week 28: Adjusted Mean Change (SE)	10.31 (1.93)	6.87 (2.00)		
Week 52: Adjusted Mean Change (SE)	10.92 (1.86)	10.38 (1.85)	0.54 [-4.57; 5.65]	0.836
Week 100: Adjusted Mean Change (SE)	8.62 (1.98)	6.24 (1.99)	2.37 [-3.10; 7.85]	0.395

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	75.80 (15.90)	75.99 (21.12)		
Week 52 Mean (SD)	89.22 (10.53)	82.14 (22.61)		
Week 100 Mean (SD)	89.42 (14.89)	82.50 (18.38)		
Week 28: Adjusted Mean Change (SE)	3.30 (3.33)	2.40 (3.71)		
Week 52: Adjusted Mean Change (SE)	11.71 (3.40)	9.53 (3.71)	2.19 [-7.68; 12.06]	0.664
Week 100: Adjusted Mean Change (SE)	10.45 (3.99)	8.16 (3.84)	2.29 [-8.58; 13.16]	0.679
European Region				
N'/ N	202 / 204	207 / 207		
Baseline Mean (SD)	80.57 (21.20)	79.07 (21.46)		
Week 52 Mean (SD)	89.52 (15.72)	85.86 (17.83)		
Week 100 Mean (SD)	89.81 (15.29)	85.37 (18.44)		
Week 28: Adjusted Mean Change (SE)	5.56 (1.19)	7.17 (1.16)		
Week 52: Adjusted Mean Change (SE)	10.54 (1.12)	8.76 (1.09)	1.79 [-1.27; 4.85]	0.252
Week 100: Adjusted Mean Change (SE)	10.23 (1.21)	7.87 (1.18)	2.36 [-0.94; 5.67]	0.160
Western Pacific Region				
N'/ N	48 / 48	57 / 57		
Baseline Mean (SD)	71.96 (23.04)	71.49 (20.73)		
Week 52 Mean (SD)	78.53 (22.71)	81.21 (18.54)		
Week 100 Mean (SD)	75.55 (21.94)	80.76 (15.68)		
Week 28: Adjusted Mean Change (SE)	7.29 (2.36)	9.05 (2.21)		
Week 52: Adjusted Mean Change (SE)	6.13 (2.23)	6.18 (2.00)	-0.05 [-5.93; 5.83]	0.987
Week 100: Adjusted Mean Change (SE)	3.01 (2.40)	5.88 (2.15)	-2.87 [-9.18; 3.45]	0.374
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.023 ***				
KESTREL: Social Functioning				
Interaction test	p=0.205			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	87.22 (18.83)	87.35 (17.84)		
Week 52 Mean (SD)	91.43 (16.28)	93.84 (14.00)		
Week 100 Mean (SD)	88.25 (18.58)	90.72 (16.74)		
Week 28: Adjusted Mean Change (SE)	1.46 (1.33)	3.71 (1.41)		
Week 52: Adjusted Mean Change (SE)	1.43 (1.50)	4.59 (1.52)	-3.16 [-7.35; 1.02]	0.138
Week 100: Adjusted Mean Change (SE)	-0.33 (1.78)	1.72 (1.81)	-2.05 [-7.03; 2.92]	0.417

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
European Region				
N'/ N	68 / 69	75 / 75		
Baseline Mean (SD)	94.12 (15.94)	93.83 (12.56)		
Week 52 Mean (SD)	96.36 (10.40)	96.11 (10.59)		
Week 100 Mean (SD)	95.83 (12.67)	97.10 (8.92)		
Week 28: Adjusted Mean Change (SE)	0.82 (1.51)	5.19 (1.46)		
Week 52: Adjusted Mean Change (SE)	3.94 (1.71)	4.74 (1.63)	-0.79 [-5.42; 3.83]	0.736
Week 100: Adjusted Mean Change (SE)	4.35 (2.05)	5.87 (1.96)	-1.51 [-7.06; 4.03]	0.592
Western Pacific Region				
N'/ N	30 / 30	29 / 29		
Baseline Mean (SD)	81.67 (22.44)	86.64 (14.15)		
Week 52 Mean (SD)	86.98 (17.86)	87.50 (16.54)		
Week 100 Mean (SD)	86.54 (18.68)	82.81 (16.41)		
Week 28: Adjusted Mean Change (SE)	3.75 (2.29)	1.75 (2.38)		
Week 52: Adjusted Mean Change (SE)	1.60 (2.59)	0.11 (2.56)	1.49 [-5.64; 8.62]	0.681
Week 100: Adjusted Mean Change (SE)	0.71 (2.90)	-4.72 (3.01)	5.43 [-2.77; 13.63]	0.194
KITE: Social Functioning				
Interaction test	p=0.826			
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	87.98 (15.20)	83.93 (22.06)		
Week 52 Mean (SD)	95.59 (8.77)	91.07 (14.23)		
Week 100 Mean (SD)	94.23 (14.98)	95.00 (13.19)		
Week 28: Adjusted Mean Change (SE)	6.25 (2.80)	2.85 (3.14)		
Week 52: Adjusted Mean Change (SE)	7.34 (2.64)	5.66 (2.90)	1.68 [-6.04; 9.39]	0.669
Week 100: Adjusted Mean Change (SE)	5.26 (3.58)	9.93 (3.40)	-4.66 [-14.37; 5.05]	0.345
European Region				
N'/ N	134 / 135	132 / 132		
Baseline Mean (SD)	87.87 (18.13)	86.17 (20.09)		
Week 52 Mean (SD)	94.98 (11.80)	91.63 (14.57)		
Week 100 Mean (SD)	94.81 (14.42)	89.35 (18.55)		
Week 28: Adjusted Mean Change (SE)	3.43 (1.22)	4.27 (1.22)		
Week 52: Adjusted Mean Change (SE)	7.53 (1.04)	4.68 (1.04)	2.85 [-0.04; 5.74]	0.053
Week 100: Adjusted Mean Change (SE)	6.71 (1.28)	2.05 (1.27)	4.66 [1.11; 8.21]	0.010 *

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Western Pacific Region				
N'/ N	18 / 18	28 / 28		
Baseline Mean (SD)	93.06 (13.71)	89.29 (17.91)		
Week 52 Mean (SD)	95.83 (16.14)	91.67 (16.35)		
Week 100 Mean (SD)	97.92 (4.87)	97.28 (5.27)		
Week 28: Adjusted Mean Change (SE)	2.11 (3.32)	2.43 (2.79)		
Week 52: Adjusted Mean Change (SE)	6.10 (2.86)	1.82 (2.28)	4.28 [-2.86; 11.42]	0.239
Week 100: Adjusted Mean Change (SE)	8.98 (3.78)	7.60 (2.78)	1.37 [-7.82; 10.57]	0.769
Pooled Analysis: Social Functioning				
Interaction test	p=0.498			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	87.22 (18.83)	87.35 (17.84)		
Week 52 Mean (SD)	91.43 (16.28)	93.84 (14.00)		
Week 100 Mean (SD)	88.25 (18.58)	90.72 (16.74)		
Week 28: Adjusted Mean Change (SE)	3.16 (1.57)	4.19 (1.64)		
Week 52: Adjusted Mean Change (SE)	3.18 (1.56)	5.10 (1.56)	-1.92 [-6.25; 2.41]	0.385
Week 100: Adjusted Mean Change (SE)	1.33 (1.84)	2.19 (1.86)	-0.86 [-5.97; 4.26]	0.743
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	87.98 (15.20)	83.93 (22.06)		
Week 52 Mean (SD)	95.59 (8.77)	91.07 (14.23)		
Week 100 Mean (SD)	94.23 (14.98)	95.00 (13.19)		
Week 28: Adjusted Mean Change (SE)	4.33 (2.73)	2.32 (3.04)		
Week 52: Adjusted Mean Change (SE)	5.69 (2.94)	5.35 (3.19)	0.34 [-8.18; 8.85]	0.938
Week 100: Adjusted Mean Change (SE)	3.68 (3.88)	9.30 (3.67)	-5.62 [-16.11; 4.86]	0.293
European Region				
N'/ N	202 / 204	207 / 207		
Baseline Mean (SD)	89.98 (17.64)	88.95 (18.09)		
Week 52 Mean (SD)	95.43 (11.34)	93.21 (13.44)		
Week 100 Mean (SD)	95.14 (13.84)	92.00 (16.32)		
Week 28: Adjusted Mean Change (SE)	2.03 (0.97)	4.46 (0.95)		
Week 52: Adjusted Mean Change (SE)	5.78 (0.95)	4.54 (0.93)	1.24 [-1.37; 3.85]	0.350
Week 100: Adjusted Mean Change (SE)	5.35 (1.15)	3.18 (1.12)	2.17 [-0.97; 5.31]	0.176

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Western Pacific Region				
N'/ N	48 / 48	57 / 57		
Baseline Mean (SD)	85.94 (20.24)	87.94 (16.02)		
Week 52 Mean (SD)	90.38 (17.55)	89.54 (16.41)		
Week 100 Mean (SD)	90.13 (16.48)	89.89 (14.19)		
Week 28: Adjusted Mean Change (SE)	3.64 (1.93)	1.87 (1.82)		
Week 52: Adjusted Mean Change (SE)	3.85 (1.91)	0.66 (1.70)	3.19 [-1.83; 8.21]	0.212
Week 100: Adjusted Mean Change (SE)	4.04 (2.29)	1.00 (2.06)	3.04 [-3.01; 9.09]	0.324
Mental Health				
Test of heterogeneity in main analysis: **p_H=0.200**				
KESTREL: Mental Health				
Interaction test	p=0.114			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	61.81 (27.16)	59.26 (25.04)		
Week 52 Mean (SD)	75.71 (20.57)	76.74 (20.35)		
Week 100 Mean (SD)	71.36 (23.24)	76.14 (22.60)		
Week 28: Adjusted Mean Change (SE)	6.08 (1.87)	10.07 (1.99)		
Week 52: Adjusted Mean Change (SE)	8.99 (1.92)	12.76 (1.95)	-3.76 [-9.11; 1.58]	0.167
Week 100: Adjusted Mean Change (SE)	7.40 (2.21)	12.96 (2.26)	-5.56 [-11.74; 0.61]	0.077
European Region				
N'/ N	68 / 69	75 / 75		
Baseline Mean (SD)	71.88 (20.73)	75.42 (17.69)		
Week 52 Mean (SD)	84.89 (14.32)	79.30 (16.16)		
Week 100 Mean (SD)	81.37 (16.70)	80.02 (19.34)		
Week 28: Adjusted Mean Change (SE)	8.46 (2.12)	7.59 (2.06)		
Week 52: Adjusted Mean Change (SE)	13.83 (2.18)	8.85 (2.09)	4.98 [-0.93; 10.90]	0.099
Week 100: Adjusted Mean Change (SE)	11.12 (2.53)	9.83 (2.43)	1.28 [-5.60; 8.17]	0.714
Western Pacific Region				
N'/ N	30 / 30	29 / 29		
Baseline Mean (SD)	62.29 (24.54)	75.43 (20.72)		
Week 52 Mean (SD)	71.09 (25.26)	82.75 (13.54)		
Week 100 Mean (SD)	71.15 (22.78)	76.04 (22.99)		
Week 28: Adjusted Mean Change (SE)	9.26 (3.20)	11.44 (3.35)		
Week 52: Adjusted Mean Change (SE)	7.38 (3.30)	12.09 (3.28)	-4.71 [-13.85; 4.44]	0.312
Week 100: Adjusted Mean Change (SE)	7.40 (3.61)	6.51 (3.75)	0.89 [-9.35; 11.13]	0.865

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Mental Health				
Interaction test	p=0.451			
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	60.34 (19.03)	58.63 (24.88)		
Week 52 Mean (SD)	81.25 (19.89)	65.63 (23.86)		
Week 100 Mean (SD)	79.81 (21.52)	72.50 (30.33)		
Week 28: Adjusted Mean Change (SE)	3.84 (3.42)	3.89 (3.84)		
Week 52: Adjusted Mean Change (SE)	17.44 (4.45)	5.24 (4.88)	12.20 [-0.76; 25.15]	0.065
Week 100: Adjusted Mean Change (SE)	13.27 (4.78)	8.63 (4.64)	4.64 [-8.42; 17.71]	0.485
European Region				
N'/ N	134 / 135	132 / 132		
Baseline Mean (SD)	70.94 (21.03)	67.95 (24.49)		
Week 52 Mean (SD)	82.42 (19.32)	77.79 (22.37)		
Week 100 Mean (SD)	84.79 (15.62)	79.11 (22.17)		
Week 28: Adjusted Mean Change (SE)	9.19 (1.49)	9.09 (1.49)		
Week 52: Adjusted Mean Change (SE)	12.80 (1.78)	9.40 (1.78)	3.41 [-1.52; 8.34]	0.175
Week 100: Adjusted Mean Change (SE)	13.50 (1.76)	10.11 (1.75)	3.39 [-1.48; 8.26]	0.172
Western Pacific Region				
N'/ N	18 / 18	28 / 28		
Baseline Mean (SD)	66.32 (26.35)	60.94 (32.48)		
Week 52 Mean (SD)	73.75 (29.99)	78.13 (28.01)		
Week 100 Mean (SD)	83.85 (14.22)	86.68 (14.14)		
Week 28: Adjusted Mean Change (SE)	8.79 (4.05)	11.71 (3.40)		
Week 52: Adjusted Mean Change (SE)	6.94 (4.87)	10.60 (3.89)	-3.66 [-15.87; 8.55]	0.556
Week 100: Adjusted Mean Change (SE)	17.06 (5.11)	19.07 (3.83)	-2.01 [-14.52; 10.50]	0.752
Pooled Analysis: Mental Health				
Interaction test	p=0.087			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	61.81 (27.16)	59.26 (25.04)		
Week 52 Mean (SD)	75.71 (20.57)	76.74 (20.35)		
Week 100 Mean (SD)	71.36 (23.24)	76.14 (22.60)		
Week 28: Adjusted Mean Change (SE)	6.70 (2.08)	11.21 (2.18)		
Week 52: Adjusted Mean Change (SE)	9.63 (2.29)	13.84 (2.30)	-4.21 [-10.55; 2.13]	0.193
Week 100: Adjusted Mean Change (SE)	8.12 (2.41)	14.09 (2.45)	-5.96 [-12.67; 0.75]	0.081

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	60.34 (19.03)	58.63 (24.88)		
Week 52 Mean (SD)	81.25 (19.89)	65.63 (23.86)		
Week 100 Mean (SD)	79.81 (21.52)	72.50 (30.33)		
Week 28: Adjusted Mean Change (SE)	3.06 (3.57)	2.77 (3.96)		
Week 52: Adjusted Mean Change (SE)	16.39 (4.28)	3.75 (4.65)	12.65 [0.24; 25.05]	0.046 *
Week 100: Adjusted Mean Change (SE)	12.58 (4.94)	7.40 (4.75)	5.18 [-8.27; 18.63]	0.450
European Region				
N'/ N	202 / 204	207 / 207		
Baseline Mean (SD)	71.26 (20.89)	70.65 (22.51)		
Week 52 Mean (SD)	83.23 (17.82)	78.32 (20.36)		
Week 100 Mean (SD)	83.68 (16.01)	79.42 (21.19)		
Week 28: Adjusted Mean Change (SE)	8.83 (1.27)	8.24 (1.24)		
Week 52: Adjusted Mean Change (SE)	13.00 (1.40)	8.92 (1.37)	4.08 [0.25; 7.91]	0.037 *
Week 100: Adjusted Mean Change (SE)	12.62 (1.49)	9.71 (1.46)	2.91 [-1.17; 6.99]	0.162
Western Pacific Region				
N'/ N	48 / 48	57 / 57		
Baseline Mean (SD)	63.80 (25.03)	68.31 (27.87)		
Week 52 Mean (SD)	72.12 (26.82)	80.48 (21.75)		
Week 100 Mean (SD)	75.16 (21.13)	81.25 (19.72)		
Week 28: Adjusted Mean Change (SE)	9.16 (2.51)	11.33 (2.35)		
Week 52: Adjusted Mean Change (SE)	7.38 (2.81)	10.99 (2.51)	-3.62 [-11.01; 3.78]	0.337
Week 100: Adjusted Mean Change (SE)	10.62 (2.97)	12.28 (2.66)	-1.65 [-9.48; 6.17]	0.678
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.132**				
KESTREL: Role Difficulties				
Interaction test	p=0.580			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	66.94 (29.59)	65.06 (28.41)		
Week 52 Mean (SD)	77.32 (27.61)	81.77 (23.64)		
Week 100 Mean (SD)	75.19 (29.64)	77.65 (27.61)		
Week 28: Adjusted Mean Change (SE)	4.39 (2.33)	7.03 (2.48)		
Week 52: Adjusted Mean Change (SE)	3.75 (2.58)	11.37 (2.61)	-7.62 [-14.81; -0.44]	0.038 *
Week 100: Adjusted Mean Change (SE)	5.30 (2.65)	7.53 (2.72)	-2.23 [-9.66; 5.20]	0.555

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
European Region				
N'/ N	68 / 69	75 / 75		
Baseline Mean (SD)	81.62 (23.61)	76.83 (23.76)		
Week 52 Mean (SD)	86.59 (20.53)	84.43 (22.90)		
Week 100 Mean (SD)	90.69 (16.17)	81.92 (24.53)		
Week 28: Adjusted Mean Change (SE)	6.33 (2.67)	10.50 (2.56)		
Week 52: Adjusted Mean Change (SE)	9.26 (2.95)	10.31 (2.80)	-1.04 [-9.02; 6.93]	0.797
Week 100: Adjusted Mean Change (SE)	12.99 (3.06)	7.75 (2.92)	5.24 [-3.05; 13.53]	0.215
Western Pacific Region				
N'/ N	30 / 30	29 / 29		
Baseline Mean (SD)	65.42 (31.09)	78.02 (24.92)		
Week 52 Mean (SD)	77.08 (26.75)	84.00 (20.89)		
Week 100 Mean (SD)	79.81 (25.76)	80.21 (20.50)		
Week 28: Adjusted Mean Change (SE)	8.94 (4.02)	10.76 (4.19)		
Week 52: Adjusted Mean Change (SE)	8.59 (4.44)	10.80 (4.42)	-2.21 [-14.52; 10.10]	0.724
Week 100: Adjusted Mean Change (SE)	11.19 (4.37)	7.87 (4.53)	3.32 [-9.06; 15.70]	0.598
KITE: Role Difficulties				
Interaction test	p=0.397			
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	59.62 (24.57)	58.33 (31.21)		
Week 52 Mean (SD)	83.09 (22.94)	71.43 (28.77)		
Week 100 Mean (SD)	80.77 (28.69)	78.33 (29.30)		
Week 28: Adjusted Mean Change (SE)	-0.27 (4.18)	7.91 (4.70)		
Week 52: Adjusted Mean Change (SE)	16.27 (4.86)	8.13 (5.31)	8.14 [-5.98; 22.26]	0.258
Week 100: Adjusted Mean Change (SE)	11.62 (5.67)	12.68 (5.50)	-1.06 [-16.56; 14.43]	0.893
European Region				
N'/ N	134 / 135	132 / 132		
Baseline Mean (SD)	74.16 (26.51)	69.89 (27.58)		
Week 52 Mean (SD)	83.93 (21.38)	79.58 (23.55)		
Week 100 Mean (SD)	86.32 (21.31)	78.82 (26.17)		
Week 28: Adjusted Mean Change (SE)	9.20 (1.82)	7.35 (1.82)		
Week 52: Adjusted Mean Change (SE)	12.48 (1.93)	9.20 (1.92)	3.28 [-2.06; 8.62]	0.228
Week 100: Adjusted Mean Change (SE)	12.37 (2.09)	7.70 (2.07)	4.67 [-1.10; 10.45]	0.112

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Western Pacific Region				
N'/ N	18 / 18	28 / 28		
Baseline Mean (SD)	64.58 (32.16)	61.16 (34.42)		
Week 52 Mean (SD)	75.00 (25.00)	75.52 (30.72)		
Week 100 Mean (SD)	78.13 (29.25)	88.59 (15.95)		
Week 28: Adjusted Mean Change (SE)	4.56 (4.96)	12.24 (4.15)		
Week 52: Adjusted Mean Change (SE)	7.32 (5.28)	4.98 (4.21)	2.33 [-10.88; 15.55]	0.728
Week 100: Adjusted Mean Change (SE)	9.90 (6.06)	17.57 (4.54)	-7.67 [-22.51; 7.17]	0.310
Pooled Analysis: Role Difficulties				
Interaction test	p=0.599			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	66.94 (29.59)	65.06 (28.41)		
Week 52 Mean (SD)	77.32 (27.61)	81.77 (23.64)		
Week 100 Mean (SD)	75.19 (29.64)	77.65 (27.61)		
Week 28: Adjusted Mean Change (SE)	5.39 (2.58)	6.87 (2.69)		
Week 52: Adjusted Mean Change (SE)	4.74 (2.76)	11.26 (2.76)	-6.51 [-14.15; 1.13]	0.095
Week 100: Adjusted Mean Change (SE)	6.27 (2.88)	7.39 (2.92)	-1.12 [-9.14; 6.89]	0.783
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	59.62 (24.57)	58.33 (31.21)		
Week 52 Mean (SD)	83.09 (22.94)	71.43 (28.77)		
Week 100 Mean (SD)	80.77 (28.69)	78.33 (29.30)		
Week 28: Adjusted Mean Change (SE)	-1.44 (4.44)	7.98 (4.93)		
Week 52: Adjusted Mean Change (SE)	15.11 (5.16)	8.26 (5.61)	6.85 [-8.10; 21.80]	0.369
Week 100: Adjusted Mean Change (SE)	10.62 (5.85)	12.73 (5.65)	-2.11 [-18.07; 13.85]	0.795
European Region				
N'/ N	202 / 204	207 / 207		
Baseline Mean (SD)	76.67 (25.76)	72.40 (26.42)		
Week 52 Mean (SD)	84.81 (21.08)	81.29 (23.37)		
Week 100 Mean (SD)	87.74 (19.84)	79.88 (25.59)		
Week 28: Adjusted Mean Change (SE)	7.95 (1.58)	8.54 (1.54)		
Week 52: Adjusted Mean Change (SE)	11.09 (1.69)	9.68 (1.65)	1.40 [-3.21; 6.02]	0.550
Week 100: Adjusted Mean Change (SE)	12.29 (1.78)	7.83 (1.73)	4.46 [-0.40; 9.33]	0.072

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Western Pacific Region				
N'/ N	48 / 48	57 / 57		
Baseline Mean (SD)	65.10 (31.15)	69.74 (30.89)		
Week 52 Mean (SD)	76.28 (25.78)	79.85 (26.25)		
Week 100 Mean (SD)	79.28 (26.52)	84.31 (18.70)		
Week 28: Adjusted Mean Change (SE)	7.52 (3.13)	11.32 (2.93)		
Week 52: Adjusted Mean Change (SE)	8.35 (3.38)	7.67 (3.02)	0.68 [-8.21; 9.57]	0.881
Week 100: Adjusted Mean Change (SE)	10.99 (3.54)	12.47 (3.17)	-1.48 [-10.81; 7.85]	0.755
Dependency				
Test of heterogeneity in main analysis: **p_H=0.019 ***				
KESTREL: Dependency				
Interaction test	p=0.647			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	76.02 (29.98)	75.60 (27.54)		
Week 52 Mean (SD)	86.19 (24.73)	89.58 (20.97)		
Week 100 Mean (SD)	83.21 (23.95)	85.35 (24.94)		
Week 28: Adjusted Mean Change (SE)	4.83 (2.01)	7.45 (2.13)		
Week 52: Adjusted Mean Change (SE)	4.09 (2.10)	7.95 (2.12)	-3.86 [-9.68; 1.96]	0.193
Week 100: Adjusted Mean Change (SE)	2.64 (2.35)	4.78 (2.40)	-2.14 [-8.71; 4.43]	0.523
European Region				
N'/ N	68 / 69	75 / 75		
Baseline Mean (SD)	89.46 (20.24)	88.89 (18.85)		
Week 52 Mean (SD)	95.30 (12.91)	95.08 (12.76)		
Week 100 Mean (SD)	92.48 (15.75)	92.56 (17.02)		
Week 28: Adjusted Mean Change (SE)	6.72 (2.29)	5.32 (2.21)		
Week 52: Adjusted Mean Change (SE)	8.78 (2.39)	9.84 (2.28)	-1.06 [-7.51; 5.39]	0.747
Week 100: Adjusted Mean Change (SE)	6.55 (2.70)	7.68 (2.59)	-1.14 [-8.46; 6.19]	0.761
Western Pacific Region				
N'/ N	30 / 30	29 / 29		
Baseline Mean (SD)	80.00 (23.22)	87.36 (18.04)		
Week 52 Mean (SD)	82.64 (26.34)	91.67 (12.03)		
Week 100 Mean (SD)	81.41 (27.42)	87.15 (15.92)		
Week 28: Adjusted Mean Change (SE)	5.46 (3.44)	9.09 (3.60)		
Week 52: Adjusted Mean Change (SE)	2.13 (3.59)	8.56 (3.58)	-6.43 [-16.38; 3.53]	0.205
Week 100: Adjusted Mean Change (SE)	0.39 (3.83)	2.92 (3.98)	-2.54 [-13.41; 8.33]	0.646

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Dependency				
Interaction test	p=0.545			
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	77.24 (22.80)	72.62 (34.58)		
Week 52 Mean (SD)	96.08 (7.86)	80.36 (25.66)		
Week 100 Mean (SD)	94.87 (9.94)	80.56 (32.83)		
Week 28: Adjusted Mean Change (SE)	5.04 (3.44)	0.13 (3.87)		
Week 52: Adjusted Mean Change (SE)	12.77 (4.00)	1.77 (4.39)	11.00 [-0.65; 22.65]	0.064
Week 100: Adjusted Mean Change (SE)	7.85 (4.66)	-0.34 (4.52)	8.19 [-4.55; 20.94]	0.207
European Region				
N'/ N	134 / 135	132 / 132		
Baseline Mean (SD)	85.76 (22.50)	83.90 (25.27)		
Week 52 Mean (SD)	91.22 (18.41)	88.17 (20.77)		
Week 100 Mean (SD)	93.40 (14.12)	86.73 (22.87)		
Week 28: Adjusted Mean Change (SE)	5.58 (1.50)	3.48 (1.50)		
Week 52: Adjusted Mean Change (SE)	6.57 (1.60)	3.91 (1.60)	2.66 [-1.77; 7.09]	0.238
Week 100: Adjusted Mean Change (SE)	6.26 (1.71)	1.78 (1.70)	4.47 [-0.26; 9.21]	0.064
Western Pacific Region				
N'/ N	18 / 18	28 / 28		
Baseline Mean (SD)	75.00 (29.57)	79.46 (27.91)		
Week 52 Mean (SD)	84.44 (30.52)	83.68 (29.02)		
Week 100 Mean (SD)	88.19 (21.46)	94.93 (12.24)		
Week 28: Adjusted Mean Change (SE)	3.12 (4.09)	2.90 (3.42)		
Week 52: Adjusted Mean Change (SE)	6.07 (4.39)	-0.16 (3.50)	6.23 [-4.76; 17.22]	0.265
Week 100: Adjusted Mean Change (SE)	8.09 (4.99)	10.27 (3.73)	-2.18 [-14.38; 10.02]	0.725
Pooled Analysis: Dependency				
Interaction test	p=0.445			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	76.02 (29.98)	75.60 (27.54)		
Week 52 Mean (SD)	86.19 (24.73)	89.58 (20.97)		
Week 100 Mean (SD)	83.21 (23.95)	85.35 (24.94)		
Week 28: Adjusted Mean Change (SE)	5.24 (2.18)	6.55 (2.27)		
Week 52: Adjusted Mean Change (SE)	4.45 (2.29)	6.97 (2.29)	-2.51 [-8.84; 3.81]	0.436
Week 100: Adjusted Mean Change (SE)	3.11 (2.46)	3.81 (2.49)	-0.71 [-7.55; 6.13]	0.839

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	77.24 (22.80)	72.62 (34.58)		
Week 52 Mean (SD)	96.08 (7.86)	80.36 (25.66)		
Week 100 Mean (SD)	94.87 (9.94)	80.56 (32.83)		
Week 28: Adjusted Mean Change (SE)	4.53 (3.74)	1.05 (4.16)		
Week 52: Adjusted Mean Change (SE)	12.49 (4.25)	2.69 (4.62)	9.80 [-2.52; 22.13]	0.119
Week 100: Adjusted Mean Change (SE)	7.91 (5.05)	0.59 (4.84)	7.33 [-6.41; 21.06]	0.295
European Region				
N'/ N	202 / 204	207 / 207		
Baseline Mean (SD)	87.00 (21.79)	85.71 (23.23)		
Week 52 Mean (SD)	92.56 (16.87)	90.61 (18.60)		
Week 100 Mean (SD)	93.10 (14.62)	88.72 (21.19)		
Week 28: Adjusted Mean Change (SE)	6.00 (1.33)	4.48 (1.30)		
Week 52: Adjusted Mean Change (SE)	7.28 (1.39)	6.38 (1.36)	0.90 [-2.91; 4.72]	0.641
Week 100: Adjusted Mean Change (SE)	6.47 (1.52)	4.25 (1.49)	2.22 [-1.94; 6.38]	0.294
Western Pacific Region				
N'/ N	48 / 48	57 / 57		
Baseline Mean (SD)	78.12 (25.59)	83.48 (23.54)		
Week 52 Mean (SD)	83.33 (27.64)	87.76 (22.19)		
Week 100 Mean (SD)	83.55 (25.59)	90.96 (14.62)		
Week 28: Adjusted Mean Change (SE)	4.32 (2.64)	5.70 (2.47)		
Week 52: Adjusted Mean Change (SE)	3.39 (2.79)	3.86 (2.50)	-0.47 [-7.82; 6.88]	0.900
Week 100: Adjusted Mean Change (SE)	2.69 (3.03)	6.09 (2.71)	-3.40 [-11.38; 4.57]	0.402
Driving				
Test of heterogeneity in main analysis: **p_H=0.792**				
KESTREL: Driving				
Interaction test	p=0.811			
Region of the Americas				
N'/ N	58 / 90	54 / 83		
Baseline Mean (SD)	76.72 (17.64)	72.84 (20.62)		
Week 52 Mean (SD)	82.80 (20.22)	81.88 (20.81)		
Week 100 Mean (SD)	81.25 (20.22)	77.92 (22.85)		
Week 28: Adjusted Mean Change (SE)	0.60 (1.99)	3.81 (2.08)		
Week 52: Adjusted Mean Change (SE)	2.27 (2.30)	5.54 (2.38)	-3.26 [-9.75; 3.22]	0.322
Week 100: Adjusted Mean Change (SE)	2.57 (2.61)	0.36 (2.67)	2.21 [-5.10; 9.52]	0.551

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
European Region				
N'/ N	43 / 69	46 / 75		
Baseline Mean (SD)	88.18 (14.46)	82.70 (18.00)		
Week 52 Mean (SD)	90.54 (15.49)	89.84 (14.16)		
Week 100 Mean (SD)	90.15 (13.25)	88.99 (17.72)		
Week 28: Adjusted Mean Change (SE)	4.06 (2.34)	9.17 (2.41)		
Week 52: Adjusted Mean Change (SE)	6.18 (2.67)	7.94 (2.81)	-1.76 [-9.32; 5.80]	0.646
Week 100: Adjusted Mean Change (SE)	4.12 (2.95)	6.54 (3.16)	-2.43 [-10.87; 6.02]	0.572
Western Pacific Region				
N'/ N	19 / 30	20 / 29		
Baseline Mean (SD)	71.05 (23.14)	76.04 (18.63)		
Week 52 Mean (SD)	73.33 (25.04)	79.76 (13.36)		
Week 100 Mean (SD)	72.40 (22.51)	68.61 (18.56)		
Week 28: Adjusted Mean Change (SE)	1.57 (3.51)	2.25 (3.63)		
Week 52: Adjusted Mean Change (SE)	1.16 (4.10)	2.22 (4.19)	-1.06 [-12.56; 10.44]	0.856
Week 100: Adjusted Mean Change (SE)	-1.64 (4.31)	-4.75 (4.40)	3.11 [-8.97; 15.20]	0.612
KITE: Driving				
Interaction test	p=0.640			
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	13 / 26	14 / 21		
Baseline Mean (SD)	69.55 (22.14)	72.02 (27.66)		
Week 52 Mean (SD)	90.63 (6.95)	81.25 (23.88)		
Week 100 Mean (SD)	83.33 (13.94)	84.09 (10.84)		
Week 28: Adjusted Mean Change (SE)	1.15 (4.71)	7.03 (4.11)		
Week 52: Adjusted Mean Change (SE)	14.48 (4.08)	2.15 (3.88)	12.32 [1.25; 23.40]	0.029 *
Week 100: Adjusted Mean Change (SE)	6.04 (5.00)	6.02 (3.89)	0.02 [-12.45; 12.49]	0.998
European Region				
N'/ N	79 / 135	68 / 132		
Baseline Mean (SD)	80.59 (20.57)	84.13 (20.31)		
Week 52 Mean (SD)	85.98 (19.01)	88.62 (15.84)		
Week 100 Mean (SD)	86.39 (15.70)	87.35 (15.76)		
Week 28: Adjusted Mean Change (SE)	0.43 (1.64)	5.17 (1.79)		
Week 52: Adjusted Mean Change (SE)	4.32 (1.42)	5.48 (1.54)	-1.16 [-5.30; 2.97]	0.580
Week 100: Adjusted Mean Change (SE)	3.76 (1.60)	2.06 (1.73)	1.70 [-2.95; 6.36]	0.471

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Western Pacific Region				
N'/ N	11 / 18	14 / 28		
Baseline Mean (SD)	78.79 (14.12)	82.14 (20.89)		
Week 52 Mean (SD)	90.00 (7.66)	88.54 (6.44)		
Week 100 Mean (SD)	87.50 (10.91)	89.17 (11.15)		
Week 28: Adjusted Mean Change (SE)	2.37 (4.30)	4.45 (4.12)		
Week 52: Adjusted Mean Change (SE)	9.22 (3.69)	2.71 (3.41)	6.51 [-3.38; 16.40]	0.196
Week 100: Adjusted Mean Change (SE)	5.33 (4.41)	3.18 (4.02)	2.14 [-9.60; 13.89]	0.719
Pooled Analysis: Driving				
Interaction test	p=0.709			
Region of the Americas				
N'/ N	58 / 90	54 / 83		
Baseline Mean (SD)	76.72 (17.64)	72.84 (20.62)		
Week 52 Mean (SD)	82.80 (20.22)	81.88 (20.81)		
Week 100 Mean (SD)	81.25 (20.22)	77.92 (22.85)		
Week 28: Adjusted Mean Change (SE)	0.30 (2.23)	3.27 (2.31)		
Week 52: Adjusted Mean Change (SE)	2.28 (2.28)	5.09 (2.35)	-2.81 [-9.19; 3.58]	0.388
Week 100: Adjusted Mean Change (SE)	2.32 (2.56)	-0.10 (2.61)	2.42 [-4.73; 9.57]	0.506
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	13 / 26	14 / 21		
Baseline Mean (SD)	69.55 (22.14)	72.02 (27.66)		
Week 52 Mean (SD)	90.63 (6.95)	81.25 (23.88)		
Week 100 Mean (SD)	83.33 (13.94)	84.09 (10.84)		
Week 28: Adjusted Mean Change (SE)	1.62 (4.86)	7.71 (4.32)		
Week 52: Adjusted Mean Change (SE)	15.76 (5.05)	2.94 (4.82)	12.83 [-0.89; 26.54]	0.067
Week 100: Adjusted Mean Change (SE)	7.07 (6.05)	6.74 (4.79)	0.33 [-14.83; 15.50]	0.966
European Region				
N'/ N	122 / 204	114 / 207		
Baseline Mean (SD)	83.27 (18.94)	83.55 (19.34)		
Week 52 Mean (SD)	87.62 (17.88)	89.06 (15.18)		
Week 100 Mean (SD)	87.67 (14.95)	87.91 (16.36)		
Week 28: Adjusted Mean Change (SE)	1.79 (1.41)	6.99 (1.49)		
Week 52: Adjusted Mean Change (SE)	5.10 (1.45)	6.73 (1.55)	-1.63 [-5.77; 2.52]	0.440
Week 100: Adjusted Mean Change (SE)	3.98 (1.60)	4.05 (1.72)	-0.07 [-4.67; 4.54]	0.978

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Western Pacific Region				
N'/ N	30 / 48	34 / 57		
Baseline Mean (SD)	73.89 (20.38)	78.55 (19.52)		
Week 52 Mean (SD)	80.00 (21.38)	83.81 (11.45)		
Week 100 Mean (SD)	77.43 (20.48)	76.83 (18.79)		
Week 28: Adjusted Mean Change (SE)	1.56 (2.72)	2.51 (2.71)		
Week 52: Adjusted Mean Change (SE)	3.89 (2.82)	1.70 (2.75)	2.19 [-5.55; 9.93]	0.579
Week 100: Adjusted Mean Change (SE)	0.57 (3.12)	-2.11 (3.04)	2.68 [-5.88; 11.25]	0.538
Color Vision				
Test of heterogeneity in main analysis: **p_H=0.477**				
KESTREL: Color Vision				
Interaction test	p=0.774			
Region of the Americas				
N'/ N	89 / 90	81 / 83		
Baseline Mean (SD)	91.29 (16.90)	92.59 (17.87)		
Week 52 Mean (SD)	95.36 (13.66)	96.01 (11.84)		
Week 100 Mean (SD)	93.56 (14.75)	93.75 (15.43)		
Week 28: Adjusted Mean Change (SE)	2.19 (1.21)	-0.00 (1.29)		
Week 52: Adjusted Mean Change (SE)	1.01 (1.26)	1.92 (1.29)	-0.91 [-4.44; 2.62]	0.612
Week 100: Adjusted Mean Change (SE)	-0.06 (1.47)	-0.23 (1.50)	0.17 [-3.94; 4.28]	0.934
European Region				
N'/ N	67 / 69	75 / 75		
Baseline Mean (SD)	96.64 (15.01)	95.67 (11.89)		
Week 52 Mean (SD)	99.07 (6.80)	97.08 (10.39)		
Week 100 Mean (SD)	99.00 (4.95)	98.21 (6.50)		
Week 28: Adjusted Mean Change (SE)	2.14 (1.38)	4.51 (1.32)		
Week 52: Adjusted Mean Change (SE)	3.88 (1.44)	2.71 (1.37)	1.17 [-2.73; 5.08]	0.555
Week 100: Adjusted Mean Change (SE)	3.80 (1.68)	3.84 (1.60)	-0.04 [-4.60; 4.52]	0.986
Western Pacific Region				
N'/ N	30 / 30	28 / 29		
Baseline Mean (SD)	90.00 (18.10)	93.75 (12.95)		
Week 52 Mean (SD)	94.79 (10.37)	92.71 (15.60)		
Week 100 Mean (SD)	89.00 (16.27)	90.91 (12.31)		
Week 28: Adjusted Mean Change (SE)	1.50 (2.06)	-0.59 (2.19)		
Week 52: Adjusted Mean Change (SE)	1.63 (2.16)	-0.96 (2.19)	2.59 [-3.44; 8.62]	0.399
Week 100: Adjusted Mean Change (SE)	-3.74 (2.40)	-3.74 (2.56)	-0.00 [-6.90; 6.89]	0.999

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Color Vision				
Interaction test	p=0.186			
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	87.50 (20.31)	88.10 (20.34)		
Week 52 Mean (SD)	97.06 (8.30)	87.50 (23.51)		
Week 100 Mean (SD)	96.15 (9.39)	93.33 (19.97)		
Week 28: Adjusted Mean Change (SE)	5.03 (2.19)	1.21 (2.46)		
Week 52: Adjusted Mean Change (SE)	7.38 (2.12)	-2.04 (2.34)	9.42 [3.22; 15.61]	0.003 *
Week 100: Adjusted Mean Change (SE)	4.93 (2.85)	3.71 (2.68)	1.22 [-6.46; 8.90]	0.755
European Region				
N'/ N	134 / 135	130 / 132		
Baseline Mean (SD)	92.16 (16.91)	92.31 (15.52)		
Week 52 Mean (SD)	97.75 (8.63)	96.33 (9.52)		
Week 100 Mean (SD)	97.38 (9.12)	94.47 (13.47)		
Week 28: Adjusted Mean Change (SE)	3.22 (0.96)	4.24 (0.96)		
Week 52: Adjusted Mean Change (SE)	5.73 (0.84)	4.52 (0.85)	1.21 [-1.12; 3.55]	0.308
Week 100: Adjusted Mean Change (SE)	5.03 (1.01)	2.49 (1.02)	2.54 [-0.28; 5.36]	0.078
Western Pacific Region				
N'/ N	18 / 18	28 / 28		
Baseline Mean (SD)	98.61 (5.89)	91.96 (15.30)		
Week 52 Mean (SD)	96.67 (8.80)	92.71 (13.75)		
Week 100 Mean (SD)	97.92 (7.22)	98.91 (5.21)		
Week 28: Adjusted Mean Change (SE)	2.79 (2.60)	5.26 (2.18)		
Week 52: Adjusted Mean Change (SE)	2.56 (2.29)	0.76 (1.82)	1.80 [-3.93; 7.52]	0.538
Week 100: Adjusted Mean Change (SE)	4.15 (2.99)	6.59 (2.18)	-2.45 [-9.70; 4.80]	0.507
Pooled Analysis: Color Vision				
Interaction test	p=0.507			
Region of the Americas				
N'/ N	89 / 90	81 / 83		
Baseline Mean (SD)	91.29 (16.90)	92.59 (17.87)		
Week 52 Mean (SD)	95.36 (13.66)	96.01 (11.84)		
Week 100 Mean (SD)	93.56 (14.75)	93.75 (15.43)		
Week 28: Adjusted Mean Change (SE)	3.37 (1.33)	0.89 (1.40)		
Week 52: Adjusted Mean Change (SE)	2.27 (1.28)	2.84 (1.29)	-0.56 [-4.12; 2.99]	0.755
Week 100: Adjusted Mean Change (SE)	1.16 (1.50)	0.66 (1.52)	0.50 [-3.68; 4.68]	0.815

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	87.50 (20.31)	88.10 (20.34)		
Week 52 Mean (SD)	97.06 (8.30)	87.50 (23.51)		
Week 100 Mean (SD)	96.15 (9.39)	93.33 (19.97)		
Week 28: Adjusted Mean Change (SE)	3.63 (2.31)	0.17 (2.57)		
Week 52: Adjusted Mean Change (SE)	6.08 (2.39)	-2.91 (2.60)	8.99 [2.05; 15.92]	0.011 *
Week 100: Adjusted Mean Change (SE)	3.81 (3.14)	2.49 (2.96)	1.31 [-7.17; 9.80]	0.761
European Region				
N'/ N	201 / 204	205 / 207		
Baseline Mean (SD)	93.66 (16.40)	93.54 (14.36)		
Week 52 Mean (SD)	98.18 (8.08)	96.60 (9.81)		
Week 100 Mean (SD)	97.90 (8.04)	95.78 (11.64)		
Week 28: Adjusted Mean Change (SE)	2.50 (0.82)	4.07 (0.81)		
Week 52: Adjusted Mean Change (SE)	4.67 (0.78)	3.59 (0.76)	1.08 [-1.06; 3.22]	0.321
Week 100: Adjusted Mean Change (SE)	4.22 (0.93)	2.64 (0.91)	1.58 [-0.97; 4.14]	0.225
Western Pacific Region				
N'/ N	48 / 48	56 / 57		
Baseline Mean (SD)	93.23 (15.25)	92.86 (14.07)		
Week 52 Mean (SD)	95.51 (9.72)	92.71 (14.55)		
Week 100 Mean (SD)	91.89 (14.50)	95.00 (10.11)		
Week 28: Adjusted Mean Change (SE)	2.48 (1.64)	2.21 (1.56)		
Week 52: Adjusted Mean Change (SE)	2.36 (1.55)	-0.29 (1.40)	2.65 [-1.46; 6.76]	0.205
Week 100: Adjusted Mean Change (SE)	-0.52 (1.87)	1.14 (1.69)	-1.66 [-6.60; 3.29]	0.510
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.003 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.436			
Region of the Americas				
N'/ N	89 / 90	82 / 83		
Baseline Mean (SD)	79.49 (23.40)	75.91 (25.59)		
Week 52 Mean (SD)	87.14 (21.17)	90.14 (17.15)		
Week 100 Mean (SD)	82.20 (24.32)	87.50 (20.69)		
Week 28: Adjusted Mean Change (SE)	3.79 (1.97)	7.43 (2.08)		
Week 52: Adjusted Mean Change (SE)	4.25 (2.02)	9.81 (2.04)	-5.56 [-11.17; 0.05]	0.052
Week 100: Adjusted Mean Change (SE)	0.66 (2.41)	6.56 (2.44)	-5.90 [-12.61; 0.82]	0.085

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
European Region				
N'/ N	68 / 69	75 / 75		
Baseline Mean (SD)	90.07 (18.90)	88.33 (17.60)		
Week 52 Mean (SD)	93.64 (13.79)	89.34 (18.52)		
Week 100 Mean (SD)	90.20 (17.38)	90.63 (21.09)		
Week 28: Adjusted Mean Change (SE)	2.55 (2.23)	7.89 (2.15)		
Week 52: Adjusted Mean Change (SE)	7.96 (2.29)	4.57 (2.18)	3.40 [-2.78; 9.58]	0.281
Week 100: Adjusted Mean Change (SE)	4.05 (2.75)	5.89 (2.63)	-1.84 [-9.29; 5.61]	0.628
Western Pacific Region				
N'/ N	30 / 30	29 / 29		
Baseline Mean (SD)	83.33 (20.06)	70.69 (23.21)		
Week 52 Mean (SD)	85.42 (24.36)	82.00 (16.96)		
Week 100 Mean (SD)	77.88 (22.72)	80.21 (19.48)		
Week 28: Adjusted Mean Change (SE)	-0.52 (3.41)	7.41 (3.53)		
Week 52: Adjusted Mean Change (SE)	3.82 (3.45)	5.50 (3.44)	-1.68 [-11.24; 7.88]	0.730
Week 100: Adjusted Mean Change (SE)	-4.20 (3.88)	3.62 (4.07)	-7.83 [-18.87; 3.22]	0.164
KITE: Peripheral Vision				
Interaction test	p=0.738			
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	81.73 (19.44)	77.38 (23.59)		
Week 52 Mean (SD)	91.18 (15.16)	82.14 (22.85)		
Week 100 Mean (SD)	92.31 (15.76)	85.00 (22.76)		
Week 28: Adjusted Mean Change (SE)	3.37 (3.19)	2.89 (3.58)		
Week 52: Adjusted Mean Change (SE)	8.62 (3.70)	4.01 (4.09)	4.61 [-6.23; 15.45]	0.404
Week 100: Adjusted Mean Change (SE)	8.00 (4.00)	5.93 (3.84)	2.07 [-8.82; 12.96]	0.708
European Region				
N'/ N	134 / 135	131 / 132		
Baseline Mean (SD)	82.84 (21.11)	84.92 (21.63)		
Week 52 Mean (SD)	89.51 (16.99)	88.29 (18.10)		
Week 100 Mean (SD)	92.92 (14.94)	86.45 (19.21)		
Week 28: Adjusted Mean Change (SE)	4.67 (1.39)	4.46 (1.40)		
Week 52: Adjusted Mean Change (SE)	6.28 (1.47)	4.22 (1.47)	2.06 [-2.02; 6.14]	0.322
Week 100: Adjusted Mean Change (SE)	8.20 (1.44)	1.64 (1.44)	6.56 [2.55; 10.56]	0.001 *

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Western Pacific Region				
N'/ N	18 / 18	28 / 28		
Baseline Mean (SD)	87.50 (12.86)	89.29 (17.25)		
Week 52 Mean (SD)	90.00 (20.70)	88.54 (23.29)		
Week 100 Mean (SD)	87.50 (16.85)	95.65 (9.69)		
Week 28: Adjusted Mean Change (SE)	5.41 (3.78)	5.66 (3.18)		
Week 52: Adjusted Mean Change (SE)	4.10 (4.01)	-0.22 (3.21)	4.31 [-5.74; 14.37]	0.399
Week 100: Adjusted Mean Change (SE)	1.94 (4.24)	6.80 (3.15)	-4.86 [-15.20; 5.48]	0.356
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.368			
Region of the Americas				
N'/ N	89 / 90	82 / 83		
Baseline Mean (SD)	79.49 (23.40)	75.91 (25.59)		
Week 52 Mean (SD)	87.14 (21.17)	90.14 (17.15)		
Week 100 Mean (SD)	82.20 (24.32)	87.50 (20.69)		
Week 28: Adjusted Mean Change (SE)	5.14 (2.06)	7.14 (2.13)		
Week 52: Adjusted Mean Change (SE)	5.55 (2.14)	9.61 (2.14)	-4.06 [-9.97; 1.84]	0.177
Week 100: Adjusted Mean Change (SE)	1.87 (2.32)	6.16 (2.33)	-4.29 [-10.71; 2.14]	0.190
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	81.73 (19.44)	77.38 (23.59)		
Week 52 Mean (SD)	91.18 (15.16)	82.14 (22.85)		
Week 100 Mean (SD)	92.31 (15.76)	85.00 (22.76)		
Week 28: Adjusted Mean Change (SE)	1.79 (3.54)	3.20 (3.94)		
Week 52: Adjusted Mean Change (SE)	7.04 (4.01)	4.24 (4.39)	2.79 [-8.89; 14.48]	0.639
Week 100: Adjusted Mean Change (SE)	6.73 (4.81)	6.09 (4.58)	0.64 [-12.40; 13.67]	0.923
European Region				
N'/ N	202 / 204	206 / 207		
Baseline Mean (SD)	85.27 (20.63)	86.17 (20.28)		
Week 52 Mean (SD)	90.87 (16.09)	88.66 (18.20)		
Week 100 Mean (SD)	92.04 (15.77)	87.88 (19.91)		
Week 28: Adjusted Mean Change (SE)	3.42 (1.26)	5.87 (1.24)		
Week 52: Adjusted Mean Change (SE)	6.27 (1.30)	4.56 (1.28)	1.71 [-1.87; 5.28]	0.349
Week 100: Adjusted Mean Change (SE)	6.26 (1.43)	3.29 (1.40)	2.97 [-0.95; 6.89]	0.138

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Western Pacific Region				
N'/ N	48 / 48	57 / 57		
Baseline Mean (SD)	84.90 (17.67)	79.82 (22.38)		
Week 52 Mean (SD)	87.18 (22.85)	85.20 (20.36)		
Week 100 Mean (SD)	80.92 (21.30)	87.77 (17.19)		
Week 28: Adjusted Mean Change (SE)	1.85 (2.53)	6.84 (2.36)		
Week 52: Adjusted Mean Change (SE)	4.10 (2.62)	2.92 (2.34)	1.17 [-5.71; 8.06]	0.738
Week 100: Adjusted Mean Change (SE)	-1.89 (2.85)	5.35 (2.56)	-7.25 [-14.76; 0.26]	0.059
General Health				
Test of heterogeneity in main analysis: **p_H=0.834**				
KESTREL: General Health				
Interaction test	p=0.514			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	45.83 (21.28)	37.95 (18.87)		
Week 52 Mean (SD)	56.07 (23.86)	48.61 (21.76)		
Week 100 Mean (SD)	51.87 (21.01)	46.21 (19.73)		
Week 28: Adjusted Mean Change (SE)	2.10 (2.00)	4.26 (2.11)		
Week 52: Adjusted Mean Change (SE)	10.97 (2.44)	7.69 (2.44)	3.29 [-3.50; 10.08]	0.341
Week 100: Adjusted Mean Change (SE)	8.29 (2.44)	4.81 (2.47)	3.48 [-3.34; 10.31]	0.316
European Region				
N'/ N	68 / 69	75 / 75		
Baseline Mean (SD)	45.96 (21.86)	41.67 (21.49)		
Week 52 Mean (SD)	52.73 (24.38)	45.49 (22.60)		
Week 100 Mean (SD)	51.96 (23.90)	53.57 (23.08)		
Week 28: Adjusted Mean Change (SE)	8.48 (2.27)	4.48 (2.18)		
Week 52: Adjusted Mean Change (SE)	8.27 (2.76)	3.62 (2.63)	4.65 [-2.84; 12.14]	0.223
Week 100: Adjusted Mean Change (SE)	9.92 (2.79)	11.46 (2.67)	-1.54 [-9.12; 6.04]	0.690
Western Pacific Region				
N'/ N	30 / 30	29 / 29		
Baseline Mean (SD)	35.00 (16.87)	31.90 (18.78)		
Week 52 Mean (SD)	37.50 (19.50)	38.00 (16.33)		
Week 100 Mean (SD)	40.38 (25.57)	41.67 (19.03)		
Week 28: Adjusted Mean Change (SE)	2.29 (3.42)	7.06 (3.59)		
Week 52: Adjusted Mean Change (SE)	1.40 (4.17)	2.51 (4.15)	-1.11 [-12.64; 10.42]	0.850
Week 100: Adjusted Mean Change (SE)	2.18 (3.96)	5.84 (4.13)	-3.66 [-14.87; 7.54]	0.521

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Health				
Interaction test	p=0.346			
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	47.12 (22.72)	45.24 (23.21)		
Week 52 Mean (SD)	50.00 (25.00)	41.07 (27.05)		
Week 100 Mean (SD)	50.00 (17.68)	55.00 (23.53)		
Week 28: Adjusted Mean Change (SE)	2.53 (3.67)	4.67 (4.12)		
Week 52: Adjusted Mean Change (SE)	6.60 (4.76)	0.38 (5.20)	6.22 [-7.63; 20.07]	0.377
Week 100: Adjusted Mean Change (SE)	4.36 (4.74)	14.80 (4.54)	-10.44 [-23.33; 2.45]	0.112
European Region				
N'/ N	134 / 135	132 / 132		
Baseline Mean (SD)	42.54 (16.52)	42.23 (19.81)		
Week 52 Mean (SD)	49.78 (20.27)	49.11 (20.11)		
Week 100 Mean (SD)	51.18 (19.02)	48.15 (19.55)		
Week 28: Adjusted Mean Change (SE)	3.05 (1.60)	3.34 (1.61)		
Week 52: Adjusted Mean Change (SE)	6.48 (1.87)	5.23 (1.87)	1.24 [-3.95; 6.43]	0.638
Week 100: Adjusted Mean Change (SE)	6.84 (1.72)	3.83 (1.70)	3.00 [-1.74; 7.75]	0.214
Western Pacific Region				
N'/ N	18 / 18	28 / 28		
Baseline Mean (SD)	50.00 (36.38)	55.36 (32.17)		
Week 52 Mean (SD)	46.67 (29.68)	60.42 (32.06)		
Week 100 Mean (SD)	47.92 (29.11)	63.04 (30.03)		
Week 28: Adjusted Mean Change (SE)	8.12 (4.36)	9.31 (3.69)		
Week 52: Adjusted Mean Change (SE)	-2.63 (5.13)	6.59 (4.10)	-9.22 [-22.04; 3.61]	0.159
Week 100: Adjusted Mean Change (SE)	2.17 (5.03)	8.10 (3.77)	-5.94 [-18.22; 6.34]	0.342
Pooled Analysis: General Health				
Interaction test	p=0.252			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	45.83 (21.28)	37.95 (18.87)		
Week 52 Mean (SD)	56.07 (23.86)	48.61 (21.76)		
Week 100 Mean (SD)	51.87 (21.01)	46.21 (19.73)		
Week 28: Adjusted Mean Change (SE)	0.51 (2.22)	3.91 (2.31)		
Week 52: Adjusted Mean Change (SE)	9.33 (2.59)	7.36 (2.57)	1.97 [-5.19; 9.14]	0.589
Week 100: Adjusted Mean Change (SE)	6.68 (2.50)	4.42 (2.53)	2.27 [-4.71; 9.24]	0.524

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	47.12 (22.72)	45.24 (23.21)		
Week 52 Mean (SD)	50.00 (25.00)	41.07 (27.05)		
Week 100 Mean (SD)	50.00 (17.68)	55.00 (23.53)		
Week 28: Adjusted Mean Change (SE)	3.82 (3.83)	5.14 (4.26)		
Week 52: Adjusted Mean Change (SE)	7.89 (4.94)	1.08 (5.38)	6.81 [-7.53; 21.14]	0.352
Week 100: Adjusted Mean Change (SE)	5.62 (5.20)	15.08 (4.95)	-9.46 [-23.56; 4.64]	0.188
European Region				
N'/ N	202 / 204	207 / 207		
Baseline Mean (SD)	43.69 (18.50)	42.03 (20.38)		
Week 52 Mean (SD)	50.75 (21.68)	47.83 (21.03)		
Week 100 Mean (SD)	51.43 (20.65)	50.00 (20.91)		
Week 28: Adjusted Mean Change (SE)	5.20 (1.36)	3.86 (1.33)		
Week 52: Adjusted Mean Change (SE)	7.40 (1.60)	4.72 (1.56)	2.68 [-1.71; 7.06]	0.231
Week 100: Adjusted Mean Change (SE)	8.23 (1.55)	6.60 (1.51)	1.63 [-2.62; 5.88]	0.451
Western Pacific Region				
N'/ N	48 / 48	57 / 57		
Baseline Mean (SD)	40.63 (26.61)	43.42 (28.55)		
Week 52 Mean (SD)	41.03 (23.98)	48.98 (27.46)		
Week 100 Mean (SD)	42.76 (26.58)	52.13 (27.00)		
Week 28: Adjusted Mean Change (SE)	4.46 (2.70)	8.67 (2.54)		
Week 52: Adjusted Mean Change (SE)	-0.15 (3.23)	5.02 (2.88)	-5.17 [-13.66; 3.32]	0.233
Week 100: Adjusted Mean Change (SE)	2.07 (3.08)	7.55 (2.76)	-5.48 [-13.61; 2.66]	0.187

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + region + treatment * region + visit * region + treatment * region * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + study + treatment * study + region + treatment * region + visit * region + treatment * region * visit.

Table 8.6 VFQ by diabetes type (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Composite Score				
Test of heterogeneity in main analysis: **p_H=0.049 ***				
KESTREL: Composite Score				
Interaction test	p=0.785			
Type 1				
N'/ N	12 / 12	6 / 6		
Baseline Mean (SD)	80.02 (8.90)	78.11 (8.47)		
Week 52 Mean (SD)	82.14 (15.46)	84.54 (13.65)		
Week 100 Mean (SD)	83.42 (17.84)	85.82 (12.44)		
Week 28: Adjusted Mean Change (SE)	7.69 (3.18)	1.96 (4.56)		
Week 52: Adjusted Mean Change (SE)	5.16 (3.52)	7.08 (4.33)	-1.93 [-12.90; 9.05]	0.730
Week 100: Adjusted Mean Change (SE)	5.16 (3.76)	8.64 (5.42)	-3.48 [-16.45; 9.49]	0.598
Type 2				
N'/ N	176 / 177	181 / 181		
Baseline Mean (SD)	76.41 (17.89)	76.77 (14.76)		
Week 52 Mean (SD)	85.20 (13.86)	85.18 (12.26)		
Week 100 Mean (SD)	83.03 (14.82)	83.26 (14.48)		
Week 28: Adjusted Mean Change (SE)	5.62 (0.82)	7.91 (0.82)		
Week 52: Adjusted Mean Change (SE)	7.12 (0.86)	8.24 (0.84)	-1.12 [-3.49; 1.25]	0.354
Week 100: Adjusted Mean Change (SE)	6.20 (0.97)	6.51 (0.95)	-0.31 [-2.97; 2.34]	0.816
KITE: Composite Score				
Interaction test	p=0.104			
Type 1				
N'/ N	19 / 19	7 / 7		
Baseline Mean (SD)	83.04 (11.40)	82.92 (12.40)		
Week 52 Mean (SD)	89.26 (7.29)	93.01 (5.28)		
Week 100 Mean (SD)	91.94 (4.89)	96.92 (4.85)		
Week 28: Adjusted Mean Change (SE)	5.79 (2.29)	11.46 (3.74)		
Week 52: Adjusted Mean Change (SE)	7.27 (2.39)	12.03 (3.85)	-4.76 [-13.66; 4.14]	0.294
Week 100: Adjusted Mean Change (SE)	9.15 (2.80)	12.68 (4.87)	-3.53 [-14.57; 7.50]	0.529

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Type 2				
N'/ N	159 / 160	174 / 174		
Baseline Mean (SD)	77.20 (15.27)	76.20 (17.83)		
Week 52 Mean (SD)	86.09 (13.47)	83.08 (15.85)		
Week 100 Mean (SD)	87.55 (12.74)	83.59 (15.37)		
Week 28: Adjusted Mean Change (SE)	5.68 (0.81)	5.64 (0.78)		
Week 52: Adjusted Mean Change (SE)	9.01 (0.88)	6.08 (0.83)	2.93 [0.55; 5.31]	0.016 *
Week 100: Adjusted Mean Change (SE)	8.94 (1.03)	5.93 (0.94)	3.01 [0.26; 5.75]	0.032 *
Pooled Analysis: Composite Score				
Interaction test	p=0.314			
Type 1				
N'/ N	31 / 31	13 / 13		
Baseline Mean (SD)	81.87 (10.45)	80.70 (10.63)		
Week 52 Mean (SD)	87.07 (10.69)	89.10 (10.53)		
Week 100 Mean (SD)	88.87 (11.77)	91.98 (10.20)		
Week 28: Adjusted Mean Change (SE)	6.34 (1.91)	7.66 (2.95)		
Week 52: Adjusted Mean Change (SE)	6.51 (2.01)	9.97 (2.90)	-3.46 [-10.38; 3.47]	0.327
Week 100: Adjusted Mean Change (SE)	7.63 (2.24)	11.23 (3.61)	-3.60 [-11.94; 4.74]	0.397

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Type 2				
N'/ N	335 / 337	355 / 355		
Baseline Mean (SD)	76.78 (16.68)	76.49 (16.31)		
Week 52 Mean (SD)	85.62 (13.66)	84.16 (14.13)		
Week 100 Mean (SD)	85.11 (14.06)	83.42 (14.91)		
Week 28: Adjusted Mean Change (SE)	5.70 (0.59)	6.75 (0.57)		
Week 52: Adjusted Mean Change (SE)	8.05 (0.62)	7.16 (0.59)	0.88 [-0.80; 2.57]	0.303
Week 100: Adjusted Mean Change (SE)	7.54 (0.70)	6.18 (0.66)	1.36 [-0.53; 3.26]	0.159
General Vision				
Test of heterogeneity in main analysis: **p_H=0.762**				
KESTREL: General Vision				
Interaction test	p=0.646			
Type 1				
N'/ N	12 / 12	6 / 6		
Baseline Mean (SD)	63.33 (11.55)	63.33 (15.06)		
Week 52 Mean (SD)	67.50 (10.35)	76.67 (8.16)		
Week 100 Mean (SD)	75.56 (16.67)	70.00 (11.55)		
Week 28: Adjusted Mean Change (SE)	10.52 (3.87)	11.27 (5.65)		
Week 52: Adjusted Mean Change (SE)	6.99 (4.36)	15.28 (5.18)	-8.29 [-21.60; 5.02]	0.221
Week 100: Adjusted Mean Change (SE)	13.50 (4.11)	8.38 (6.07)	5.12 [-9.31; 19.54]	0.486
Type 2				
N'/ N	176 / 177	181 / 181		
Baseline Mean (SD)	61.14 (17.59)	60.11 (14.68)		
Week 52 Mean (SD)	73.33 (14.28)	70.92 (12.99)		
Week 100 Mean (SD)	73.48 (14.83)	72.39 (12.08)		
Week 28: Adjusted Mean Change (SE)	11.42 (1.00)	10.72 (1.00)		
Week 52: Adjusted Mean Change (SE)	12.03 (1.05)	10.46 (1.02)	1.57 [-1.31; 4.45]	0.284
Week 100: Adjusted Mean Change (SE)	12.98 (1.06)	11.92 (1.03)	1.06 [-1.85; 3.97]	0.474

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Vision				
Interaction test	p=0.379			
Type 1				
N'/ N	19 / 19	7 / 7		
Baseline Mean (SD)	61.05 (18.23)	71.43 (10.69)		
Week 52 Mean (SD)	75.56 (8.56)	77.14 (13.80)		
Week 100 Mean (SD)	76.25 (8.06)	84.00 (16.73)		
Week 28: Adjusted Mean Change (SE)	9.99 (3.07)	17.37 (5.03)		
Week 52: Adjusted Mean Change (SE)	13.28 (3.29)	11.65 (5.30)	1.63 [-10.64; 13.91]	0.794
Week 100: Adjusted Mean Change (SE)	14.90 (3.41)	18.43 (6.00)	-3.53 [-17.10; 10.05]	0.610
Type 2				
N'/ N	159 / 160	174 / 174		
Baseline Mean (SD)	61.89 (15.88)	59.43 (18.43)		
Week 52 Mean (SD)	72.38 (15.15)	70.21 (17.26)		
Week 100 Mean (SD)	73.39 (14.44)	70.07 (16.32)		
Week 28: Adjusted Mean Change (SE)	9.27 (1.09)	9.19 (1.05)		
Week 52: Adjusted Mean Change (SE)	11.49 (1.22)	10.19 (1.15)	1.30 [-2.01; 4.61]	0.441
Week 100: Adjusted Mean Change (SE)	11.84 (1.26)	9.20 (1.15)	2.65 [-0.71; 6.01]	0.122
Pooled Analysis: General Vision				
Interaction test	p=0.303			
Type 1				
N'/ N	31 / 31	13 / 13		
Baseline Mean (SD)	61.94 (15.79)	67.69 (13.01)		
Week 52 Mean (SD)	73.08 (9.70)	76.92 (11.09)		
Week 100 Mean (SD)	76.00 (11.55)	77.78 (15.63)		
Week 28: Adjusted Mean Change (SE)	10.22 (2.41)	15.41 (3.76)		
Week 52: Adjusted Mean Change (SE)	11.50 (2.60)	13.71 (3.72)	-2.21 [-11.12; 6.71]	0.627
Week 100: Adjusted Mean Change (SE)	14.44 (2.60)	14.43 (4.25)	0.01 [-9.77; 9.80]	0.998
Type 2				
N'/ N	335 / 337	355 / 355		
Baseline Mean (SD)	61.49 (16.78)	59.77 (16.60)		
Week 52 Mean (SD)	72.88 (14.67)	70.58 (15.19)		
Week 100 Mean (SD)	73.44 (14.62)	71.24 (14.37)		
Week 28: Adjusted Mean Change (SE)	10.39 (0.74)	9.94 (0.73)		
Week 52: Adjusted Mean Change (SE)	11.75 (0.81)	10.31 (0.77)	1.45 [-0.74; 3.64]	0.195
Week 100: Adjusted Mean Change (SE)	12.48 (0.82)	10.56 (0.77)	1.92 [-0.29; 4.12]	0.088

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Ocular Pain				
Test of heterogeneity in main analysis: **p_H=0.664**				
KESTREL: Ocular Pain				
Interaction test	p=0.848			
Type 1				
N'/ N	12 / 12	6 / 6		
Baseline Mean (SD)	89.58 (15.84)	89.58 (14.61)		
Week 52 Mean (SD)	92.19 (13.26)	85.42 (14.61)		
Week 100 Mean (SD)	87.50 (17.68)	100.00 (0.00)		
Week 28: Adjusted Mean Change (SE)	7.35 (5.26)	-0.60 (7.65)		
Week 52: Adjusted Mean Change (SE)	6.56 (5.17)	0.51 (6.22)	6.04 [-9.86; 21.94]	0.455
Week 100: Adjusted Mean Change (SE)	1.79 (5.36)	12.23 (7.87)	-10.44 [-29.15; 8.27]	0.273
Type 2				
N'/ N	176 / 177	181 / 181		
Baseline Mean (SD)	82.95 (20.15)	81.91 (20.64)		
Week 52 Mean (SD)	88.39 (16.00)	86.76 (16.29)		
Week 100 Mean (SD)	85.93 (17.51)	83.54 (20.38)		
Week 28: Adjusted Mean Change (SE)	2.47 (1.36)	4.64 (1.35)		
Week 52: Adjusted Mean Change (SE)	4.88 (1.25)	4.62 (1.22)	0.27 [-3.17; 3.70]	0.879
Week 100: Adjusted Mean Change (SE)	3.09 (1.38)	1.60 (1.35)	1.49 [-2.30; 5.28]	0.440
KITE: Ocular Pain				
Interaction test	p=0.555			
Type 1				
N'/ N	19 / 19	7 / 7		
Baseline Mean (SD)	83.55 (18.66)	83.93 (15.67)		
Week 52 Mean (SD)	88.19 (18.92)	83.93 (23.62)		
Week 100 Mean (SD)	90.63 (16.14)	97.50 (5.59)		
Week 28: Adjusted Mean Change (SE)	5.01 (3.51)	8.96 (5.76)		
Week 52: Adjusted Mean Change (SE)	4.32 (3.53)	0.03 (5.66)	4.29 [-8.84; 17.42]	0.521
Week 100: Adjusted Mean Change (SE)	5.87 (3.63)	12.91 (6.40)	-7.04 [-21.51; 7.43]	0.339

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Type 2				
N'/ N	159 / 160	174 / 174		
Baseline Mean (SD)	84.36 (17.95)	82.40 (20.78)		
Week 52 Mean (SD)	88.89 (16.30)	87.50 (17.55)		
Week 100 Mean (SD)	90.33 (15.36)	88.92 (16.51)		
Week 28: Adjusted Mean Change (SE)	4.31 (1.26)	3.56 (1.20)		
Week 52: Adjusted Mean Change (SE)	4.83 (1.32)	3.95 (1.24)	0.87 [-2.69; 4.44]	0.630
Week 100: Adjusted Mean Change (SE)	6.04 (1.35)	5.14 (1.22)	0.90 [-2.68; 4.48]	0.621
Pooled Analysis: Ocular Pain				
Interaction test	p=0.734			
Type 1				
N'/ N	31 / 31	13 / 13		
Baseline Mean (SD)	85.89 (17.60)	86.54 (14.84)		
Week 52 Mean (SD)	89.42 (17.21)	84.62 (19.20)		
Week 100 Mean (SD)	89.50 (16.41)	98.61 (4.17)		
Week 28: Adjusted Mean Change (SE)	5.44 (3.01)	4.71 (4.70)		
Week 52: Adjusted Mean Change (SE)	4.58 (2.94)	0.10 (4.20)	4.47 [-5.60; 14.55]	0.383
Week 100: Adjusted Mean Change (SE)	4.12 (3.06)	12.50 (5.00)	-8.39 [-19.90; 3.12]	0.153
Type 2				
N'/ N	335 / 337	355 / 355		
Baseline Mean (SD)	83.62 (19.12)	82.15 (20.68)		
Week 52 Mean (SD)	88.62 (16.11)	87.12 (16.89)		
Week 100 Mean (SD)	87.95 (16.67)	86.22 (18.71)		
Week 28: Adjusted Mean Change (SE)	3.39 (0.93)	4.09 (0.91)		
Week 52: Adjusted Mean Change (SE)	4.92 (0.91)	4.29 (0.87)	0.63 [-1.85; 3.11]	0.617
Week 100: Adjusted Mean Change (SE)	4.55 (0.96)	3.34 (0.91)	1.21 [-1.39; 3.80]	0.361

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.450**				
KESTREL: Near Activities				
Interaction test	p=0.570			
Type 1				
N'/ N	12 / 12	6 / 6		
Baseline Mean (SD)	63.54 (19.39)	61.11 (21.52)		
Week 52 Mean (SD)	76.04 (22.47)	81.94 (20.01)		
Week 100 Mean (SD)	75.93 (22.99)	77.08 (17.18)		
Week 28: Adjusted Mean Change (SE)	12.62 (5.43)	15.69 (7.90)		
Week 52: Adjusted Mean Change (SE)	12.64 (6.36)	18.66 (7.63)	-6.02 [-25.56; 13.52]	0.545
Week 100: Adjusted Mean Change (SE)	11.06 (5.86)	14.64 (8.55)	-3.58 [-23.96; 16.81]	0.730
Type 2				
N'/ N	176 / 177	181 / 181		
Baseline Mean (SD)	63.49 (26.59)	65.79 (21.87)		
Week 52 Mean (SD)	79.40 (21.33)	78.56 (20.17)		
Week 100 Mean (SD)	79.75 (20.67)	77.00 (21.27)		
Week 28: Adjusted Mean Change (SE)	12.24 (1.40)	14.25 (1.40)		
Week 52: Adjusted Mean Change (SE)	13.32 (1.54)	13.35 (1.50)	-0.03 [-4.26; 4.20]	0.990
Week 100: Adjusted Mean Change (SE)	14.64 (1.51)	11.60 (1.48)	3.04 [-1.11; 7.19]	0.150
KITE: Near Activities				
Interaction test	p=0.108			
Type 1				
N'/ N	19 / 19	7 / 7		
Baseline Mean (SD)	78.07 (18.68)	78.57 (18.54)		
Week 52 Mean (SD)	86.57 (18.99)	91.67 (9.62)		
Week 100 Mean (SD)	88.02 (17.20)	96.67 (7.45)		
Week 28: Adjusted Mean Change (SE)	7.00 (4.10)	19.16 (6.70)		
Week 52: Adjusted Mean Change (SE)	11.28 (4.04)	16.77 (6.48)	-5.50 [-20.50; 9.50]	0.472
Week 100: Adjusted Mean Change (SE)	10.38 (4.37)	17.81 (7.61)	-7.43 [-24.68; 9.81]	0.397

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Type 2				
N'/ N	158 / 160	174 / 174		
Baseline Mean (SD)	69.20 (22.66)	69.04 (24.04)		
Week 52 Mean (SD)	79.17 (20.78)	78.00 (22.34)		
Week 100 Mean (SD)	83.30 (18.87)	77.36 (23.17)		
Week 28: Adjusted Mean Change (SE)	6.23 (1.46)	5.34 (1.39)		
Week 52: Adjusted Mean Change (SE)	10.08 (1.49)	8.68 (1.40)	1.40 [-2.63; 5.42]	0.495
Week 100: Adjusted Mean Change (SE)	12.31 (1.61)	7.17 (1.47)	5.14 [0.85; 9.42]	0.019 *
Pooled Analysis: Near Activities				
Interaction test	p=0.111			
Type 1				
N'/ N	31 / 31	13 / 13		
Baseline Mean (SD)	72.45 (19.97)	70.51 (21.14)		
Week 52 Mean (SD)	83.33 (20.28)	87.18 (15.45)		
Week 100 Mean (SD)	83.67 (19.91)	87.96 (15.65)		
Week 28: Adjusted Mean Change (SE)	9.86 (3.32)	18.74 (5.16)		
Week 52: Adjusted Mean Change (SE)	12.85 (3.50)	18.46 (5.02)	-5.61 [-17.62; 6.41]	0.360
Week 100: Adjusted Mean Change (SE)	11.55 (3.51)	17.31 (5.68)	-5.76 [-18.87; 7.34]	0.388
Type 2				
N'/ N	334 / 337	355 / 355		
Baseline Mean (SD)	66.19 (24.94)	67.38 (22.99)		
Week 52 Mean (SD)	79.29 (21.03)	78.29 (21.21)		
Week 100 Mean (SD)	81.38 (19.90)	77.18 (22.20)		
Week 28: Adjusted Mean Change (SE)	9.43 (1.02)	9.75 (1.00)		
Week 52: Adjusted Mean Change (SE)	11.72 (1.08)	10.99 (1.03)	0.73 [-2.21; 3.67]	0.625
Week 100: Adjusted Mean Change (SE)	13.51 (1.10)	9.36 (1.04)	4.14 [1.17; 7.12]	0.006 *

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Distance Activities				
Test of heterogeneity in main analysis: **p_H=0.046 ***				
KESTREL: Distance Activities				
Interaction test	p=0.608			
Type 1				
N'/ N	12 / 12	6 / 6		
Baseline Mean (SD)	85.07 (15.02)	73.61 (18.57)		
Week 52 Mean (SD)	81.25 (21.25)	81.94 (22.00)		
Week 100 Mean (SD)	84.26 (22.99)	91.67 (9.62)		
Week 28: Adjusted Mean Change (SE)	6.37 (4.79)	8.01 (6.90)		
Week 52: Adjusted Mean Change (SE)	4.26 (4.82)	7.47 (5.85)	-3.21 [-18.13; 11.70]	0.672
Week 100: Adjusted Mean Change (SE)	5.20 (5.06)	13.37 (7.37)	-8.17 [-25.74; 9.41]	0.361
Type 2				
N'/ N	176 / 177	181 / 181		
Baseline Mean (SD)	74.60 (24.21)	75.41 (21.26)		
Week 52 Mean (SD)	85.64 (17.02)	85.20 (16.92)		
Week 100 Mean (SD)	81.64 (19.80)	82.95 (18.82)		
Week 28: Adjusted Mean Change (SE)	7.42 (1.24)	8.98 (1.23)		
Week 52: Adjusted Mean Change (SE)	9.24 (1.17)	9.54 (1.14)	-0.31 [-3.53; 2.91]	0.852
Week 100: Adjusted Mean Change (SE)	6.64 (1.30)	7.43 (1.27)	-0.78 [-4.35; 2.79]	0.668
KITE: Distance Activities				
Interaction test	p=0.050 *			
Type 1				
N'/ N	19 / 19	7 / 7		
Baseline Mean (SD)	85.96 (11.47)	84.52 (18.28)		
Week 52 Mean (SD)	92.36 (10.33)	96.43 (9.45)		
Week 100 Mean (SD)	94.01 (8.05)	100.00 (0.00)		
Week 28: Adjusted Mean Change (SE)	3.44 (3.57)	14.31 (5.84)		
Week 52: Adjusted Mean Change (SE)	8.64 (3.27)	15.50 (5.22)	-6.86 [-18.96; 5.24]	0.266
Week 100: Adjusted Mean Change (SE)	10.62 (3.60)	14.96 (6.27)	-4.34 [-18.55; 9.86]	0.548

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Type 2				
N'/ N	159 / 160	174 / 174		
Baseline Mean (SD)	75.81 (22.14)	75.86 (22.57)		
Week 52 Mean (SD)	87.30 (18.23)	83.80 (18.88)		
Week 100 Mean (SD)	88.51 (16.63)	83.24 (18.89)		
Week 28: Adjusted Mean Change (SE)	6.46 (1.27)	4.90 (1.21)		
Week 52: Adjusted Mean Change (SE)	11.63 (1.21)	7.65 (1.14)	3.98 [0.72; 7.24]	0.017 *
Week 100: Adjusted Mean Change (SE)	11.36 (1.32)	6.47 (1.21)	4.89 [1.36; 8.41]	0.007 *
Pooled Analysis: Distance Activities				
Interaction test	p=0.078			
Type 1				
N'/ N	31 / 31	13 / 13		
Baseline Mean (SD)	85.62 (12.72)	79.49 (18.51)		
Week 52 Mean (SD)	88.94 (15.04)	89.74 (17.40)		
Week 100 Mean (SD)	90.50 (15.47)	96.30 (7.35)		
Week 28: Adjusted Mean Change (SE)	4.18 (2.90)	11.74 (4.51)		
Week 52: Adjusted Mean Change (SE)	6.84 (2.74)	12.09 (3.92)	-5.25 [-14.64; 4.14]	0.273
Week 100: Adjusted Mean Change (SE)	8.36 (2.96)	14.40 (4.79)	-6.03 [-17.07; 5.01]	0.284
Type 2				
N'/ N	335 / 337	355 / 355		
Baseline Mean (SD)	75.17 (23.22)	75.63 (21.88)		
Week 52 Mean (SD)	86.42 (17.58)	84.52 (17.88)		
Week 100 Mean (SD)	84.80 (18.69)	83.10 (18.82)		
Week 28: Adjusted Mean Change (SE)	7.03 (0.89)	6.94 (0.87)		
Week 52: Adjusted Mean Change (SE)	10.44 (0.85)	8.61 (0.81)	1.83 [-0.47; 4.12]	0.118
Week 100: Adjusted Mean Change (SE)	8.90 (0.92)	6.95 (0.87)	1.95 [-0.54; 4.45]	0.125

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.023 ***				
KESTREL: Social Functioning				
Interaction test	p=0.766			
Type 1				
N'/ N	12 / 12	6 / 6		
Baseline Mean (SD)	94.79 (8.36)	91.67 (12.91)		
Week 52 Mean (SD)	89.06 (16.95)	91.67 (20.41)		
Week 100 Mean (SD)	88.89 (17.05)	100.00 (0.00)		
Week 28: Adjusted Mean Change (SE)	2.38 (3.63)	-3.28 (5.32)		
Week 52: Adjusted Mean Change (SE)	-1.17 (4.40)	1.43 (5.22)	-2.60 [-16.03; 10.83]	0.704
Week 100: Adjusted Mean Change (SE)	-2.15 (4.95)	10.29 (7.26)	-12.44 [-29.72; 4.84]	0.158
Type 2				
N'/ N	176 / 177	181 / 181		
Baseline Mean (SD)	88.42 (19.37)	89.78 (15.73)		
Week 52 Mean (SD)	92.73 (14.88)	93.79 (13.22)		
Week 100 Mean (SD)	90.74 (17.14)	91.64 (15.09)		
Week 28: Adjusted Mean Change (SE)	1.53 (0.94)	4.24 (0.94)		
Week 52: Adjusted Mean Change (SE)	2.58 (1.06)	4.02 (1.03)	-1.44 [-4.35; 1.48]	0.333
Week 100: Adjusted Mean Change (SE)	1.77 (1.27)	2.06 (1.24)	-0.29 [-3.79; 3.21]	0.870
KITE: Social Functioning				
Interaction test	p=0.450			
Type 1				
N'/ N	19 / 19	7 / 7		
Baseline Mean (SD)	92.11 (13.31)	92.86 (18.90)		
Week 52 Mean (SD)	98.61 (4.04)	100.00 (0.00)		
Week 100 Mean (SD)	100.00 (0.00)	100.00 (0.00)		
Week 28: Adjusted Mean Change (SE)	5.92 (3.14)	10.09 (5.15)		
Week 52: Adjusted Mean Change (SE)	8.86 (2.61)	10.09 (4.17)	-1.22 [-10.90; 8.45]	0.804
Week 100: Adjusted Mean Change (SE)	9.75 (3.34)	8.70 (5.89)	1.05 [-12.25; 14.36]	0.877

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Type 2				
N'/ N	159 / 160	174 / 174		
Baseline Mean (SD)	87.97 (17.73)	86.14 (20.00)		
Week 52 Mean (SD)	94.64 (12.59)	91.17 (14.97)		
Week 100 Mean (SD)	94.35 (14.65)	90.87 (17.09)		
Week 28: Adjusted Mean Change (SE)	3.43 (1.12)	3.58 (1.07)		
Week 52: Adjusted Mean Change (SE)	7.17 (0.97)	4.07 (0.91)	3.10 [0.48; 5.73]	0.021 *
Week 100: Adjusted Mean Change (SE)	6.40 (1.24)	3.53 (1.12)	2.87 [-0.42; 6.16]	0.087
Pooled Analysis: Social Functioning				
Interaction test	p=0.475			
Type 1				
N'/ N	31 / 31	13 / 13		
Baseline Mean (SD)	93.15 (11.56)	92.31 (15.76)		
Week 52 Mean (SD)	95.67 (10.57)	96.15 (13.87)		
Week 100 Mean (SD)	96.00 (11.25)	100.00 (0.00)		
Week 28: Adjusted Mean Change (SE)	3.86 (2.37)	4.44 (3.71)		
Week 52: Adjusted Mean Change (SE)	4.65 (2.34)	6.08 (3.33)	-1.44 [-9.43; 6.56]	0.724
Week 100: Adjusted Mean Change (SE)	4.78 (2.83)	9.31 (4.62)	-4.53 [-15.17; 6.10]	0.403
Type 2				
N'/ N	335 / 337	355 / 355		
Baseline Mean (SD)	88.21 (18.58)	87.99 (18.02)		
Week 52 Mean (SD)	93.63 (13.85)	92.52 (14.13)		
Week 100 Mean (SD)	92.40 (16.11)	91.25 (16.09)		
Week 28: Adjusted Mean Change (SE)	2.56 (0.73)	3.87 (0.71)		
Week 52: Adjusted Mean Change (SE)	4.92 (0.73)	4.02 (0.69)	0.90 [-1.07; 2.87]	0.369
Week 100: Adjusted Mean Change (SE)	4.08 (0.89)	2.72 (0.84)	1.36 [-1.04; 3.76]	0.265

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Mental Health				
Test of heterogeneity in main analysis: **p_H=0.200**				
KESTREL: Mental Health				
Interaction test	p=0.207			
Type 1				
N'/ N	12 / 12	6 / 6		
Baseline Mean (SD)	63.54 (17.84)	61.46 (22.85)		
Week 52 Mean (SD)	73.44 (25.17)	71.88 (16.18)		
Week 100 Mean (SD)	72.22 (29.99)	78.13 (23.11)		
Week 28: Adjusted Mean Change (SE)	16.99 (5.05)	-7.42 (7.37)		
Week 52: Adjusted Mean Change (SE)	7.96 (5.64)	7.42 (6.75)	0.55 [-16.74; 17.84]	0.950
Week 100: Adjusted Mean Change (SE)	8.97 (6.06)	11.45 (8.87)	-2.48 [-23.61; 18.64]	0.817
Type 2				
N'/ N	176 / 177	181 / 181		
Baseline Mean (SD)	65.66 (25.37)	68.47 (23.07)		
Week 52 Mean (SD)	78.63 (19.71)	78.95 (17.93)		
Week 100 Mean (SD)	75.05 (20.92)	77.60 (21.45)		
Week 28: Adjusted Mean Change (SE)	6.80 (1.31)	9.82 (1.30)		
Week 52: Adjusted Mean Change (SE)	10.62 (1.37)	11.24 (1.32)	-0.62 [-4.36; 3.12]	0.744
Week 100: Adjusted Mean Change (SE)	8.72 (1.56)	10.68 (1.53)	-1.96 [-6.26; 2.33]	0.369
KITE: Mental Health				
Interaction test	p=0.256			
Type 1				
N'/ N	19 / 19	7 / 7		
Baseline Mean (SD)	74.01 (16.44)	77.68 (13.91)		
Week 52 Mean (SD)	82.29 (15.79)	91.96 (8.63)		
Week 100 Mean (SD)	87.50 (7.91)	97.50 (5.59)		
Week 28: Adjusted Mean Change (SE)	9.84 (3.87)	11.94 (6.32)		
Week 52: Adjusted Mean Change (SE)	11.03 (4.48)	19.08 (7.20)	-8.04 [-24.70; 8.61]	0.343
Week 100: Adjusted Mean Change (SE)	14.77 (4.54)	22.03 (7.90)	-7.26 [-25.15; 10.63]	0.425

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Type 2				
N'/ N	159 / 160	174 / 174		
Baseline Mean (SD)	68.32 (22.06)	65.30 (26.29)		
Week 52 Mean (SD)	81.25 (21.37)	75.96 (23.84)		
Week 100 Mean (SD)	83.75 (16.90)	78.99 (22.36)		
Week 28: Adjusted Mean Change (SE)	8.18 (1.37)	8.78 (1.32)		
Week 52: Adjusted Mean Change (SE)	12.91 (1.66)	8.67 (1.56)	4.25 [-0.23; 8.72]	0.063
Week 100: Adjusted Mean Change (SE)	13.59 (1.67)	10.93 (1.53)	2.66 [-1.80; 7.12]	0.242
Pooled Analysis: Mental Health				
Interaction test	p=0.926			
Type 1				
N'/ N	31 / 31	13 / 13		
Baseline Mean (SD)	69.96 (17.49)	70.19 (19.62)		
Week 52 Mean (SD)	79.57 (19.09)	82.69 (15.97)		
Week 100 Mean (SD)	82.00 (19.87)	88.89 (17.89)		
Week 28: Adjusted Mean Change (SE)	12.16 (3.08)	3.84 (4.80)		
Week 52: Adjusted Mean Change (SE)	9.81 (3.45)	13.84 (4.95)	-4.03 [-15.87; 7.81]	0.504
Week 100: Adjusted Mean Change (SE)	12.46 (3.64)	17.70 (5.90)	-5.24 [-18.84; 8.36]	0.450
Type 2				
N'/ N	335 / 337	355 / 355		
Baseline Mean (SD)	66.92 (23.86)	66.92 (24.71)		
Week 52 Mean (SD)	79.87 (20.52)	77.50 (21.02)		
Week 100 Mean (SD)	79.05 (19.62)	78.29 (21.88)		
Week 28: Adjusted Mean Change (SE)	7.53 (0.95)	9.27 (0.93)		
Week 52: Adjusted Mean Change (SE)	11.78 (1.07)	9.94 (1.02)	1.83 [-1.07; 4.73]	0.215
Week 100: Adjusted Mean Change (SE)	11.12 (1.14)	10.76 (1.08)	0.36 [-2.73; 3.44]	0.820

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.132**				
KESTREL: Role Difficulties				
Interaction test	p=0.567			
Type 1				
N'/ N	12 / 12	6 / 6		
Baseline Mean (SD)	67.71 (28.43)	75.00 (15.81)		
Week 52 Mean (SD)	76.56 (21.59)	85.42 (14.61)		
Week 100 Mean (SD)	83.33 (22.53)	75.00 (22.82)		
Week 28: Adjusted Mean Change (SE)	13.68 (6.39)	8.88 (9.29)		
Week 52: Adjusted Mean Change (SE)	8.78 (7.51)	12.14 (9.03)	-3.36 [-26.47; 19.74]	0.775
Week 100: Adjusted Mean Change (SE)	12.62 (7.30)	4.62 (10.63)	8.00 [-17.36; 33.36]	0.535
Type 2				
N'/ N	176 / 177	181 / 181		
Baseline Mean (SD)	72.30 (28.69)	71.69 (26.96)		
Week 52 Mean (SD)	80.94 (25.56)	83.06 (23.13)		
Week 100 Mean (SD)	81.39 (26.00)	79.84 (25.43)		
Week 28: Adjusted Mean Change (SE)	5.27 (1.65)	9.02 (1.64)		
Week 52: Adjusted Mean Change (SE)	6.37 (1.82)	10.82 (1.77)	-4.45 [-9.45; 0.55]	0.081
Week 100: Adjusted Mean Change (SE)	8.81 (1.88)	7.75 (1.84)	1.06 [-4.10; 6.23]	0.686
KITE: Role Difficulties				
Interaction test	p=0.249			
Type 1				
N'/ N	19 / 19	7 / 7		
Baseline Mean (SD)	77.63 (23.78)	80.36 (22.66)		
Week 52 Mean (SD)	84.03 (18.59)	92.86 (9.83)		
Week 100 Mean (SD)	89.84 (14.59)	97.50 (5.59)		
Week 28: Adjusted Mean Change (SE)	5.86 (4.73)	14.19 (7.74)		
Week 52: Adjusted Mean Change (SE)	7.84 (4.85)	17.76 (7.77)	-9.92 [-27.91; 8.07]	0.279
Week 100: Adjusted Mean Change (SE)	12.75 (5.41)	15.23 (9.40)	-2.48 [-23.79; 18.83]	0.819

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Type 2				
N'/ N	159 / 160	174 / 174		
Baseline Mean (SD)	70.28 (27.62)	66.67 (29.49)		
Week 52 Mean (SD)	82.74 (22.46)	77.45 (25.58)		
Week 100 Mean (SD)	84.35 (23.75)	79.70 (25.51)		
Week 28: Adjusted Mean Change (SE)	7.55 (1.68)	7.88 (1.61)		
Week 52: Adjusted Mean Change (SE)	12.94 (1.80)	7.99 (1.69)	4.95 [0.09; 9.81]	0.046 *
Week 100: Adjusted Mean Change (SE)	11.73 (1.99)	9.52 (1.82)	2.20 [-3.11; 7.52]	0.415
Pooled Analysis: Role Difficulties				
Interaction test	p=0.623			
Type 1				
N'/ N	31 / 31	13 / 13		
Baseline Mean (SD)	73.79 (25.69)	77.88 (19.20)		
Week 52 Mean (SD)	81.73 (19.44)	89.42 (12.34)		
Week 100 Mean (SD)	87.50 (17.68)	87.50 (18.75)		
Week 28: Adjusted Mean Change (SE)	8.52 (3.84)	12.15 (5.98)		
Week 52: Adjusted Mean Change (SE)	8.00 (4.13)	15.38 (5.92)	-7.38 [-21.55; 6.78]	0.307
Week 100: Adjusted Mean Change (SE)	12.62 (4.35)	10.90 (7.02)	1.72 [-14.50; 17.93]	0.835
Type 2				
N'/ N	335 / 337	355 / 355		
Baseline Mean (SD)	71.34 (28.16)	69.23 (28.30)		
Week 52 Mean (SD)	81.79 (24.12)	80.34 (24.46)		
Week 100 Mean (SD)	82.75 (24.99)	79.77 (25.43)		
Week 28: Adjusted Mean Change (SE)	6.41 (1.18)	8.42 (1.15)		
Week 52: Adjusted Mean Change (SE)	9.51 (1.28)	9.44 (1.22)	0.08 [-3.40; 3.55]	0.965
Week 100: Adjusted Mean Change (SE)	10.29 (1.36)	8.62 (1.29)	1.67 [-2.01; 5.35]	0.373

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Dependency				
Test of heterogeneity in main analysis: **p_H=0.019 ***				
KESTREL: Dependency				
Interaction test	p=0.160			
Type 1				
N'/ N	12 / 12	6 / 6		
Baseline Mean (SD)	82.64 (19.93)	76.39 (23.22)		
Week 52 Mean (SD)	86.46 (15.39)	83.33 (18.26)		
Week 100 Mean (SD)	87.04 (19.59)	77.08 (31.46)		
Week 28: Adjusted Mean Change (SE)	8.43 (5.45)	-11.69 (7.94)		
Week 52: Adjusted Mean Change (SE)	3.52 (6.10)	2.72 (7.33)	0.81 [-17.95; 19.57]	0.933
Week 100: Adjusted Mean Change (SE)	3.59 (6.44)	-1.62 (9.42)	5.21 [-17.23; 27.66]	0.648
Type 2				
N'/ N	176 / 177	181 / 181		
Baseline Mean (SD)	81.44 (26.81)	82.97 (23.84)		
Week 52 Mean (SD)	89.13 (22.23)	92.38 (16.94)		
Week 100 Mean (SD)	86.11 (22.72)	88.73 (20.68)		
Week 28: Adjusted Mean Change (SE)	5.42 (1.41)	7.41 (1.41)		
Week 52: Adjusted Mean Change (SE)	5.60 (1.48)	8.96 (1.44)	-3.36 [-7.42; 0.70]	0.104
Week 100: Adjusted Mean Change (SE)	3.66 (1.66)	5.80 (1.62)	-2.13 [-6.69; 2.42]	0.358
KITE: Dependency				
Interaction test	p=0.506			
Type 1				
N'/ N	19 / 19	7 / 7		
Baseline Mean (SD)	92.11 (14.56)	90.48 (16.96)		
Week 52 Mean (SD)	96.30 (8.20)	97.62 (4.07)		
Week 100 Mean (SD)	97.92 (6.45)	100.00 (0.00)		
Week 28: Adjusted Mean Change (SE)	7.85 (3.87)	8.03 (6.32)		
Week 52: Adjusted Mean Change (SE)	8.29 (4.04)	10.42 (6.49)	-2.12 [-17.14; 12.90]	0.781
Week 100: Adjusted Mean Change (SE)	8.29 (4.45)	8.94 (7.73)	-0.65 [-18.18; 16.87]	0.942

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Type 2				
N'/ N	159 / 160	174 / 174		
Baseline Mean (SD)	82.39 (24.23)	81.56 (27.29)		
Week 52 Mean (SD)	90.34 (20.20)	86.19 (23.11)		
Week 100 Mean (SD)	92.39 (15.24)	86.94 (23.24)		
Week 28: Adjusted Mean Change (SE)	4.91 (1.38)	2.82 (1.31)		
Week 52: Adjusted Mean Change (SE)	7.12 (1.49)	2.68 (1.40)	4.44 [0.40; 8.47]	0.031 *
Week 100: Adjusted Mean Change (SE)	6.41 (1.64)	2.65 (1.50)	3.75 [-0.61; 8.12]	0.092
Pooled Analysis: Dependency				
Interaction test	p=0.659			
Type 1				
N'/ N	31 / 31	13 / 13		
Baseline Mean (SD)	88.44 (17.17)	83.97 (20.54)		
Week 52 Mean (SD)	93.27 (11.55)	91.03 (14.22)		
Week 100 Mean (SD)	94.00 (13.51)	89.81 (22.74)		
Week 28: Adjusted Mean Change (SE)	8.10 (3.23)	0.45 (5.02)		
Week 52: Adjusted Mean Change (SE)	6.82 (3.42)	7.55 (4.91)	-0.73 [-12.48; 11.01]	0.903
Week 100: Adjusted Mean Change (SE)	6.75 (3.72)	5.36 (6.02)	1.38 [-12.50; 15.27]	0.845
Type 2				
N'/ N	335 / 337	355 / 355		
Baseline Mean (SD)	81.89 (25.58)	82.28 (25.56)		
Week 52 Mean (SD)	89.70 (21.27)	89.38 (20.37)		
Week 100 Mean (SD)	89.00 (19.85)	87.84 (21.97)		
Week 28: Adjusted Mean Change (SE)	5.24 (1.00)	5.09 (0.97)		
Week 52: Adjusted Mean Change (SE)	6.34 (1.06)	5.84 (1.01)	0.50 [-2.37; 3.38]	0.730
Week 100: Adjusted Mean Change (SE)	5.09 (1.17)	4.21 (1.10)	0.87 [-2.27; 4.02]	0.586

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Driving				
Test of heterogeneity in main analysis: **p_H=0.792**				
KESTREL: Driving				
Interaction test	p=0.254			
Type 1				
N'/ N	9 / 12	4 / 6		
Baseline Mean (SD)	85.19 (13.03)	81.25 (21.92)		
Week 52 Mean (SD)	81.67 (14.91)	91.67 (14.43)		
Week 100 Mean (SD)	73.33 (29.70)	100.00 (0.00)		
Week 28: Adjusted Mean Change (SE)	-0.57 (5.50)	6.34 (8.42)		
Week 52: Adjusted Mean Change (SE)	3.57 (6.81)	11.90 (9.44)	-8.33 [-31.25; 14.59]	0.475
Week 100: Adjusted Mean Change (SE)	-9.77 (7.37)	12.62 (11.39)	-22.39 [-49.09; 4.32]	0.100
Type 2				
N'/ N	111 / 177	116 / 181		
Baseline Mean (SD)	79.50 (18.96)	77.01 (19.70)		
Week 52 Mean (SD)	84.40 (20.38)	84.08 (18.15)		
Week 100 Mean (SD)	83.53 (18.61)	79.48 (21.57)		
Week 28: Adjusted Mean Change (SE)	2.13 (1.43)	5.49 (1.46)		
Week 52: Adjusted Mean Change (SE)	3.53 (1.64)	5.69 (1.68)	-2.16 [-6.80; 2.47]	0.359
Week 100: Adjusted Mean Change (SE)	3.03 (1.82)	1.34 (1.85)	1.69 [-3.42; 6.80]	0.515
KITE: Driving				
Interaction test	p=0.451			
Type 1				
N'/ N	14 / 19	5 / 7		
Baseline Mean (SD)	80.95 (20.78)	83.33 (15.59)		
Week 52 Mean (SD)	88.46 (12.97)	95.00 (11.18)		
Week 100 Mean (SD)	90.91 (10.84)	97.92 (4.17)		
Week 28: Adjusted Mean Change (SE)	1.67 (3.91)	6.12 (6.34)		
Week 52: Adjusted Mean Change (SE)	5.59 (3.25)	12.78 (5.29)	-7.19 [-19.47; 5.09]	0.249
Week 100: Adjusted Mean Change (SE)	7.24 (3.72)	10.56 (6.19)	-3.32 [-17.58; 10.95]	0.647

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Type 2				
N'/ N	89 / 160	91 / 174		
Baseline Mean (SD)	78.70 (20.39)	82.01 (22.11)		
Week 52 Mean (SD)	86.62 (17.95)	87.32 (15.97)		
Week 100 Mean (SD)	85.51 (15.55)	86.50 (14.66)		
Week 28: Adjusted Mean Change (SE)	0.57 (1.57)	5.30 (1.56)		
Week 52: Adjusted Mean Change (SE)	5.87 (1.38)	4.24 (1.36)	1.63 [-2.20; 5.46]	0.403
Week 100: Adjusted Mean Change (SE)	3.74 (1.53)	2.34 (1.48)	1.40 [-2.81; 5.61]	0.513
Pooled Analysis: Driving				
Interaction test	p=0.168			
Type 1				
N'/ N	23 / 31	9 / 13		
Baseline Mean (SD)	82.61 (17.93)	82.41 (17.40)		
Week 52 Mean (SD)	86.57 (13.45)	93.75 (11.57)		
Week 100 Mean (SD)	85.42 (19.60)	98.61 (3.40)		
Week 28: Adjusted Mean Change (SE)	0.62 (3.22)	6.88 (5.09)		
Week 52: Adjusted Mean Change (SE)	4.49 (3.30)	13.13 (5.06)	-8.64 [-20.51; 3.24]	0.154
Week 100: Adjusted Mean Change (SE)	1.65 (3.74)	11.77 (6.04)	-10.12 [-24.08; 3.84]	0.155
Type 2				
N'/ N	200 / 337	207 / 355		
Baseline Mean (SD)	79.15 (19.56)	79.21 (20.89)		
Week 52 Mean (SD)	85.35 (19.35)	85.52 (17.24)		
Week 100 Mean (SD)	84.41 (17.29)	82.76 (18.93)		
Week 28: Adjusted Mean Change (SE)	1.48 (1.06)	5.34 (1.07)		
Week 52: Adjusted Mean Change (SE)	4.70 (1.09)	5.04 (1.10)	-0.33 [-3.37; 2.71]	0.831
Week 100: Adjusted Mean Change (SE)	3.37 (1.23)	1.80 (1.22)	1.57 [-1.83; 4.97]	0.365

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Color Vision				
Test of heterogeneity in main analysis: **p_H=0.477**				
KESTREL: Color Vision				
Interaction test	p=0.852			
Type 1				
N'/ N	12 / 12	6 / 6		
Baseline Mean (SD)	95.83 (14.43)	100.00 (0.00)		
Week 52 Mean (SD)	90.63 (18.60)	95.83 (10.21)		
Week 100 Mean (SD)	94.44 (16.67)	100.00 (0.00)		
Week 28: Adjusted Mean Change (SE)	0.89 (3.31)	-5.32 (4.85)		
Week 52: Adjusted Mean Change (SE)	-2.85 (3.65)	0.23 (4.35)	-3.08 [-14.26; 8.10]	0.589
Week 100: Adjusted Mean Change (SE)	0.64 (4.06)	5.73 (5.96)	-5.08 [-19.26; 9.09]	0.481
Type 2				
N'/ N	174 / 177	178 / 181		
Baseline Mean (SD)	92.82 (16.75)	93.82 (15.16)		
Week 52 Mean (SD)	96.96 (10.59)	95.92 (12.08)		
Week 100 Mean (SD)	94.70 (12.75)	94.93 (12.51)		
Week 28: Adjusted Mean Change (SE)	2.14 (0.86)	2.00 (0.86)		
Week 52: Adjusted Mean Change (SE)	2.47 (0.89)	1.86 (0.87)	0.61 [-1.84; 3.05]	0.626
Week 100: Adjusted Mean Change (SE)	0.66 (1.06)	0.71 (1.04)	-0.05 [-2.96; 2.86]	0.973
KITE: Color Vision				
Interaction test	p=0.415			
Type 1				
N'/ N	19 / 19	7 / 7		
Baseline Mean (SD)	96.05 (12.54)	92.86 (12.20)		
Week 52 Mean (SD)	98.61 (5.89)	100.00 (0.00)		
Week 100 Mean (SD)	100.00 (0.00)	100.00 (0.00)		
Week 28: Adjusted Mean Change (SE)	6.76 (2.45)	7.76 (4.03)		
Week 52: Adjusted Mean Change (SE)	5.44 (2.14)	7.76 (3.41)	-2.32 [-10.23; 5.60]	0.565
Week 100: Adjusted Mean Change (SE)	5.70 (2.61)	7.20 (4.62)	-1.50 [-11.93; 8.93]	0.777

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Type 2				
N'/ N	159 / 160	172 / 174		
Baseline Mean (SD)	91.67 (17.26)	91.72 (16.23)		
Week 52 Mean (SD)	97.40 (8.88)	94.64 (12.65)		
Week 100 Mean (SD)	96.93 (9.49)	94.89 (13.61)		
Week 28: Adjusted Mean Change (SE)	3.01 (0.88)	3.88 (0.84)		
Week 52: Adjusted Mean Change (SE)	5.64 (0.80)	3.04 (0.76)	2.60 [0.43; 4.76]	0.019 *
Week 100: Adjusted Mean Change (SE)	4.86 (0.97)	3.13 (0.89)	1.72 [-0.86; 4.31]	0.191
Pooled Analysis: Color Vision				
Interaction test	p=0.616			
Type 1				
N'/ N	31 / 31	13 / 13		
Baseline Mean (SD)	95.97 (13.07)	96.15 (9.39)		
Week 52 Mean (SD)	96.15 (11.60)	98.08 (6.93)		
Week 100 Mean (SD)	98.00 (10.00)	100.00 (0.00)		
Week 28: Adjusted Mean Change (SE)	4.20 (2.01)	1.89 (3.15)		
Week 52: Adjusted Mean Change (SE)	2.22 (1.92)	4.01 (2.73)	-1.79 [-8.36; 4.77]	0.592
Week 100: Adjusted Mean Change (SE)	3.74 (2.28)	6.26 (3.74)	-2.52 [-11.12; 6.07]	0.565
Type 2				
N'/ N	333 / 337	350 / 355		
Baseline Mean (SD)	92.27 (16.98)	92.79 (15.71)		
Week 52 Mean (SD)	97.17 (9.80)	95.30 (12.35)		
Week 100 Mean (SD)	95.73 (11.39)	94.91 (13.04)		
Week 28: Adjusted Mean Change (SE)	2.65 (0.62)	2.91 (0.61)		
Week 52: Adjusted Mean Change (SE)	4.04 (0.60)	2.43 (0.58)	1.61 [-0.02; 3.24]	0.053
Week 100: Adjusted Mean Change (SE)	2.74 (0.72)	1.79 (0.68)	0.95 [-1.00; 2.90]	0.340

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.003 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.950			
Type 1				
N'/ N	12 / 12	6 / 6		
Baseline Mean (SD)	89.58 (12.87)	87.50 (20.92)		
Week 52 Mean (SD)	87.50 (18.90)	91.67 (20.41)		
Week 100 Mean (SD)	86.11 (22.05)	87.50 (25.00)		
Week 28: Adjusted Mean Change (SE)	4.41 (5.35)	6.68 (7.85)		
Week 52: Adjusted Mean Change (SE)	3.20 (5.93)	7.54 (6.98)	-4.34 [-22.35; 13.67]	0.636
Week 100: Adjusted Mean Change (SE)	0.41 (6.57)	6.50 (9.71)	-6.10 [-29.16; 16.96]	0.603
Type 2				
N'/ N	175 / 177	180 / 181		
Baseline Mean (SD)	83.57 (22.22)	79.86 (23.35)		
Week 52 Mean (SD)	89.36 (19.65)	88.41 (17.74)		
Week 100 Mean (SD)	84.14 (22.22)	87.50 (20.79)		
Week 28: Adjusted Mean Change (SE)	2.50 (1.39)	7.67 (1.38)		
Week 52: Adjusted Mean Change (SE)	5.69 (1.43)	7.07 (1.38)	-1.38 [-5.30; 2.53]	0.488
Week 100: Adjusted Mean Change (SE)	1.07 (1.70)	5.81 (1.65)	-4.74 [-9.41; -0.08]	0.046 *
KITE: Peripheral Vision				
Interaction test	p=0.039 *			
Type 1				
N'/ N	19 / 19	7 / 7		
Baseline Mean (SD)	93.42 (14.05)	78.57 (22.49)		
Week 52 Mean (SD)	90.28 (15.19)	96.43 (9.45)		
Week 100 Mean (SD)	96.88 (8.54)	95.00 (11.18)		
Week 28: Adjusted Mean Change (SE)	4.22 (3.58)	11.44 (5.85)		
Week 52: Adjusted Mean Change (SE)	0.80 (3.66)	15.01 (5.84)	-14.21 [-27.79; -0.64]	0.040 *
Week 100: Adjusted Mean Change (SE)	5.80 (3.77)	8.92 (6.59)	-3.12 [-18.06; 11.82]	0.682

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Type 2				
N'/ N	159 / 160	173 / 174		
Baseline Mean (SD)	81.92 (20.46)	84.97 (21.35)		
Week 52 Mean (SD)	89.68 (17.40)	87.32 (19.69)		
Week 100 Mean (SD)	91.74 (15.78)	87.50 (18.85)		
Week 28: Adjusted Mean Change (SE)	4.61 (1.27)	4.16 (1.22)		
Week 52: Adjusted Mean Change (SE)	7.12 (1.36)	2.93 (1.28)	4.19 [0.51; 7.88]	0.026 *
Week 100: Adjusted Mean Change (SE)	7.84 (1.39)	2.65 (1.27)	5.20 [1.50; 8.89]	0.006 *
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.181			
Type 1				
N'/ N	31 / 31	13 / 13		
Baseline Mean (SD)	91.94 (13.52)	82.69 (21.37)		
Week 52 Mean (SD)	89.42 (16.08)	94.23 (14.98)		
Week 100 Mean (SD)	93.00 (15.34)	91.67 (17.68)		
Week 28: Adjusted Mean Change (SE)	3.93 (3.08)	9.31 (4.80)		
Week 52: Adjusted Mean Change (SE)	1.15 (3.21)	11.35 (4.55)	-10.20 [-21.14; 0.74]	0.068
Week 100: Adjusted Mean Change (SE)	3.49 (3.53)	7.90 (5.78)	-4.41 [-17.70; 8.89]	0.515
Type 2				
N'/ N	334 / 337	353 / 355		
Baseline Mean (SD)	82.78 (21.38)	82.37 (22.51)		
Week 52 Mean (SD)	89.51 (18.59)	87.88 (18.69)		
Week 100 Mean (SD)	87.65 (19.84)	87.50 (19.81)		
Week 28: Adjusted Mean Change (SE)	3.46 (0.95)	6.04 (0.93)		
Week 52: Adjusted Mean Change (SE)	6.31 (0.99)	5.19 (0.95)	1.12 [-1.58; 3.81]	0.417
Week 100: Adjusted Mean Change (SE)	4.17 (1.11)	4.30 (1.05)	-0.13 [-3.12; 2.86]	0.933

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
General Health				
Test of heterogeneity in main analysis: **p_H=0.834**				
KESTREL: General Health				
Interaction test	p=0.703			
Type 1				
N'/ N	12 / 12	6 / 6		
Baseline Mean (SD)	52.08 (24.91)	45.83 (18.82)		
Week 52 Mean (SD)	50.00 (18.90)	45.83 (18.82)		
Week 100 Mean (SD)	58.33 (27.95)	56.25 (31.46)		
Week 28: Adjusted Mean Change (SE)	3.13 (5.50)	-6.35 (8.00)		
Week 52: Adjusted Mean Change (SE)	5.35 (7.19)	2.28 (8.51)	3.06 [-18.83; 24.96]	0.783
Week 100: Adjusted Mean Change (SE)	9.88 (6.73)	10.39 (9.88)	-0.51 [-23.98; 22.97]	0.966
Type 2				
N'/ N	176 / 177	181 / 181		
Baseline Mean (SD)	43.61 (20.83)	38.26 (20.16)		
Week 52 Mean (SD)	51.95 (24.47)	45.72 (21.68)		
Week 100 Mean (SD)	49.26 (22.84)	48.06 (21.07)		
Week 28: Adjusted Mean Change (SE)	4.54 (1.42)	5.17 (1.41)		
Week 52: Adjusted Mean Change (SE)	8.53 (1.73)	5.43 (1.68)	3.10 [-1.66; 7.86]	0.201
Week 100: Adjusted Mean Change (SE)	7.63 (1.73)	7.49 (1.69)	0.15 [-4.61; 4.90]	0.952
KITE: General Health				
Interaction test	p=0.405			
Type 1				
N'/ N	19 / 19	7 / 7		
Baseline Mean (SD)	44.74 (17.83)	46.43 (22.49)		
Week 52 Mean (SD)	56.94 (25.45)	53.57 (17.25)		
Week 100 Mean (SD)	50.00 (22.36)	65.00 (13.69)		
Week 28: Adjusted Mean Change (SE)	3.80 (4.13)	11.52 (6.77)		
Week 52: Adjusted Mean Change (SE)	11.76 (4.71)	7.95 (7.55)	3.81 [-13.69; 21.31]	0.669
Week 100: Adjusted Mean Change (SE)	5.96 (4.43)	18.40 (7.75)	-12.44 [-29.99; 5.11]	0.164

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Type 2				
N'/ N	159 / 160	174 / 174		
Baseline Mean (SD)	43.87 (20.61)	44.54 (22.94)		
Week 52 Mean (SD)	48.41 (21.15)	50.00 (23.74)		
Week 100 Mean (SD)	50.87 (19.57)	50.71 (22.55)		
Week 28: Adjusted Mean Change (SE)	3.47 (1.48)	4.04 (1.41)		
Week 52: Adjusted Mean Change (SE)	4.66 (1.77)	4.94 (1.65)	-0.28 [-5.04; 4.48]	0.909
Week 100: Adjusted Mean Change (SE)	6.17 (1.64)	5.13 (1.49)	1.04 [-3.32; 5.40]	0.638
Pooled Analysis: General Health				
Interaction test	p=0.761			
Type 1				
N'/ N	31 / 31	13 / 13		
Baseline Mean (SD)	47.58 (20.77)	46.15 (20.02)		
Week 52 Mean (SD)	54.81 (23.47)	50.00 (17.68)		
Week 100 Mean (SD)	53.00 (24.28)	61.11 (22.05)		
Week 28: Adjusted Mean Change (SE)	3.47 (3.32)	4.00 (5.19)		
Week 52: Adjusted Mean Change (SE)	9.74 (3.98)	5.32 (5.66)	4.41 [-9.17; 17.99]	0.524
Week 100: Adjusted Mean Change (SE)	7.26 (3.79)	14.85 (6.19)	-7.59 [-21.84; 6.66]	0.296
Type 2				
N'/ N	335 / 337	355 / 355		
Baseline Mean (SD)	43.73 (20.70)	41.34 (21.77)		
Week 52 Mean (SD)	50.28 (22.99)	47.80 (22.76)		
Week 100 Mean (SD)	50.00 (21.37)	49.38 (21.82)		
Week 28: Adjusted Mean Change (SE)	3.93 (1.02)	4.68 (1.00)		
Week 52: Adjusted Mean Change (SE)	6.59 (1.24)	5.25 (1.18)	1.35 [-2.00; 4.70]	0.430
Week 100: Adjusted Mean Change (SE)	6.85 (1.19)	6.42 (1.12)	0.44 [-2.78; 3.65]	0.790

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + diabetes type + treatment * diabetes type + visit * diabetes type + treatment * diabetes type * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + study + treatment * study + diabetes type + treatment * diabetes type + visit * diabetes type + treatment * diabetes type * visit.

Table 8.7 VFQ by HbA1c (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Composite Score				
Test of heterogeneity in main analysis: **p_H=0.049 ***				
KESTREL: Composite Score				
Interaction test	p=0.072			
< 7.5 %				
N'/ N	76 / 76	107 / 107		
Baseline Mean (SD)	77.80 (17.48)	76.20 (14.52)		
Week 52 Mean (SD)	87.25 (11.63)	84.41 (12.16)		
Week 100 Mean (SD)	84.38 (13.31)	83.26 (14.46)		
Week 28: Adjusted Mean Change (SE)	7.03 (1.25)	7.21 (1.06)		
Week 52: Adjusted Mean Change (SE)	9.02 (1.29)	7.47 (1.07)	1.55 [-1.75; 4.85]	0.357
Week 100: Adjusted Mean Change (SE)	7.96 (1.47)	6.80 (1.20)	1.16 [-2.57; 4.89]	0.542
≥ 7.5 %				
N'/ N	111 / 112	80 / 80		
Baseline Mean (SD)	76.15 (17.28)	77.63 (14.72)		
Week 52 Mean (SD)	83.41 (15.22)	86.22 (12.44)		
Week 100 Mean (SD)	82.41 (15.89)	83.43 (14.43)		
Week 28: Adjusted Mean Change (SE)	4.75 (1.03)	8.37 (1.23)		
Week 52: Adjusted Mean Change (SE)	5.51 (1.09)	9.16 (1.27)	-3.64 [-6.95; -0.34]	0.031 *
Week 100: Adjusted Mean Change (SE)	4.84 (1.21)	5.99 (1.48)	-1.16 [-4.92; 2.60]	0.546
KITE: Composite Score				
Interaction test	p=0.306			
< 7.5 %				
N'/ N	81 / 82	96 / 96		
Baseline Mean (SD)	77.79 (14.96)	74.14 (18.89)		
Week 52 Mean (SD)	86.30 (12.53)	82.86 (16.06)		
Week 100 Mean (SD)	86.84 (13.85)	83.44 (14.77)		
Week 28: Adjusted Mean Change (SE)	6.77 (1.14)	6.23 (1.04)		
Week 52: Adjusted Mean Change (SE)	8.43 (1.24)	7.25 (1.12)	1.18 [-2.10; 4.47]	0.478
Week 100: Adjusted Mean Change (SE)	7.84 (1.43)	7.44 (1.28)	0.40 [-3.37; 4.18]	0.834

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 7.5 %				
N'/ N	97 / 97	85 / 85		
Baseline Mean (SD)	77.85 (15.09)	79.08 (15.89)		
Week 52 Mean (SD)	86.62 (13.24)	84.30 (15.26)		
Week 100 Mean (SD)	89.13 (10.45)	84.69 (15.96)		
Week 28: Adjusted Mean Change (SE)	4.79 (1.03)	5.45 (1.11)		
Week 52: Adjusted Mean Change (SE)	9.06 (1.11)	5.29 (1.19)	3.77 [0.57; 6.97]	0.021 *
Week 100: Adjusted Mean Change (SE)	9.87 (1.30)	4.84 (1.34)	5.03 [1.36; 8.70]	0.007 *
Pooled Analysis: Composite Score				
Interaction test	p=0.484			
< 7.5 %				
N'/ N	157 / 158	203 / 203		
Baseline Mean (SD)	77.79 (16.17)	75.23 (16.72)		
Week 52 Mean (SD)	86.77 (12.05)	83.70 (14.06)		
Week 100 Mean (SD)	85.64 (13.59)	83.34 (14.56)		
Week 28: Adjusted Mean Change (SE)	6.90 (0.85)	6.67 (0.75)		
Week 52: Adjusted Mean Change (SE)	8.73 (0.90)	7.28 (0.78)	1.45 [-0.89; 3.79]	0.224
Week 100: Adjusted Mean Change (SE)	7.95 (1.02)	6.97 (0.87)	0.98 [-1.66; 3.62]	0.468

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 7.5 %				
N'/ N	208 / 209	165 / 165		
Baseline Mean (SD)	76.94 (16.28)	78.38 (15.31)		
Week 52 Mean (SD)	84.96 (14.35)	85.22 (13.97)		
Week 100 Mean (SD)	85.45 (14.07)	84.13 (15.26)		
Week 28: Adjusted Mean Change (SE)	4.84 (0.74)	6.90 (0.84)		
Week 52: Adjusted Mean Change (SE)	7.25 (0.79)	7.23 (0.88)	0.02 [-2.29; 2.33]	0.988
Week 100: Adjusted Mean Change (SE)	7.22 (0.89)	5.51 (0.99)	1.72 [-0.89; 4.33]	0.196
General Vision				
Test of heterogeneity in main analysis: **p_H=0.762**				
KESTREL: General Vision				
Interaction test	p=0.780			
< 7.5 %				
N'/ N	76 / 76	107 / 107		
Baseline Mean (SD)	62.11 (17.76)	60.19 (14.14)		
Week 52 Mean (SD)	73.97 (12.25)	72.04 (12.56)		
Week 100 Mean (SD)	73.33 (12.15)	72.44 (12.57)		
Week 28: Adjusted Mean Change (SE)	12.40 (1.53)	10.36 (1.30)		
Week 52: Adjusted Mean Change (SE)	11.92 (1.58)	11.23 (1.31)	0.69 [-3.35; 4.72]	0.739
Week 100: Adjusted Mean Change (SE)	12.89 (1.62)	11.72 (1.30)	1.17 [-2.92; 5.26]	0.574
≥ 7.5 %				
N'/ N	111 / 112	80 / 80		
Baseline Mean (SD)	61.08 (16.59)	60.25 (15.42)		
Week 52 Mean (SD)	72.33 (15.39)	69.85 (13.29)		
Week 100 Mean (SD)	73.72 (16.60)	72.14 (11.24)		
Week 28: Adjusted Mean Change (SE)	10.53 (1.26)	11.13 (1.51)		
Week 52: Adjusted Mean Change (SE)	11.49 (1.35)	9.68 (1.56)	1.82 [-2.24; 5.87]	0.378
Week 100: Adjusted Mean Change (SE)	12.75 (1.33)	11.88 (1.63)	0.87 [-3.27; 5.01]	0.680

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Vision				
Interaction test	p=0.610			
< 7.5 %				
N'/ N	81 / 82	96 / 96		
Baseline Mean (SD)	59.75 (15.00)	56.25 (18.42)		
Week 52 Mean (SD)	71.56 (14.61)	68.86 (16.56)		
Week 100 Mean (SD)	73.33 (14.57)	69.07 (15.87)		
Week 28: Adjusted Mean Change (SE)	10.80 (1.53)	9.11 (1.41)		
Week 52: Adjusted Mean Change (SE)	11.35 (1.72)	10.26 (1.55)	1.09 [-3.46; 5.64]	0.638
Week 100: Adjusted Mean Change (SE)	13.01 (1.76)	9.85 (1.58)	3.16 [-1.49; 7.80]	0.182
≥ 7.5 %				
N'/ N	97 / 97	85 / 85		
Baseline Mean (SD)	63.51 (16.84)	64.00 (17.40)		
Week 52 Mean (SD)	73.75 (14.44)	72.39 (17.68)		
Week 100 Mean (SD)	74.08 (13.26)	72.11 (17.06)		
Week 28: Adjusted Mean Change (SE)	8.15 (1.39)	10.02 (1.50)		
Week 52: Adjusted Mean Change (SE)	11.99 (1.54)	10.22 (1.64)	1.77 [-2.65; 6.19]	0.432
Week 100: Adjusted Mean Change (SE)	11.54 (1.61)	9.19 (1.64)	2.34 [-2.17; 6.85]	0.308
Pooled Analysis: General Vision				
Interaction test	p=0.550			
< 7.5 %				
N'/ N	157 / 158	203 / 203		
Baseline Mean (SD)	60.89 (16.38)	58.33 (16.38)		
Week 52 Mean (SD)	72.76 (13.49)	70.58 (14.58)		
Week 100 Mean (SD)	73.33 (13.39)	70.91 (14.22)		
Week 28: Adjusted Mean Change (SE)	11.47 (1.09)	9.62 (0.96)		
Week 52: Adjusted Mean Change (SE)	11.50 (1.17)	10.62 (1.01)	0.88 [-2.15; 3.92]	0.568
Week 100: Adjusted Mean Change (SE)	12.92 (1.19)	10.69 (1.01)	2.23 [-0.84; 5.29]	0.154
≥ 7.5 %				
N'/ N	208 / 209	165 / 165		
Baseline Mean (SD)	62.21 (16.71)	62.18 (16.53)		
Week 52 Mean (SD)	73.01 (14.91)	71.18 (15.73)		
Week 100 Mean (SD)	73.89 (15.13)	72.13 (14.73)		
Week 28: Adjusted Mean Change (SE)	9.48 (0.94)	10.71 (1.06)		
Week 52: Adjusted Mean Change (SE)	11.82 (1.02)	10.16 (1.14)	1.66 [-1.34; 4.66]	0.278
Week 100: Adjusted Mean Change (SE)	12.27 (1.03)	10.64 (1.15)	1.64 [-1.39; 4.66]	0.289

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Ocular Pain				
Test of heterogeneity in main analysis: **p_H=0.664**				
KESTREL: Ocular Pain				
Interaction test	p=0.009 *			
< 7.5 %				
N'/ N	76 / 76	107 / 107		
Baseline Mean (SD)	84.54 (20.30)	82.36 (20.67)		
Week 52 Mean (SD)	91.47 (13.25)	86.42 (16.65)		
Week 100 Mean (SD)	88.60 (16.58)	84.31 (20.14)		
Week 28: Adjusted Mean Change (SE)	6.56 (2.05)	2.23 (1.74)		
Week 52: Adjusted Mean Change (SE)	7.85 (1.87)	3.51 (1.55)	4.34 [-0.44; 9.12]	0.075
Week 100: Adjusted Mean Change (SE)	5.56 (2.12)	1.96 (1.70)	3.60 [-1.75; 8.94]	0.187
≥ 7.5 %				
N'/ N	111 / 112	80 / 80		
Baseline Mean (SD)	83.00 (19.35)	81.88 (20.37)		
Week 52 Mean (SD)	86.48 (17.28)	87.12 (15.62)		
Week 100 Mean (SD)	84.59 (17.85)	83.48 (20.66)		
Week 28: Adjusted Mean Change (SE)	0.25 (1.69)	7.36 (2.02)		
Week 52: Adjusted Mean Change (SE)	2.94 (1.59)	5.61 (1.84)	-2.68 [-7.47; 2.12]	0.273
Week 100: Adjusted Mean Change (SE)	1.22 (1.74)	1.41 (2.13)	-0.19 [-5.60; 5.22]	0.945
KITE: Ocular Pain				
Interaction test	p=0.671			
< 7.5 %				
N'/ N	81 / 82	96 / 96		
Baseline Mean (SD)	84.88 (16.97)	82.03 (23.56)		
Week 52 Mean (SD)	88.09 (17.02)	88.45 (17.19)		
Week 100 Mean (SD)	90.00 (15.23)	89.00 (16.94)		
Week 28: Adjusted Mean Change (SE)	6.09 (1.76)	3.78 (1.61)		
Week 52: Adjusted Mean Change (SE)	3.82 (1.85)	4.92 (1.66)	-1.10 [-6.00; 3.79]	0.658
Week 100: Adjusted Mean Change (SE)	4.97 (1.87)	5.48 (1.67)	-0.51 [-5.44; 4.43]	0.840

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 7.5 %				
N'/ N	97 / 97	85 / 85		
Baseline Mean (SD)	83.76 (18.85)	82.94 (16.69)		
Week 52 Mean (SD)	89.38 (16.29)	86.09 (18.49)		
Week 100 Mean (SD)	90.67 (15.63)	89.44 (15.76)		
Week 28: Adjusted Mean Change (SE)	2.98 (1.59)	3.78 (1.71)		
Week 52: Adjusted Mean Change (SE)	5.50 (1.65)	2.45 (1.76)	3.05 [-1.70; 7.80]	0.208
Week 100: Adjusted Mean Change (SE)	6.89 (1.71)	5.27 (1.73)	1.62 [-3.16; 6.41]	0.505
Pooled Analysis: Ocular Pain				
Interaction test	p=0.080			
< 7.5 %				
N'/ N	157 / 158	203 / 203		
Baseline Mean (SD)	84.71 (18.59)	82.20 (22.03)		
Week 52 Mean (SD)	89.76 (15.30)	87.35 (16.88)		
Week 100 Mean (SD)	89.32 (15.85)	86.44 (18.85)		
Week 28: Adjusted Mean Change (SE)	6.31 (1.35)	3.00 (1.19)		
Week 52: Adjusted Mean Change (SE)	5.82 (1.32)	4.20 (1.14)	1.62 [-1.81; 5.05]	0.354
Week 100: Adjusted Mean Change (SE)	5.32 (1.41)	3.59 (1.19)	1.72 [-1.90; 5.35]	0.351
≥ 7.5 %				
N'/ N	208 / 209	165 / 165		
Baseline Mean (SD)	83.35 (19.08)	82.42 (18.51)		
Week 52 Mean (SD)	87.88 (16.82)	86.58 (17.12)		
Week 100 Mean (SD)	87.34 (17.10)	86.81 (18.25)		
Week 28: Adjusted Mean Change (SE)	1.56 (1.17)	5.41 (1.32)		
Week 52: Adjusted Mean Change (SE)	4.19 (1.16)	3.92 (1.28)	0.27 [-3.13; 3.66]	0.878
Week 100: Adjusted Mean Change (SE)	3.88 (1.22)	3.55 (1.36)	0.33 [-3.25; 3.91]	0.858

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.450**				
KESTREL: Near Activities				
Interaction test	p=0.283			
< 7.5 %				
N'/ N	76 / 76	107 / 107		
Baseline Mean (SD)	65.57 (26.92)	65.03 (20.99)		
Week 52 Mean (SD)	81.48 (19.65)	78.63 (18.93)		
Week 100 Mean (SD)	81.21 (20.64)	76.44 (21.52)		
Week 28: Adjusted Mean Change (SE)	14.57 (2.13)	14.57 (1.81)		
Week 52: Adjusted Mean Change (SE)	14.92 (2.31)	13.31 (1.92)	1.61 [-4.30; 7.52]	0.592
Week 100: Adjusted Mean Change (SE)	16.78 (2.30)	11.58 (1.86)	5.20 [-0.62; 11.02]	0.080
≥ 7.5 %				
N'/ N	111 / 112	80 / 80		
Baseline Mean (SD)	62.20 (25.73)	66.46 (22.99)		
Week 52 Mean (SD)	77.57 (22.44)	78.78 (21.85)		
Week 100 Mean (SD)	78.83 (20.61)	77.90 (20.61)		
Week 28: Adjusted Mean Change (SE)	10.59 (1.77)	13.91 (2.11)		
Week 52: Adjusted Mean Change (SE)	12.20 (1.97)	13.87 (2.28)	-1.68 [-7.61; 4.26]	0.579
Week 100: Adjusted Mean Change (SE)	13.12 (1.89)	11.88 (2.31)	1.25 [-4.62; 7.12]	0.676
KITE: Near Activities				
Interaction test	p=0.607			
< 7.5 %				
N'/ N	81 / 82	96 / 96		
Baseline Mean (SD)	67.85 (23.21)	67.19 (24.37)		
Week 52 Mean (SD)	78.78 (21.20)	76.74 (23.43)		
Week 100 Mean (SD)	82.15 (20.76)	77.11 (21.36)		
Week 28: Adjusted Mean Change (SE)	8.09 (2.05)	4.50 (1.87)		
Week 52: Adjusted Mean Change (SE)	10.16 (2.09)	8.88 (1.89)	1.28 [-4.26; 6.81]	0.651
Week 100: Adjusted Mean Change (SE)	12.28 (2.24)	8.53 (2.01)	3.75 [-2.17; 9.66]	0.214

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 7.5 %				
N'/ N	96 / 97	85 / 85		
Baseline Mean (SD)	72.09 (21.61)	71.91 (23.22)		
Week 52 Mean (SD)	81.15 (20.27)	80.75 (20.43)		
Week 100 Mean (SD)	85.33 (16.74)	78.99 (24.88)		
Week 28: Adjusted Mean Change (SE)	4.84 (1.86)	7.49 (2.00)		
Week 52: Adjusted Mean Change (SE)	10.25 (1.88)	9.18 (2.01)	1.07 [-4.33; 6.47]	0.697
Week 100: Adjusted Mean Change (SE)	11.84 (2.05)	6.64 (2.09)	5.20 [-0.56; 10.96]	0.077
Pooled Analysis: Near Activities				
Interaction test	p=0.284			
< 7.5 %				
N'/ N	157 / 158	203 / 203		
Baseline Mean (SD)	66.75 (25.02)	66.05 (22.62)		
Week 52 Mean (SD)	80.12 (20.41)	77.76 (21.07)		
Week 100 Mean (SD)	81.70 (20.62)	76.74 (21.39)		
Week 28: Adjusted Mean Change (SE)	11.28 (1.50)	9.59 (1.32)		
Week 52: Adjusted Mean Change (SE)	12.47 (1.57)	10.98 (1.36)	1.49 [-2.59; 5.57]	0.474
Week 100: Adjusted Mean Change (SE)	14.54 (1.60)	9.87 (1.36)	4.67 [0.54; 8.81]	0.027 *
≥ 7.5 %				
N'/ N	207 / 209	165 / 165		
Baseline Mean (SD)	66.79 (24.36)	69.27 (23.20)		
Week 52 Mean (SD)	79.29 (21.43)	79.81 (21.06)		
Week 100 Mean (SD)	81.77 (19.18)	78.51 (23.01)		
Week 28: Adjusted Mean Change (SE)	8.05 (1.30)	10.66 (1.47)		
Week 52: Adjusted Mean Change (SE)	11.35 (1.37)	11.63 (1.53)	-0.28 [-4.31; 3.76]	0.893
Week 100: Adjusted Mean Change (SE)	12.58 (1.39)	9.31 (1.55)	3.27 [-0.81; 7.35]	0.117

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Distance Activities				
Test of heterogeneity in main analysis: **p_H=0.046 ***				
KESTREL: Distance Activities				
Interaction test	p=0.017 *			
< 7.5 %				
N'/ N	76 / 76	107 / 107		
Baseline Mean (SD)	75.27 (25.40)	75.08 (20.42)		
Week 52 Mean (SD)	85.98 (15.83)	83.38 (18.18)		
Week 100 Mean (SD)	81.21 (19.05)	82.45 (19.18)		
Week 28: Adjusted Mean Change (SE)	10.42 (1.86)	6.75 (1.58)		
Week 52: Adjusted Mean Change (SE)	10.33 (1.76)	7.58 (1.46)	2.75 [-1.74; 7.23]	0.230
Week 100: Adjusted Mean Change (SE)	8.02 (1.99)	7.28 (1.61)	0.74 [-4.30; 5.77]	0.774
≥ 7.5 %				
N'/ N	111 / 112	80 / 80		
Baseline Mean (SD)	75.60 (22.65)	75.73 (22.19)		
Week 52 Mean (SD)	84.98 (18.24)	87.50 (15.13)		
Week 100 Mean (SD)	82.56 (20.41)	84.37 (17.93)		
Week 28: Adjusted Mean Change (SE)	5.19 (1.54)	11.81 (1.84)		
Week 52: Adjusted Mean Change (SE)	8.00 (1.49)	11.99 (1.73)	-3.99 [-8.48; 0.51]	0.082
Week 100: Adjusted Mean Change (SE)	5.61 (1.63)	7.67 (2.00)	-2.05 [-7.14; 3.03]	0.428
KITE: Distance Activities				
Interaction test	p=0.777			
< 7.5 %				
N'/ N	81 / 82	96 / 96		
Baseline Mean (SD)	75.57 (21.30)	74.91 (22.87)		
Week 52 Mean (SD)	87.17 (16.22)	84.70 (18.58)		
Week 100 Mean (SD)	88.61 (17.17)	83.67 (17.98)		
Week 28: Adjusted Mean Change (SE)	6.58 (1.79)	4.38 (1.63)		
Week 52: Adjusted Mean Change (SE)	11.13 (1.70)	9.12 (1.53)	2.01 [-2.48; 6.51]	0.379
Week 100: Adjusted Mean Change (SE)	11.15 (1.84)	7.84 (1.65)	3.31 [-1.55; 8.18]	0.181

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 7.5 %				
N'/ N	97 / 97	85 / 85		
Baseline Mean (SD)	78.01 (21.65)	77.65 (21.98)		
Week 52 Mean (SD)	88.54 (18.52)	84.04 (18.99)		
Week 100 Mean (SD)	89.67 (14.87)	83.98 (19.78)		
Week 28: Adjusted Mean Change (SE)	5.74 (1.62)	6.26 (1.75)		
Week 52: Adjusted Mean Change (SE)	11.37 (1.52)	6.74 (1.62)	4.64 [0.26; 9.01]	0.038 *
Week 100: Adjusted Mean Change (SE)	11.38 (1.68)	5.72 (1.72)	5.67 [0.93; 10.40]	0.019 *
Pooled Analysis: Distance Activities				
Interaction test	p=0.120			
< 7.5 %				
N'/ N	157 / 158	203 / 203		
Baseline Mean (SD)	75.42 (23.30)	75.00 (21.56)		
Week 52 Mean (SD)	86.58 (15.97)	83.99 (18.32)		
Week 100 Mean (SD)	85.01 (18.41)	83.01 (18.59)		
Week 28: Adjusted Mean Change (SE)	8.41 (1.30)	5.62 (1.15)		
Week 52: Adjusted Mean Change (SE)	10.72 (1.23)	8.25 (1.06)	2.47 [-0.72; 5.66]	0.129
Week 100: Adjusted Mean Change (SE)	9.65 (1.35)	7.47 (1.15)	2.18 [-1.31; 5.66]	0.220
≥ 7.5 %				
N'/ N	208 / 209	165 / 165		
Baseline Mean (SD)	76.72 (22.17)	76.72 (22.04)		
Week 52 Mean (SD)	86.70 (18.41)	85.69 (17.28)		
Week 100 Mean (SD)	85.77 (18.41)	84.15 (18.91)		
Week 28: Adjusted Mean Change (SE)	5.52 (1.13)	8.92 (1.28)		
Week 52: Adjusted Mean Change (SE)	9.66 (1.07)	9.30 (1.19)	0.35 [-2.80; 3.50]	0.825
Week 100: Adjusted Mean Change (SE)	8.30 (1.17)	6.76 (1.31)	1.54 [-1.90; 4.98]	0.381

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.023 ***				
KESTREL: Social Functioning				
Interaction test	p=0.413			
< 7.5 %				
N'/ N	76 / 76	107 / 107		
Baseline Mean (SD)	89.14 (20.55)	89.02 (16.71)		
Week 52 Mean (SD)	94.84 (12.01)	93.89 (12.64)		
Week 100 Mean (SD)	91.01 (17.64)	92.50 (14.12)		
Week 28: Adjusted Mean Change (SE)	2.78 (1.44)	3.40 (1.22)		
Week 52: Adjusted Mean Change (SE)	4.98 (1.58)	4.37 (1.31)	0.61 [-3.43; 4.66]	0.766
Week 100: Adjusted Mean Change (SE)	2.67 (1.94)	3.35 (1.56)	-0.68 [-5.58; 4.21]	0.784
≥ 7.5 %				
N'/ N	111 / 112	80 / 80		
Baseline Mean (SD)	88.51 (17.85)	90.94 (14.06)		
Week 52 Mean (SD)	90.84 (16.65)	93.46 (14.68)		
Week 100 Mean (SD)	90.70 (16.63)	90.85 (16.25)		
Week 28: Adjusted Mean Change (SE)	0.85 (1.19)	4.88 (1.42)		
Week 52: Adjusted Mean Change (SE)	0.63 (1.35)	3.32 (1.56)	-2.68 [-6.75; 1.38]	0.194
Week 100: Adjusted Mean Change (SE)	1.09 (1.59)	0.57 (1.95)	0.51 [-4.44; 5.47]	0.839
KITE: Social Functioning				
Interaction test	p=0.449			
< 7.5 %				
N'/ N	81 / 82	96 / 96		
Baseline Mean (SD)	87.35 (18.49)	85.42 (19.08)		
Week 52 Mean (SD)	94.73 (11.95)	90.98 (14.29)		
Week 100 Mean (SD)	91.67 (18.51)	90.67 (16.19)		
Week 28: Adjusted Mean Change (SE)	4.05 (1.57)	3.41 (1.44)		
Week 52: Adjusted Mean Change (SE)	7.42 (1.37)	4.43 (1.24)	2.99 [-0.64; 6.62]	0.106
Week 100: Adjusted Mean Change (SE)	3.70 (1.70)	4.03 (1.52)	-0.33 [-4.81; 4.15]	0.884

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 7.5 %				
N'/ N	97 / 97	85 / 85		
Baseline Mean (SD)	89.30 (16.34)	87.50 (20.95)		
Week 52 Mean (SD)	95.47 (11.97)	92.25 (15.29)		
Week 100 Mean (SD)	97.89 (7.00)	91.73 (17.67)		
Week 28: Adjusted Mean Change (SE)	3.41 (1.43)	4.34 (1.54)		
Week 52: Adjusted Mean Change (SE)	7.33 (1.23)	4.24 (1.31)	3.10 [-0.43; 6.62]	0.085
Week 100: Adjusted Mean Change (SE)	9.43 (1.55)	3.44 (1.57)	5.99 [1.64; 10.34]	0.007 *
Pooled Analysis: Social Functioning				
Interaction test	p=0.947			
< 7.5 %				
N'/ N	157 / 158	203 / 203		
Baseline Mean (SD)	88.22 (19.47)	87.32 (17.92)		
Week 52 Mean (SD)	94.78 (11.94)	92.54 (13.46)		
Week 100 Mean (SD)	91.35 (18.01)	91.67 (15.08)		
Week 28: Adjusted Mean Change (SE)	3.41 (1.07)	3.43 (0.94)		
Week 52: Adjusted Mean Change (SE)	6.23 (1.05)	4.44 (0.91)	1.80 [-0.93; 4.52]	0.196
Week 100: Adjusted Mean Change (SE)	3.20 (1.29)	3.65 (1.09)	-0.45 [-3.77; 2.87]	0.789
≥ 7.5 %				
N'/ N	208 / 209	165 / 165		
Baseline Mean (SD)	88.88 (17.12)	89.17 (17.97)		
Week 52 Mean (SD)	93.07 (14.73)	92.83 (14.96)		
Week 100 Mean (SD)	93.95 (13.62)	91.34 (17.00)		
Week 28: Adjusted Mean Change (SE)	2.17 (0.93)	4.47 (1.05)		
Week 52: Adjusted Mean Change (SE)	3.94 (0.92)	3.69 (1.02)	0.26 [-2.44; 2.95]	0.853
Week 100: Adjusted Mean Change (SE)	5.05 (1.12)	2.00 (1.24)	3.05 [-0.23; 6.33]	0.068

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Mental Health				
Test of heterogeneity in main analysis: **p_H=0.200**				
KESTREL: Mental Health				
Interaction test	p=0.179			
< 7.5 %				
N'/ N	76 / 76	107 / 107		
Baseline Mean (SD)	68.91 (23.61)	66.94 (23.62)		
Week 52 Mean (SD)	81.94 (16.50)	76.68 (18.57)		
Week 100 Mean (SD)	77.74 (18.11)	77.85 (21.51)		
Week 28: Adjusted Mean Change (SE)	6.88 (2.02)	8.55 (1.71)		
Week 52: Adjusted Mean Change (SE)	12.90 (2.03)	9.25 (1.68)	3.65 [-1.55; 8.84]	0.168
Week 100: Adjusted Mean Change (SE)	10.90 (2.37)	11.12 (1.91)	-0.21 [-6.20; 5.78]	0.944
≥ 7.5 %				
N'/ N	111 / 112	80 / 80		
Baseline Mean (SD)	63.74 (25.17)	70.00 (22.25)		
Week 52 Mean (SD)	75.73 (21.89)	81.54 (16.55)		
Week 100 Mean (SD)	72.89 (23.44)	77.23 (21.43)		
Week 28: Adjusted Mean Change (SE)	7.70 (1.67)	10.15 (1.99)		
Week 52: Adjusted Mean Change (SE)	8.50 (1.73)	13.62 (2.01)	-5.12 [-10.33; 0.10]	0.054
Week 100: Adjusted Mean Change (SE)	6.72 (1.95)	9.64 (2.38)	-2.93 [-8.98; 3.13]	0.342
KITE: Mental Health				
Interaction test	p=0.080			
< 7.5 %				
N'/ N	81 / 82	96 / 96		
Baseline Mean (SD)	71.84 (19.27)	60.81 (27.45)		
Week 52 Mean (SD)	82.71 (18.82)	75.87 (24.93)		
Week 100 Mean (SD)	82.71 (17.43)	79.33 (21.38)		
Week 28: Adjusted Mean Change (SE)	9.28 (1.92)	10.95 (1.77)		
Week 52: Adjusted Mean Change (SE)	12.19 (2.34)	10.85 (2.11)	1.34 [-4.87; 7.55]	0.671
Week 100: Adjusted Mean Change (SE)	10.84 (2.32)	13.88 (2.08)	-3.04 [-9.18; 3.11]	0.332

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 7.5 %				
N'/ N	97 / 97	85 / 85		
Baseline Mean (SD)	66.49 (23.13)	71.40 (23.17)		
Week 52 Mean (SD)	80.31 (22.17)	77.64 (22.13)		
Week 100 Mean (SD)	85.48 (14.89)	79.93 (23.29)		
Week 28: Adjusted Mean Change (SE)	7.58 (1.73)	6.61 (1.88)		
Week 52: Adjusted Mean Change (SE)	13.01 (2.09)	7.17 (2.23)	5.84 [-0.18; 11.86]	0.057
Week 100: Adjusted Mean Change (SE)	16.09 (2.11)	8.55 (2.17)	7.53 [1.57; 13.49]	0.013 *
Pooled Analysis: Mental Health				
Interaction test	p=0.770			
< 7.5 %				
N'/ N	157 / 158	203 / 203		
Baseline Mean (SD)	70.42 (21.46)	64.04 (25.63)		
Week 52 Mean (SD)	82.33 (17.64)	76.31 (21.66)		
Week 100 Mean (SD)	80.29 (17.86)	78.52 (21.40)		
Week 28: Adjusted Mean Change (SE)	8.12 (1.39)	9.64 (1.23)		
Week 52: Adjusted Mean Change (SE)	12.58 (1.55)	9.91 (1.34)	2.67 [-1.37; 6.70]	0.195
Week 100: Adjusted Mean Change (SE)	10.96 (1.66)	12.29 (1.41)	-1.33 [-5.62; 2.96]	0.543
≥ 7.5 %				
N'/ N	208 / 209	165 / 165		
Baseline Mean (SD)	65.02 (24.22)	70.72 (22.67)		
Week 52 Mean (SD)	77.94 (22.08)	79.50 (19.69)		
Week 100 Mean (SD)	78.58 (20.94)	78.74 (22.44)		
Week 28: Adjusted Mean Change (SE)	7.75 (1.20)	8.30 (1.37)		
Week 52: Adjusted Mean Change (SE)	10.72 (1.36)	10.29 (1.51)	0.43 [-3.56; 4.41]	0.834
Week 100: Adjusted Mean Change (SE)	11.16 (1.44)	9.23 (1.61)	1.93 [-2.30; 6.16]	0.371

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.132**				
KESTREL: Role Difficulties				
Interaction test	p=0.356			
< 7.5 %				
N'/ N	76 / 76	107 / 107		
Baseline Mean (SD)	75.49 (28.75)	71.03 (27.29)		
Week 52 Mean (SD)	84.72 (23.05)	82.53 (21.66)		
Week 100 Mean (SD)	84.21 (22.72)	79.31 (25.29)		
Week 28: Adjusted Mean Change (SE)	6.55 (2.52)	9.81 (2.14)		
Week 52: Adjusted Mean Change (SE)	9.90 (2.73)	10.15 (2.26)	-0.25 [-7.22; 6.71]	0.943
Week 100: Adjusted Mean Change (SE)	11.54 (2.87)	7.44 (2.32)	4.10 [-3.16; 11.36]	0.267
≥ 7.5 %				
N'/ N	111 / 112	80 / 80		
Baseline Mean (SD)	70.05 (28.22)	72.81 (25.91)		
Week 52 Mean (SD)	77.76 (26.60)	84.04 (24.56)		
Week 100 Mean (SD)	80.38 (27.02)	80.36 (25.55)		
Week 28: Adjusted Mean Change (SE)	5.36 (2.08)	7.81 (2.49)		
Week 52: Adjusted Mean Change (SE)	4.20 (2.32)	11.80 (2.69)	-7.60 [-14.58; -0.61]	0.033 *
Week 100: Adjusted Mean Change (SE)	7.61 (2.36)	7.90 (2.88)	-0.29 [-7.61; 7.03]	0.938
KITE: Role Difficulties				
Interaction test	p=0.510			
< 7.5 %				
N'/ N	81 / 82	96 / 96		
Baseline Mean (SD)	72.53 (26.77)	62.37 (31.91)		
Week 52 Mean (SD)	82.62 (23.10)	77.85 (25.00)		
Week 100 Mean (SD)	84.58 (23.51)	78.83 (26.47)		
Week 28: Adjusted Mean Change (SE)	9.13 (2.36)	7.79 (2.17)		
Week 52: Adjusted Mean Change (SE)	11.14 (2.53)	10.37 (2.28)	0.77 [-5.93; 7.48]	0.821
Week 100: Adjusted Mean Change (SE)	11.09 (2.77)	11.70 (2.48)	-0.61 [-7.94; 6.72]	0.870

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 7.5 %				
N'/ N	97 / 97	85 / 85		
Baseline Mean (SD)	69.85 (27.76)	72.65 (25.18)		
Week 52 Mean (SD)	83.13 (21.15)	78.52 (25.72)		
Week 100 Mean (SD)	85.39 (22.46)	81.87 (24.07)		
Week 28: Adjusted Mean Change (SE)	5.89 (2.13)	8.51 (2.30)		
Week 52: Adjusted Mean Change (SE)	13.21 (2.26)	6.24 (2.42)	6.97 [0.46; 13.49]	0.036 *
Week 100: Adjusted Mean Change (SE)	12.44 (2.53)	7.69 (2.59)	4.75 [-2.37; 11.87]	0.190
Pooled Analysis: Role Difficulties				
Interaction test	p=0.759			
< 7.5 %				
N'/ N	157 / 158	203 / 203		
Baseline Mean (SD)	73.96 (27.70)	66.93 (29.81)		
Week 52 Mean (SD)	83.66 (23.01)	80.38 (23.30)		
Week 100 Mean (SD)	84.40 (23.03)	79.09 (25.76)		
Week 28: Adjusted Mean Change (SE)	7.82 (1.73)	8.71 (1.53)		
Week 52: Adjusted Mean Change (SE)	10.48 (1.86)	10.15 (1.61)	0.33 [-4.50; 5.16]	0.892
Week 100: Adjusted Mean Change (SE)	11.32 (1.99)	9.22 (1.69)	2.11 [-3.02; 7.23]	0.420
≥ 7.5 %				
N'/ N	208 / 209	165 / 165		
Baseline Mean (SD)	69.95 (27.94)	72.73 (25.46)		
Week 52 Mean (SD)	80.35 (24.20)	81.16 (25.23)		
Week 100 Mean (SD)	82.64 (25.11)	81.20 (24.64)		
Week 28: Adjusted Mean Change (SE)	5.72 (1.49)	8.29 (1.70)		
Week 52: Adjusted Mean Change (SE)	8.59 (1.62)	9.02 (1.80)	-0.43 [-5.19; 4.34]	0.861
Week 100: Adjusted Mean Change (SE)	10.03 (1.72)	8.01 (1.92)	2.03 [-3.03; 7.08]	0.432

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Dependency				
Test of heterogeneity in main analysis: **p_H=0.019 ***				
KESTREL: Dependency				
Interaction test	p=0.533			
< 7.5 %				
N'/ N	76 / 76	107 / 107		
Baseline Mean (SD)	82.46 (26.30)	82.32 (22.80)		
Week 52 Mean (SD)	90.74 (22.00)	90.68 (18.79)		
Week 100 Mean (SD)	88.74 (19.70)	89.63 (19.53)		
Week 28: Adjusted Mean Change (SE)	5.69 (2.17)	6.88 (1.84)		
Week 52: Adjusted Mean Change (SE)	7.00 (2.22)	7.75 (1.84)	-0.75 [-6.42; 4.92]	0.795
Week 100: Adjusted Mean Change (SE)	6.68 (2.53)	7.05 (2.04)	-0.37 [-6.75; 6.01]	0.909
≥ 7.5 %				
N'/ N	111 / 112	80 / 80		
Baseline Mean (SD)	81.01 (26.62)	83.33 (25.19)		
Week 52 Mean (SD)	87.69 (21.83)	93.97 (14.01)		
Week 100 Mean (SD)	84.69 (24.15)	86.46 (23.17)		
Week 28: Adjusted Mean Change (SE)	5.42 (1.79)	6.71 (2.14)		
Week 52: Adjusted Mean Change (SE)	4.37 (1.89)	10.16 (2.19)	-5.79 [-11.47; -0.10]	0.046 *
Week 100: Adjusted Mean Change (SE)	1.74 (2.07)	3.08 (2.54)	-1.33 [-7.79; 5.12]	0.685
KITE: Dependency				
Interaction test	p=0.123			
< 7.5 %				
N'/ N	81 / 82	96 / 96		
Baseline Mean (SD)	87.35 (20.46)	76.48 (30.87)		
Week 52 Mean (SD)	91.93 (18.12)	85.23 (24.49)		
Week 100 Mean (SD)	92.22 (13.88)	86.56 (22.63)		
Week 28: Adjusted Mean Change (SE)	5.33 (1.93)	4.23 (1.77)		
Week 52: Adjusted Mean Change (SE)	5.34 (2.10)	3.74 (1.90)	1.60 [-3.98; 7.18]	0.573
Week 100: Adjusted Mean Change (SE)	4.26 (2.27)	4.46 (2.03)	-0.20 [-6.22; 5.81]	0.947

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 7.5 %				
N'/ N	97 / 97	85 / 85		
Baseline Mean (SD)	80.15 (25.50)	88.04 (20.27)		
Week 52 Mean (SD)	90.42 (20.11)	88.38 (20.58)		
Week 100 Mean (SD)	93.78 (15.15)	88.26 (23.43)		
Week 28: Adjusted Mean Change (SE)	5.17 (1.75)	1.69 (1.89)		
Week 52: Adjusted Mean Change (SE)	8.77 (1.88)	2.19 (2.01)	6.58 [1.15; 12.01]	0.018 *
Week 100: Adjusted Mean Change (SE)	8.57 (2.07)	1.19 (2.12)	7.39 [1.54; 13.23]	0.013 *
Pooled Analysis: Dependency				
Interaction test	p=0.765			
< 7.5 %				
N'/ N	157 / 158	203 / 203		
Baseline Mean (SD)	84.98 (23.52)	79.56 (27.01)		
Week 52 Mean (SD)	91.34 (20.07)	88.18 (21.70)		
Week 100 Mean (SD)	90.53 (16.98)	88.23 (20.98)		
Week 28: Adjusted Mean Change (SE)	5.71 (1.46)	5.34 (1.29)		
Week 52: Adjusted Mean Change (SE)	6.39 (1.54)	5.61 (1.33)	0.79 [-3.21; 4.78]	0.700
Week 100: Adjusted Mean Change (SE)	5.72 (1.70)	5.57 (1.44)	0.15 [-4.23; 4.53]	0.948
≥ 7.5 %				
N'/ N	208 / 209	165 / 165		
Baseline Mean (SD)	80.61 (26.04)	85.76 (22.84)		
Week 52 Mean (SD)	89.01 (21.00)	91.05 (17.91)		
Week 100 Mean (SD)	88.80 (21.01)	87.47 (23.24)		
Week 28: Adjusted Mean Change (SE)	5.25 (1.26)	4.40 (1.43)		
Week 52: Adjusted Mean Change (SE)	6.37 (1.34)	6.28 (1.49)	0.08 [-3.86; 4.03]	0.967
Week 100: Adjusted Mean Change (SE)	4.94 (1.47)	2.51 (1.64)	2.42 [-1.90; 6.75]	0.271

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Driving				
Test of heterogeneity in main analysis: **p_H=0.792**				
KESTREL: Driving				
Interaction test	p=0.274			
< 7.5 %				
N'/ N	50 / 76	69 / 107		
Baseline Mean (SD)	79.83 (19.93)	75.97 (18.81)		
Week 52 Mean (SD)	88.01 (17.48)	83.95 (16.26)		
Week 100 Mean (SD)	82.66 (19.28)	79.00 (20.63)		
Week 28: Adjusted Mean Change (SE)	4.46 (2.11)	6.32 (1.89)		
Week 52: Adjusted Mean Change (SE)	7.34 (2.44)	6.52 (2.14)	0.82 [-5.58; 7.22]	0.801
Week 100: Adjusted Mean Change (SE)	4.97 (2.75)	1.55 (2.38)	3.41 [-3.76; 10.59]	0.350
≥ 7.5 %				
N'/ N	70 / 112	51 / 80		
Baseline Mean (SD)	80.00 (17.74)	78.76 (20.90)		
Week 52 Mean (SD)	81.61 (21.50)	84.87 (20.49)		
Week 100 Mean (SD)	83.17 (19.49)	81.51 (23.16)		
Week 28: Adjusted Mean Change (SE)	0.12 (1.82)	4.40 (2.18)		
Week 52: Adjusted Mean Change (SE)	0.72 (2.07)	4.99 (2.53)	-4.28 [-10.72; 2.17]	0.192
Week 100: Adjusted Mean Change (SE)	0.29 (2.34)	1.91 (2.93)	-1.62 [-9.01; 5.76]	0.665
KITE: Driving				
Interaction test	p=0.190			
< 7.5 %				
N'/ N	47 / 82	49 / 96		
Baseline Mean (SD)	80.23 (18.54)	79.51 (24.02)		
Week 52 Mean (SD)	89.74 (15.35)	86.95 (16.39)		
Week 100 Mean (SD)	86.54 (14.00)	84.76 (17.44)		
Week 28: Adjusted Mean Change (SE)	2.72 (2.13)	5.71 (2.16)		
Week 52: Adjusted Mean Change (SE)	8.36 (1.85)	3.89 (1.87)	4.47 [-0.73; 9.67]	0.092
Week 100: Adjusted Mean Change (SE)	4.92 (2.04)	1.78 (2.11)	3.14 [-2.64; 8.92]	0.286

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 7.5 %				
N'/ N	56 / 97	47 / 85		
Baseline Mean (SD)	77.98 (21.87)	84.75 (19.00)		
Week 52 Mean (SD)	84.44 (18.51)	88.71 (15.28)		
Week 100 Mean (SD)	86.00 (16.18)	89.17 (11.20)		
Week 28: Adjusted Mean Change (SE)	-0.94 (1.97)	5.02 (2.10)		
Week 52: Adjusted Mean Change (SE)	3.65 (1.73)	5.63 (1.86)	-1.98 [-7.00; 3.03]	0.436
Week 100: Adjusted Mean Change (SE)	3.75 (1.99)	3.72 (2.01)	0.02 [-5.57; 5.61]	0.993
Pooled Analysis: Driving				
Interaction test	p=0.121			
< 7.5 %				
N'/ N	97 / 158	118 / 203		
Baseline Mean (SD)	80.03 (19.17)	77.44 (21.11)		
Week 52 Mean (SD)	88.85 (16.40)	85.19 (16.29)		
Week 100 Mean (SD)	84.65 (16.78)	81.35 (19.50)		
Week 28: Adjusted Mean Change (SE)	3.55 (1.50)	6.20 (1.42)		
Week 52: Adjusted Mean Change (SE)	7.97 (1.54)	5.57 (1.44)	2.40 [-1.75; 6.56]	0.256
Week 100: Adjusted Mean Change (SE)	4.93 (1.74)	1.76 (1.63)	3.17 [-1.50; 7.84]	0.183
≥ 7.5 %				
N'/ N	126 / 209	98 / 165		
Baseline Mean (SD)	79.10 (19.63)	81.63 (20.14)		
Week 52 Mean (SD)	82.85 (20.21)	86.79 (18.06)		
Week 100 Mean (SD)	84.39 (18.10)	85.76 (17.83)		
Week 28: Adjusted Mean Change (SE)	-0.31 (1.34)	4.49 (1.52)		
Week 52: Adjusted Mean Change (SE)	2.10 (1.37)	5.20 (1.58)	-3.10 [-7.21; 1.00]	0.138
Week 100: Adjusted Mean Change (SE)	1.85 (1.57)	2.74 (1.78)	-0.90 [-5.56; 3.76]	0.705

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Color Vision				
Test of heterogeneity in main analysis: **p_H=0.477**				
KESTREL: Color Vision				
Interaction test	p=0.334			
< 7.5 %				
N'/ N	76 / 76	106 / 107		
Baseline Mean (SD)	92.76 (15.71)	92.69 (16.54)		
Week 52 Mean (SD)	96.83 (11.44)	96.74 (9.96)		
Week 100 Mean (SD)	95.18 (11.99)	96.02 (10.64)		
Week 28: Adjusted Mean Change (SE)	2.45 (1.31)	2.53 (1.12)		
Week 52: Adjusted Mean Change (SE)	2.56 (1.32)	3.01 (1.10)	-0.44 [-3.83; 2.95]	0.798
Week 100: Adjusted Mean Change (SE)	1.69 (1.59)	2.37 (1.29)	-0.67 [-4.71; 3.36]	0.743
≥ 7.5 %				
N'/ N	110 / 112	78 / 80		
Baseline Mean (SD)	93.18 (17.24)	95.83 (12.36)		
Week 52 Mean (SD)	96.47 (11.01)	94.67 (14.52)		
Week 100 Mean (SD)	94.35 (13.64)	93.52 (14.72)		
Week 28: Adjusted Mean Change (SE)	1.80 (1.09)	0.74 (1.31)		
Week 52: Adjusted Mean Change (SE)	1.90 (1.13)	0.04 (1.35)	1.86 [-1.60; 5.32]	0.292
Week 100: Adjusted Mean Change (SE)	-0.02 (1.32)	-1.52 (1.63)	1.50 [-2.64; 5.63]	0.477
KITE: Color Vision				
Interaction test	p=0.478			
< 7.5 %				
N'/ N	81 / 82	96 / 96		
Baseline Mean (SD)	91.67 (18.54)	90.89 (17.06)		
Week 52 Mean (SD)	96.48 (10.79)	93.99 (13.41)		
Week 100 Mean (SD)	96.61 (9.80)	95.27 (13.52)		
Week 28: Adjusted Mean Change (SE)	3.51 (1.23)	4.16 (1.13)		
Week 52: Adjusted Mean Change (SE)	4.96 (1.12)	3.01 (1.01)	1.95 [-1.01; 4.91]	0.197
Week 100: Adjusted Mean Change (SE)	4.36 (1.35)	4.06 (1.20)	0.31 [-3.25; 3.86]	0.865

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 7.5 %				
N'/ N	97 / 97	83 / 85		
Baseline Mean (SD)	92.53 (15.38)	92.77 (14.88)		
Week 52 Mean (SD)	98.42 (6.13)	95.96 (11.11)		
Week 100 Mean (SD)	97.89 (8.18)	94.85 (13.35)		
Week 28: Adjusted Mean Change (SE)	3.38 (1.13)	3.90 (1.22)		
Week 52: Adjusted Mean Change (SE)	6.13 (1.01)	3.55 (1.09)	2.58 [-0.34; 5.49]	0.083
Week 100: Adjusted Mean Change (SE)	5.43 (1.23)	2.44 (1.26)	2.99 [-0.47; 6.45]	0.090
Pooled Analysis: Color Vision				
Interaction test	p=0.245			
< 7.5 %				
N'/ N	157 / 158	202 / 203		
Baseline Mean (SD)	92.20 (17.18)	91.83 (16.77)		
Week 52 Mean (SD)	96.65 (11.07)	95.47 (11.72)		
Week 100 Mean (SD)	95.91 (10.91)	95.68 (12.01)		
Week 28: Adjusted Mean Change (SE)	3.00 (0.91)	3.38 (0.80)		
Week 52: Adjusted Mean Change (SE)	3.80 (0.86)	3.08 (0.75)	0.72 [-1.52; 2.96]	0.528
Week 100: Adjusted Mean Change (SE)	3.14 (1.05)	3.12 (0.89)	0.03 [-2.67; 2.72]	0.985
≥ 7.5 %				
N'/ N	207 / 209	161 / 165		
Baseline Mean (SD)	92.87 (16.36)	94.25 (13.76)		
Week 52 Mean (SD)	97.41 (9.02)	95.35 (12.80)		
Week 100 Mean (SD)	95.97 (11.57)	94.26 (13.93)		
Week 28: Adjusted Mean Change (SE)	2.63 (0.79)	2.23 (0.90)		
Week 52: Adjusted Mean Change (SE)	3.93 (0.76)	1.73 (0.86)	2.20 [-0.05; 4.45]	0.055
Week 100: Adjusted Mean Change (SE)	2.60 (0.91)	0.38 (1.02)	2.22 [-0.47; 4.91]	0.105

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.003 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.004 *			
< 7.5 %				
N'/ N	76 / 76	106 / 107		
Baseline Mean (SD)	84.54 (21.20)	79.25 (23.52)		
Week 52 Mean (SD)	92.46 (14.64)	85.48 (19.62)		
Week 100 Mean (SD)	85.96 (20.05)	85.56 (23.10)		
Week 28: Adjusted Mean Change (SE)	3.68 (2.10)	5.93 (1.79)		
Week 52: Adjusted Mean Change (SE)	9.08 (2.10)	4.06 (1.73)	5.02 [-0.33; 10.38]	0.066
Week 100: Adjusted Mean Change (SE)	3.35 (2.59)	4.48 (2.08)	-1.13 [-7.66; 5.40]	0.734
≥ 7.5 %				
N'/ N	111 / 112	80 / 80		
Baseline Mean (SD)	83.56 (22.23)	81.25 (23.02)		
Week 52 Mean (SD)	86.92 (22.27)	92.97 (13.71)		
Week 100 Mean (SD)	83.14 (23.47)	90.63 (16.21)		
Week 28: Adjusted Mean Change (SE)	1.88 (1.75)	9.95 (2.08)		
Week 52: Adjusted Mean Change (SE)	2.99 (1.79)	11.42 (2.08)	-8.42 [-13.83; -3.02]	0.002 *
Week 100: Adjusted Mean Change (SE)	-0.59 (2.12)	7.69 (2.60)	-8.27 [-14.88; -1.67]	0.014 *
KITE: Peripheral Vision				
Interaction test	p=0.307			
< 7.5 %				
N'/ N	81 / 82	96 / 96		
Baseline Mean (SD)	81.17 (19.58)	85.68 (20.11)		
Week 52 Mean (SD)	90.63 (15.75)	86.71 (20.35)		
Week 100 Mean (SD)	89.58 (17.40)	86.33 (20.26)		
Week 28: Adjusted Mean Change (SE)	6.31 (1.79)	3.87 (1.63)		
Week 52: Adjusted Mean Change (SE)	7.83 (1.92)	2.59 (1.73)	5.24 [0.15; 10.34]	0.044 *
Week 100: Adjusted Mean Change (SE)	5.69 (1.91)	1.73 (1.71)	3.96 [-1.08; 9.01]	0.123

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 7.5 %				
N'/ N	97 / 97	84 / 85		
Baseline Mean (SD)	84.79 (20.59)	83.63 (22.79)		
Week 52 Mean (SD)	89.06 (18.16)	88.93 (18.37)		
Week 100 Mean (SD)	94.72 (12.62)	89.29 (16.80)		
Week 28: Adjusted Mean Change (SE)	3.12 (1.62)	5.17 (1.75)		
Week 52: Adjusted Mean Change (SE)	5.10 (1.72)	4.51 (1.85)	0.59 [-4.37; 5.55]	0.815
Week 100: Adjusted Mean Change (SE)	9.21 (1.75)	4.20 (1.79)	5.01 [0.10; 9.92]	0.046 *
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.005 *			
< 7.5 %				
N'/ N	157 / 158	202 / 203		
Baseline Mean (SD)	82.80 (20.38)	82.30 (22.15)		
Week 52 Mean (SD)	91.54 (15.18)	86.05 (19.91)		
Week 100 Mean (SD)	87.82 (18.75)	85.91 (21.79)		
Week 28: Adjusted Mean Change (SE)	4.85 (1.38)	5.06 (1.22)		
Week 52: Adjusted Mean Change (SE)	8.32 (1.43)	3.47 (1.23)	4.85 [1.14; 8.56]	0.011 *
Week 100: Adjusted Mean Change (SE)	4.46 (1.61)	3.29 (1.37)	1.17 [-2.98; 5.32]	0.581
≥ 7.5 %				
N'/ N	208 / 209	164 / 165		
Baseline Mean (SD)	84.13 (21.44)	82.47 (22.87)		
Week 52 Mean (SD)	87.95 (20.36)	90.86 (16.38)		
Week 100 Mean (SD)	88.38 (20.12)	89.88 (16.49)		
Week 28: Adjusted Mean Change (SE)	2.49 (1.20)	7.56 (1.36)		
Week 52: Adjusted Mean Change (SE)	3.96 (1.25)	7.97 (1.40)	-4.00 [-7.68; -0.32]	0.033 *
Week 100: Adjusted Mean Change (SE)	3.83 (1.40)	5.89 (1.56)	-2.06 [-6.17; 2.05]	0.325

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
General Health				
Test of heterogeneity in main analysis: **p_H=0.834**				
KESTREL: General Health				
Interaction test	p=0.412			
< 7.5 %				
N'/ N	76 / 76	107 / 107		
Baseline Mean (SD)	49.67 (22.17)	39.72 (19.71)		
Week 52 Mean (SD)	56.75 (24.68)	45.70 (21.37)		
Week 100 Mean (SD)	53.51 (20.29)	48.89 (20.15)		
Week 28: Adjusted Mean Change (SE)	3.85 (2.19)	4.62 (1.84)		
Week 52: Adjusted Mean Change (SE)	10.51 (2.61)	4.62 (2.14)	5.89 [-0.77; 12.56]	0.083
Week 100: Adjusted Mean Change (SE)	10.48 (2.65)	8.18 (2.12)	2.30 [-4.38; 8.98]	0.499
≥ 7.5 %				
N'/ N	111 / 112	80 / 80		
Baseline Mean (SD)	40.54 (19.67)	36.88 (20.66)		
Week 52 Mean (SD)	48.26 (23.26)	45.77 (21.91)		
Week 100 Mean (SD)	47.09 (24.68)	47.32 (23.20)		
Week 28: Adjusted Mean Change (SE)	4.71 (1.79)	5.04 (2.14)		
Week 52: Adjusted Mean Change (SE)	6.64 (2.21)	6.28 (2.56)	0.36 [-6.28; 7.01]	0.915
Week 100: Adjusted Mean Change (SE)	5.54 (2.15)	6.45 (2.65)	-0.91 [-7.63; 5.81]	0.790
KITE: General Health				
Interaction test	p=0.912			
< 7.5 %				
N'/ N	81 / 82	96 / 96		
Baseline Mean (SD)	43.21 (20.54)	43.49 (23.01)		
Week 52 Mean (SD)	50.00 (20.41)	50.00 (23.68)		
Week 100 Mean (SD)	50.00 (18.98)	50.00 (22.51)		
Week 28: Adjusted Mean Change (SE)	3.31 (2.07)	4.32 (1.90)		
Week 52: Adjusted Mean Change (SE)	6.12 (2.48)	5.01 (2.23)	1.12 [-5.45; 7.68]	0.738
Week 100: Adjusted Mean Change (SE)	4.93 (2.28)	5.42 (2.04)	-0.49 [-6.51; 5.53]	0.872

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 7.5 %				
N'/ N	97 / 97	85 / 85		
Baseline Mean (SD)	44.59 (20.16)	45.88 (22.77)		
Week 52 Mean (SD)	49.06 (23.00)	50.35 (23.33)		
Week 100 Mean (SD)	51.41 (20.65)	52.46 (22.42)		
Week 28: Adjusted Mean Change (SE)	3.66 (1.88)	4.38 (2.02)		
Week 52: Adjusted Mean Change (SE)	5.09 (2.22)	5.11 (2.36)	-0.02 [-6.40; 6.36]	0.995
Week 100: Adjusted Mean Change (SE)	7.20 (2.09)	5.79 (2.12)	1.41 [-4.44; 7.27]	0.636
Pooled Analysis: General Health				
Interaction test	p=0.636			
< 7.5 %				
N'/ N	157 / 158	203 / 203		
Baseline Mean (SD)	46.34 (21.52)	41.50 (21.37)		
Week 52 Mean (SD)	53.35 (22.79)	47.67 (22.50)		
Week 100 Mean (SD)	51.71 (19.62)	49.39 (21.20)		
Week 28: Adjusted Mean Change (SE)	3.39 (1.50)	4.51 (1.32)		
Week 52: Adjusted Mean Change (SE)	8.06 (1.79)	4.81 (1.54)	3.25 [-1.40; 7.89]	0.170
Week 100: Adjusted Mean Change (SE)	7.51 (1.74)	6.97 (1.47)	0.54 [-3.94; 5.02]	0.812
≥ 7.5 %				
N'/ N	208 / 209	165 / 165		
Baseline Mean (SD)	42.43 (19.96)	41.52 (22.17)		
Week 52 Mean (SD)	48.64 (23.07)	48.16 (22.70)		
Week 100 Mean (SD)	49.04 (22.98)	50.20 (22.82)		
Week 28: Adjusted Mean Change (SE)	4.17 (1.30)	4.82 (1.47)		
Week 52: Adjusted Mean Change (SE)	5.86 (1.56)	5.78 (1.73)	0.09 [-4.50; 4.67]	0.970
Week 100: Adjusted Mean Change (SE)	6.20 (1.50)	6.28 (1.68)	-0.08 [-4.50; 4.34]	0.971

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + HbA1c + treatment * HbA1c + visit * HbA1c + treatment * HbA1c * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + study + treatment * study + HbA1c + treatment * HbA1c + visit * HbA1c + treatment * HbA1c * visit.

Table 8.8 VFQ by duration of DME (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Composite Score				
Test of heterogeneity in main analysis: **p_H=0.049 ***				
KESTREL: Composite Score				
Interaction test	p=0.674			
≤ 3 months				
N'/ N	120 / 120	110 / 110		
Baseline Mean (SD)	77.59 (17.64)	77.65 (15.11)		
Week 52 Mean (SD)	85.92 (14.14)	86.88 (12.38)		
Week 100 Mean (SD)	83.93 (15.60)	84.81 (14.26)		
Week 28: Adjusted Mean Change (SE)	6.30 (0.98)	8.96 (1.04)		
Week 52: Adjusted Mean Change (SE)	7.25 (1.03)	9.27 (1.07)	-2.02 [-4.93; 0.90]	0.175
Week 100: Adjusted Mean Change (SE)	6.34 (1.16)	7.34 (1.21)	-1.00 [-4.30; 2.29]	0.550
> 3 - < 12 months				
N'/ N	30 / 30	39 / 39		
Baseline Mean (SD)	77.40 (13.15)	75.14 (13.31)		
Week 52 Mean (SD)	85.85 (11.03)	83.60 (13.07)		
Week 100 Mean (SD)	84.00 (10.87)	82.70 (14.88)		
Week 28: Adjusted Mean Change (SE)	3.87 (2.03)	7.59 (1.74)		
Week 52: Adjusted Mean Change (SE)	8.03 (2.19)	7.63 (1.85)	0.40 [-5.24; 6.05]	0.888
Week 100: Adjusted Mean Change (SE)	7.78 (2.39)	6.76 (2.13)	1.02 [-5.28; 7.33]	0.749
≥ 12 months				
N'/ N	38 / 39	38 / 38		
Baseline Mean (SD)	73.03 (19.70)	76.09 (14.47)		
Week 52 Mean (SD)	81.06 (14.76)	81.71 (10.47)		
Week 100 Mean (SD)	79.35 (15.38)	79.98 (14.19)		
Week 28: Adjusted Mean Change (SE)	5.37 (1.78)	4.29 (1.78)		
Week 52: Adjusted Mean Change (SE)	5.49 (1.95)	5.67 (1.81)	-0.18 [-5.40; 5.04]	0.947
Week 100: Adjusted Mean Change (SE)	4.16 (2.14)	4.14 (1.99)	0.02 [-5.71; 5.75]	0.994

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Composite Score				
Interaction test	p=0.390			
≤ 3 months				
N'/ N	84 / 85	92 / 92		
Baseline Mean (SD)	79.25 (14.46)	79.36 (17.03)		
Week 52 Mean (SD)	88.63 (10.33)	85.20 (15.34)		
Week 100 Mean (SD)	90.21 (9.83)	85.35 (15.03)		
Week 28: Adjusted Mean Change (SE)	6.06 (1.12)	5.30 (1.07)		
Week 52: Adjusted Mean Change (SE)	10.03 (1.21)	6.09 (1.15)	3.93 [0.65; 7.22]	0.019 *
Week 100: Adjusted Mean Change (SE)	9.97 (1.45)	5.74 (1.31)	4.23 [0.38; 8.07]	0.031 *
> 3 - < 12 months				
N'/ N	51 / 51	49 / 49		
Baseline Mean (SD)	75.12 (15.84)	70.23 (18.41)		
Week 52 Mean (SD)	82.07 (16.37)	78.33 (17.81)		
Week 100 Mean (SD)	84.90 (14.31)	80.52 (16.54)		
Week 28: Adjusted Mean Change (SE)	5.69 (1.42)	6.19 (1.49)		
Week 52: Adjusted Mean Change (SE)	7.20 (1.52)	5.03 (1.56)	2.17 [-2.10; 6.43]	0.318
Week 100: Adjusted Mean Change (SE)	8.68 (1.73)	7.22 (1.82)	1.45 [-3.48; 6.38]	0.563
≥ 12 months				
N'/ N	43 / 43	40 / 40		
Baseline Mean (SD)	78.23 (14.88)	77.44 (16.66)		
Week 52 Mean (SD)	87.82 (11.34)	86.39 (11.94)		
Week 100 Mean (SD)	88.49 (12.23)	85.17 (14.36)		
Week 28: Adjusted Mean Change (SE)	4.94 (1.57)	6.87 (1.64)		
Week 52: Adjusted Mean Change (SE)	8.36 (1.70)	8.52 (1.72)	-0.16 [-4.91; 4.60]	0.949
Week 100: Adjusted Mean Change (SE)	7.39 (1.97)	6.15 (1.93)	1.24 [-4.17; 6.65]	0.652
Pooled Analysis: Composite Score				
Interaction test	p=0.970			
≤ 3 months				
N'/ N	204 / 205	202 / 202		
Baseline Mean (SD)	78.27 (16.39)	78.43 (15.99)		
Week 52 Mean (SD)	87.00 (12.80)	86.14 (13.74)		
Week 100 Mean (SD)	86.30 (14.01)	85.06 (14.57)		
Week 28: Adjusted Mean Change (SE)	6.39 (0.75)	7.24 (0.76)		
Week 52: Adjusted Mean Change (SE)	8.53 (0.79)	7.83 (0.79)	0.70 [-1.48; 2.89]	0.527
Week 100: Adjusted Mean Change (SE)	7.92 (0.90)	6.56 (0.89)	1.35 [-1.13; 3.84]	0.284

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 3 - < 12 months				
N'/ N	81 / 81	88 / 88		
Baseline Mean (SD)	75.97 (14.86)	72.41 (16.44)		
Week 52 Mean (SD)	83.31 (14.85)	80.56 (16.09)		
Week 100 Mean (SD)	84.59 (13.15)	81.43 (15.79)		
Week 28: Adjusted Mean Change (SE)	4.72 (1.20)	6.64 (1.15)		
Week 52: Adjusted Mean Change (SE)	7.02 (1.27)	5.99 (1.20)	1.03 [-2.40; 4.47]	0.556
Week 100: Adjusted Mean Change (SE)	8.03 (1.41)	6.87 (1.38)	1.16 [-2.71; 5.02]	0.557
≥ 12 months				
N'/ N	81 / 82	78 / 78		
Baseline Mean (SD)	75.79 (17.39)	76.78 (15.54)		
Week 52 Mean (SD)	84.83 (13.29)	84.09 (11.40)		
Week 100 Mean (SD)	84.22 (14.42)	82.65 (14.41)		
Week 28: Adjusted Mean Change (SE)	5.18 (1.20)	5.75 (1.23)		
Week 52: Adjusted Mean Change (SE)	7.17 (1.29)	7.26 (1.26)	-0.09 [-3.63; 3.45]	0.960
Week 100: Adjusted Mean Change (SE)	6.04 (1.44)	5.32 (1.38)	0.72 [-3.18; 4.63]	0.716
General Vision				
Test of heterogeneity in main analysis: **p_H=0.762**				
KESTREL: General Vision				
Interaction test	p=0.823			
≤ 3 months				
N'/ N	120 / 120	110 / 110		
Baseline Mean (SD)	61.17 (18.02)	60.91 (15.18)		
Week 52 Mean (SD)	73.86 (14.07)	72.98 (11.25)		
Week 100 Mean (SD)	74.89 (14.94)	73.95 (11.09)		
Week 28: Adjusted Mean Change (SE)	12.65 (1.19)	12.98 (1.26)		
Week 52: Adjusted Mean Change (SE)	12.52 (1.25)	12.07 (1.29)	0.45 [-3.08; 3.99]	0.801
Week 100: Adjusted Mean Change (SE)	14.36 (1.26)	13.11 (1.32)	1.25 [-2.34; 4.83]	0.495
> 3 - < 12 months				
N'/ N	30 / 30	39 / 39		
Baseline Mean (SD)	62.67 (14.61)	56.41 (14.42)		
Week 52 Mean (SD)	73.33 (13.17)	69.68 (17.03)		
Week 100 Mean (SD)	73.64 (12.93)	71.85 (13.88)		
Week 28: Adjusted Mean Change (SE)	8.47 (2.46)	8.40 (2.11)		
Week 52: Adjusted Mean Change (SE)	11.78 (2.70)	10.68 (2.25)	1.10 [-5.83; 8.03]	0.755
Week 100: Adjusted Mean Change (SE)	12.63 (2.61)	12.35 (2.35)	0.28 [-6.62; 7.19]	0.936

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 12 months				
N'/ N	38 / 39	38 / 38		
Baseline Mean (SD)	60.53 (17.08)	62.11 (12.98)		
Week 52 Mean (SD)	69.63 (15.06)	67.27 (12.06)		
Week 100 Mean (SD)	69.29 (15.85)	68.48 (12.28)		
Week 28: Adjusted Mean Change (SE)	9.37 (2.14)	6.67 (2.16)		
Week 52: Adjusted Mean Change (SE)	9.18 (2.39)	6.55 (2.19)	2.64 [-3.73; 9.00]	0.416
Week 100: Adjusted Mean Change (SE)	8.81 (2.32)	7.88 (2.15)	0.94 [-5.27; 7.14]	0.767
KITE: General Vision				
Interaction test	p=0.726			
≤ 3 months				
N'/ N	84 / 85	92 / 92		
Baseline Mean (SD)	63.10 (16.28)	61.30 (18.94)		
Week 52 Mean (SD)	72.54 (15.11)	70.54 (18.79)		
Week 100 Mean (SD)	75.44 (14.65)	70.41 (18.29)		
Week 28: Adjusted Mean Change (SE)	9.49 (1.51)	9.48 (1.44)		
Week 52: Adjusted Mean Change (SE)	10.96 (1.68)	8.93 (1.60)	2.02 [-2.53; 6.58]	0.383
Week 100: Adjusted Mean Change (SE)	12.90 (1.79)	8.36 (1.60)	4.54 [-0.19; 9.27]	0.060
> 3 - < 12 months				
N'/ N	51 / 51	49 / 49		
Baseline Mean (SD)	59.22 (17.87)	55.51 (18.83)		
Week 52 Mean (SD)	70.23 (14.72)	68.10 (17.70)		
Week 100 Mean (SD)	72.38 (13.94)	69.47 (15.24)		
Week 28: Adjusted Mean Change (SE)	10.31 (1.90)	9.18 (2.00)		
Week 52: Adjusted Mean Change (SE)	10.93 (2.10)	10.62 (2.15)	0.31 [-5.58; 6.21]	0.916
Week 100: Adjusted Mean Change (SE)	12.93 (2.11)	11.29 (2.22)	1.64 [-4.39; 7.66]	0.593
≥ 12 months				
N'/ N	43 / 43	40 / 40		
Baseline Mean (SD)	62.33 (13.24)	62.00 (15.56)		
Week 52 Mean (SD)	76.47 (12.52)	73.53 (11.78)		
Week 100 Mean (SD)	72.50 (12.18)	72.00 (13.89)		
Week 28: Adjusted Mean Change (SE)	7.92 (2.11)	10.13 (2.20)		
Week 52: Adjusted Mean Change (SE)	14.19 (2.35)	12.65 (2.38)	1.54 [-5.04; 8.12]	0.645
Week 100: Adjusted Mean Change (SE)	10.06 (2.41)	10.06 (2.34)	0.00 [-6.60; 6.60]	1.000

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: General Vision				
Interaction test	p=0.951			
≤ 3 months				
N'/ N	204 / 205	202 / 202		
Baseline Mean (SD)	61.96 (17.31)	61.09 (16.95)		
Week 52 Mean (SD)	73.33 (14.46)	71.90 (15.04)		
Week 100 Mean (SD)	75.10 (14.78)	72.33 (14.89)		
Week 28: Adjusted Mean Change (SE)	11.33 (0.95)	11.33 (0.96)		
Week 52: Adjusted Mean Change (SE)	11.85 (1.02)	10.63 (1.02)	1.22 [-1.62; 4.06]	0.401
Week 100: Adjusted Mean Change (SE)	13.81 (1.05)	10.92 (1.03)	2.88 [0.00; 5.77]	0.050 *
> 3 - < 12 months				
N'/ N	81 / 81	88 / 88		
Baseline Mean (SD)	60.49 (16.73)	55.91 (16.93)		
Week 52 Mean (SD)	71.25 (14.20)	68.77 (17.32)		
Week 100 Mean (SD)	72.81 (13.51)	70.46 (14.62)		
Week 28: Adjusted Mean Change (SE)	9.60 (1.52)	8.81 (1.46)		
Week 52: Adjusted Mean Change (SE)	11.08 (1.66)	10.65 (1.56)	0.43 [-4.04; 4.90]	0.850
Week 100: Adjusted Mean Change (SE)	12.73 (1.63)	11.74 (1.60)	0.99 [-3.49; 5.48]	0.663
≥ 12 months				
N'/ N	81 / 82	78 / 78		
Baseline Mean (SD)	61.48 (15.09)	62.05 (14.27)		
Week 52 Mean (SD)	73.44 (14.01)	70.45 (12.24)		
Week 100 Mean (SD)	71.00 (13.99)	70.29 (13.15)		
Week 28: Adjusted Mean Change (SE)	8.71 (1.51)	8.53 (1.55)		
Week 52: Adjusted Mean Change (SE)	12.14 (1.68)	9.70 (1.63)	2.44 [-2.15; 7.04]	0.297
Week 100: Adjusted Mean Change (SE)	9.68 (1.67)	9.09 (1.58)	0.58 [-3.93; 5.09]	0.799

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Ocular Pain				
Test of heterogeneity in main analysis: **p_H=0.664**				
KESTREL: Ocular Pain				
Interaction test	p=0.047 *			
≤ 3 months				
N'/ N	120 / 120	110 / 110		
Baseline Mean (SD)	84.69 (19.88)	82.50 (20.75)		
Week 52 Mean (SD)	88.00 (16.10)	87.63 (16.55)		
Week 100 Mean (SD)	85.37 (18.48)	84.59 (19.62)		
Week 28: Adjusted Mean Change (SE)	1.73 (1.63)	6.35 (1.73)		
Week 52: Adjusted Mean Change (SE)	3.87 (1.49)	5.38 (1.55)	-1.51 [-5.74; 2.72]	0.483
Week 100: Adjusted Mean Change (SE)	1.86 (1.66)	2.76 (1.73)	-0.90 [-5.61; 3.80]	0.706
> 3 - < 12 months				
N'/ N	30 / 30	39 / 39		
Baseline Mean (SD)	85.83 (18.78)	84.29 (16.15)		
Week 52 Mean (SD)	92.86 (12.85)	85.08 (16.90)		
Week 100 Mean (SD)	92.05 (11.28)	85.65 (19.52)		
Week 28: Adjusted Mean Change (SE)	8.51 (3.38)	2.32 (2.89)		
Week 52: Adjusted Mean Change (SE)	8.53 (3.21)	2.17 (2.68)	6.35 [-1.88; 14.59]	0.130
Week 100: Adjusted Mean Change (SE)	9.10 (3.42)	1.17 (3.07)	7.93 [-1.11; 16.97]	0.085
≥ 12 months				
N'/ N	38 / 39	38 / 38		
Baseline Mean (SD)	77.30 (20.31)	78.95 (23.63)		
Week 52 Mean (SD)	87.50 (16.98)	85.61 (14.70)		
Week 100 Mean (SD)	83.48 (17.37)	81.06 (22.78)		
Week 28: Adjusted Mean Change (SE)	1.78 (2.94)	1.24 (2.97)		
Week 52: Adjusted Mean Change (SE)	6.13 (2.85)	4.05 (2.63)	2.08 [-5.51; 9.67]	0.590
Week 100: Adjusted Mean Change (SE)	2.16 (3.05)	0.12 (2.82)	2.04 [-6.10; 10.18]	0.622

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Ocular Pain				
Interaction test	p=0.963			
≤ 3 months				
N'/ N	84 / 85	92 / 92		
Baseline Mean (SD)	85.27 (17.80)	82.74 (21.76)		
Week 52 Mean (SD)	89.55 (16.22)	89.36 (16.38)		
Week 100 Mean (SD)	92.11 (12.19)	90.75 (14.74)		
Week 28: Adjusted Mean Change (SE)	5.11 (1.74)	4.23 (1.65)		
Week 52: Adjusted Mean Change (SE)	5.35 (1.80)	5.16 (1.71)	0.19 [-4.69; 5.07]	0.939
Week 100: Adjusted Mean Change (SE)	7.79 (1.90)	6.29 (1.70)	1.50 [-3.53; 6.52]	0.558
> 3 - < 12 months				
N'/ N	51 / 51	49 / 49		
Baseline Mean (SD)	84.80 (15.68)	81.89 (20.74)		
Week 52 Mean (SD)	85.76 (17.80)	82.74 (21.20)		
Week 100 Mean (SD)	87.80 (17.35)	88.49 (17.29)		
Week 28: Adjusted Mean Change (SE)	2.91 (2.18)	1.93 (2.27)		
Week 52: Adjusted Mean Change (SE)	1.72 (2.24)	-0.66 (2.28)	2.39 [-3.91; 8.68]	0.456
Week 100: Adjusted Mean Change (SE)	3.62 (2.24)	5.97 (2.35)	-2.35 [-8.73; 4.03]	0.470
≥ 12 months				
N'/ N	43 / 43	40 / 40		
Baseline Mean (SD)	81.69 (20.84)	82.50 (17.86)		
Week 52 Mean (SD)	91.18 (15.55)	88.60 (15.50)		
Week 100 Mean (SD)	90.63 (17.68)	86.79 (18.43)		
Week 28: Adjusted Mean Change (SE)	4.80 (2.41)	5.03 (2.51)		
Week 52: Adjusted Mean Change (SE)	7.39 (2.52)	6.14 (2.54)	1.25 [-5.78; 8.28]	0.727
Week 100: Adjusted Mean Change (SE)	5.93 (2.56)	3.08 (2.47)	2.85 [-4.14; 9.83]	0.423
Pooled Analysis: Ocular Pain				
Interaction test	p=0.298			
≤ 3 months				
N'/ N	204 / 205	202 / 202		
Baseline Mean (SD)	84.93 (19.01)	82.61 (21.16)		
Week 52 Mean (SD)	88.62 (16.12)	88.39 (16.45)		
Week 100 Mean (SD)	87.91 (16.67)	87.42 (17.76)		
Week 28: Adjusted Mean Change (SE)	3.25 (1.19)	5.38 (1.20)		
Week 52: Adjusted Mean Change (SE)	4.67 (1.15)	5.30 (1.15)	-0.63 [-3.83; 2.57]	0.700
Week 100: Adjusted Mean Change (SE)	4.33 (1.25)	4.37 (1.21)	-0.04 [-3.45; 3.37]	0.983

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 3 - < 12 months				
N'/ N	81 / 81	88 / 88		
Baseline Mean (SD)	85.19 (16.78)	82.95 (18.78)		
Week 52 Mean (SD)	88.09 (16.58)	83.73 (19.40)		
Week 100 Mean (SD)	89.26 (15.57)	87.31 (18.15)		
Week 28: Adjusted Mean Change (SE)	4.63 (1.90)	2.01 (1.82)		
Week 52: Adjusted Mean Change (SE)	3.81 (1.87)	0.43 (1.75)	3.38 [-1.65; 8.40]	0.187
Week 100: Adjusted Mean Change (SE)	5.33 (1.92)	3.90 (1.89)	1.43 [-3.86; 6.73]	0.595
≥ 12 months				
N'/ N	81 / 82	78 / 78		
Baseline Mean (SD)	79.63 (20.58)	80.77 (20.81)		
Week 52 Mean (SD)	89.55 (16.17)	87.13 (15.07)		
Week 100 Mean (SD)	87.29 (17.75)	84.01 (20.70)		
Week 28: Adjusted Mean Change (SE)	3.32 (1.90)	3.16 (1.95)		
Week 52: Adjusted Mean Change (SE)	6.64 (1.90)	5.13 (1.83)	1.51 [-3.67; 6.68]	0.568
Week 100: Adjusted Mean Change (SE)	4.09 (1.97)	1.62 (1.87)	2.47 [-2.86; 7.80]	0.363
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.450**				
KESTREL: Near Activities				
Interaction test	p=0.494			
≤ 3 months				
N'/ N	120 / 120	110 / 110		
Baseline Mean (SD)	63.89 (25.19)	67.58 (22.18)		
Week 52 Mean (SD)	80.40 (20.90)	81.52 (19.36)		
Week 100 Mean (SD)	81.78 (22.48)	78.54 (22.54)		
Week 28: Adjusted Mean Change (SE)	14.98 (1.66)	15.19 (1.77)		
Week 52: Adjusted Mean Change (SE)	14.17 (1.83)	15.17 (1.90)	-1.00 [-6.18; 4.19]	0.706
Week 100: Adjusted Mean Change (SE)	16.17 (1.81)	12.00 (1.89)	4.17 [-0.97; 9.31]	0.112
> 3 - < 12 months				
N'/ N	30 / 30	39 / 39		
Baseline Mean (SD)	64.72 (25.30)	59.40 (21.02)		
Week 52 Mean (SD)	80.95 (21.27)	73.92 (23.74)		
Week 100 Mean (SD)	76.70 (13.40)	76.39 (17.72)		
Week 28: Adjusted Mean Change (SE)	4.70 (3.44)	16.33 (2.95)		
Week 52: Adjusted Mean Change (SE)	14.02 (3.94)	11.96 (3.30)	2.06 [-8.05; 12.17]	0.689
Week 100: Adjusted Mean Change (SE)	11.55 (3.73)	14.35 (3.34)	-2.80 [-12.64; 7.04]	0.576

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 12 months				
N'/ N	38 / 39	38 / 38		
Baseline Mean (SD)	61.29 (30.12)	66.45 (20.91)		
Week 52 Mean (SD)	73.46 (22.77)	75.13 (17.57)		
Week 100 Mean (SD)	74.11 (18.61)	73.48 (19.92)		
Week 28: Adjusted Mean Change (SE)	9.19 (3.00)	9.60 (3.03)		
Week 52: Adjusted Mean Change (SE)	10.00 (3.50)	10.28 (3.22)	-0.28 [-9.61; 9.04]	0.952
Week 100: Adjusted Mean Change (SE)	11.01 (3.32)	8.40 (3.11)	2.61 [-6.32; 11.53]	0.566
KITE: Near Activities				
Interaction test	p=0.345			
≤ 3 months				
N'/ N	83 / 85	92 / 92		
Baseline Mean (SD)	70.73 (22.34)	73.37 (23.17)		
Week 52 Mean (SD)	82.96 (18.94)	80.41 (22.63)		
Week 100 Mean (SD)	87.06 (15.82)	80.59 (23.53)		
Week 28: Adjusted Mean Change (SE)	6.38 (2.03)	4.43 (1.92)		
Week 52: Adjusted Mean Change (SE)	12.49 (2.04)	8.26 (1.94)	4.23 [-1.30; 9.77]	0.134
Week 100: Adjusted Mean Change (SE)	14.22 (2.27)	8.05 (2.05)	6.17 [0.16; 12.17]	0.044 *
> 3 - < 12 months				
N'/ N	51 / 51	49 / 49		
Baseline Mean (SD)	64.87 (22.69)	63.52 (24.30)		
Week 52 Mean (SD)	71.90 (24.60)	74.11 (22.50)		
Week 100 Mean (SD)	78.97 (20.60)	72.15 (24.98)		
Week 28: Adjusted Mean Change (SE)	6.97 (2.55)	6.71 (2.66)		
Week 52: Adjusted Mean Change (SE)	6.64 (2.56)	7.97 (2.61)	-1.33 [-8.49; 5.83]	0.716
Week 100: Adjusted Mean Change (SE)	11.94 (2.70)	5.58 (2.83)	6.36 [-1.30; 14.02]	0.103
≥ 12 months				
N'/ N	43 / 43	40 / 40		
Baseline Mean (SD)	75.29 (21.25)	67.50 (23.86)		
Week 52 Mean (SD)	84.80 (15.28)	80.39 (20.09)		
Week 100 Mean (SD)	84.64 (19.95)	79.05 (19.11)		
Week 28: Adjusted Mean Change (SE)	5.30 (2.83)	8.37 (2.94)		
Week 52: Adjusted Mean Change (SE)	10.33 (2.87)	12.07 (2.90)	-1.74 [-9.77; 6.29]	0.670
Week 100: Adjusted Mean Change (SE)	8.19 (3.07)	8.97 (2.99)	-0.78 [-9.21; 7.66]	0.856

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Near Activities				
Interaction test	p=0.349			
≤ 3 months				
N'/ N	203 / 205	202 / 202		
Baseline Mean (SD)	66.69 (24.24)	70.21 (22.76)		
Week 52 Mean (SD)	81.42 (20.12)	81.03 (20.80)		
Week 100 Mean (SD)	83.77 (20.33)	79.48 (22.95)		
Week 28: Adjusted Mean Change (SE)	11.38 (1.32)	9.98 (1.32)		
Week 52: Adjusted Mean Change (SE)	13.28 (1.38)	11.83 (1.37)	1.45 [-2.36; 5.27]	0.455
Week 100: Adjusted Mean Change (SE)	15.15 (1.42)	9.99 (1.39)	5.16 [1.27; 9.05]	0.009 *
> 3 - < 12 months				
N'/ N	81 / 81	88 / 88		
Baseline Mean (SD)	64.81 (23.53)	61.70 (22.87)		
Week 52 Mean (SD)	74.87 (23.78)	74.03 (22.87)		
Week 100 Mean (SD)	78.19 (18.36)	73.91 (22.20)		
Week 28: Adjusted Mean Change (SE)	6.46 (2.09)	11.19 (2.01)		
Week 52: Adjusted Mean Change (SE)	9.03 (2.22)	10.06 (2.09)	-1.03 [-7.02; 4.95]	0.735
Week 100: Adjusted Mean Change (SE)	11.93 (2.20)	9.65 (2.16)	2.28 [-3.76; 8.32]	0.459
≥ 12 months				
N'/ N	81 / 82	78 / 78		
Baseline Mean (SD)	68.72 (26.57)	66.99 (22.33)		
Week 52 Mean (SD)	79.78 (19.63)	77.80 (18.93)		
Week 100 Mean (SD)	79.72 (19.89)	76.35 (19.56)		
Week 28: Adjusted Mean Change (SE)	7.63 (2.09)	9.04 (2.14)		
Week 52: Adjusted Mean Change (SE)	10.86 (2.26)	11.22 (2.19)	-0.36 [-6.53; 5.81]	0.909
Week 100: Adjusted Mean Change (SE)	10.14 (2.25)	8.75 (2.15)	1.40 [-4.71; 7.50]	0.654

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Distance Activities				
Test of heterogeneity in main analysis: **p_H=0.046 ***				
KESTREL: Distance Activities				
Interaction test	p=0.981			
≤ 3 months				
N'/ N	120 / 120	110 / 110		
Baseline Mean (SD)	75.56 (24.56)	77.05 (21.16)		
Week 52 Mean (SD)	87.00 (16.40)	87.46 (15.85)		
Week 100 Mean (SD)	84.13 (19.21)	85.27 (18.86)		
Week 28: Adjusted Mean Change (SE)	8.18 (1.48)	11.09 (1.57)		
Week 52: Adjusted Mean Change (SE)	9.77 (1.40)	10.62 (1.45)	-0.84 [-4.81; 3.12]	0.675
Week 100: Adjusted Mean Change (SE)	8.33 (1.55)	8.59 (1.62)	-0.26 [-4.67; 4.15]	0.909
> 3 - < 12 months				
N'/ N	30 / 30	39 / 39		
Baseline Mean (SD)	77.36 (19.26)	74.15 (23.06)		
Week 52 Mean (SD)	83.93 (16.99)	80.38 (20.10)		
Week 100 Mean (SD)	80.68 (18.44)	83.49 (20.69)		
Week 28: Adjusted Mean Change (SE)	5.05 (3.05)	7.14 (2.62)		
Week 52: Adjusted Mean Change (SE)	6.96 (3.00)	5.78 (2.51)	1.18 [-6.51; 8.87]	0.764
Week 100: Adjusted Mean Change (SE)	4.67 (3.20)	8.15 (2.87)	-3.48 [-11.93; 4.97]	0.419
≥ 12 months				
N'/ N	38 / 39	38 / 38		
Baseline Mean (SD)	72.70 (25.11)	71.71 (18.91)		
Week 52 Mean (SD)	80.56 (19.85)	82.70 (16.61)		
Week 100 Mean (SD)	74.85 (22.32)	77.53 (15.55)		
Week 28: Adjusted Mean Change (SE)	6.46 (2.66)	4.44 (2.68)		
Week 52: Adjusted Mean Change (SE)	7.73 (2.66)	9.59 (2.47)	-1.86 [-8.97; 5.24]	0.606
Week 100: Adjusted Mean Change (SE)	2.10 (2.85)	4.39 (2.66)	-2.30 [-9.95; 5.35]	0.555

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Distance Activities				
Interaction test	p=0.297			
≤ 3 months				
N'/ N	84 / 85	92 / 92		
Baseline Mean (SD)	79.86 (19.08)	80.25 (20.20)		
Week 52 Mean (SD)	90.24 (15.09)	86.37 (17.51)		
Week 100 Mean (SD)	92.98 (11.89)	86.19 (16.05)		
Week 28: Adjusted Mean Change (SE)	6.98 (1.76)	5.45 (1.68)		
Week 52: Adjusted Mean Change (SE)	12.32 (1.66)	7.67 (1.59)	4.65 [0.13; 9.17]	0.044 *
Week 100: Adjusted Mean Change (SE)	13.67 (1.86)	7.18 (1.68)	6.49 [1.56; 11.42]	0.010 *
> 3 - < 12 months				
N'/ N	51 / 51	49 / 49		
Baseline Mean (SD)	73.28 (23.62)	69.22 (23.98)		
Week 52 Mean (SD)	84.79 (21.72)	79.46 (21.61)		
Week 100 Mean (SD)	85.81 (18.52)	78.73 (22.00)		
Week 28: Adjusted Mean Change (SE)	6.16 (2.22)	3.81 (2.33)		
Week 52: Adjusted Mean Change (SE)	11.15 (2.09)	6.79 (2.13)	4.36 [-1.48; 10.21]	0.143
Week 100: Adjusted Mean Change (SE)	10.87 (2.21)	6.20 (2.33)	4.67 [-1.63; 10.98]	0.146
≥ 12 months				
N'/ N	43 / 43	40 / 40		
Baseline Mean (SD)	75.39 (22.87)	75.42 (23.72)		
Week 52 Mean (SD)	87.38 (15.67)	86.15 (16.75)		
Week 100 Mean (SD)	86.85 (17.46)	84.40 (19.89)		
Week 28: Adjusted Mean Change (SE)	4.35 (2.46)	6.68 (2.56)		
Week 52: Adjusted Mean Change (SE)	9.35 (2.34)	10.16 (2.36)	-0.80 [-7.34; 5.73]	0.809
Week 100: Adjusted Mean Change (SE)	7.46 (2.52)	6.78 (2.46)	0.68 [-6.24; 7.60]	0.847
Pooled Analysis: Distance Activities				
Interaction test	p=0.592			
≤ 3 months				
N'/ N	204 / 205	202 / 202		
Baseline Mean (SD)	77.33 (22.52)	78.51 (20.74)		
Week 52 Mean (SD)	88.29 (15.92)	86.98 (16.56)		
Week 100 Mean (SD)	87.47 (17.32)	85.69 (17.57)		
Week 28: Adjusted Mean Change (SE)	7.99 (1.14)	8.45 (1.15)		
Week 52: Adjusted Mean Change (SE)	11.10 (1.07)	9.25 (1.07)	1.86 [-1.12; 4.83]	0.221
Week 100: Adjusted Mean Change (SE)	10.64 (1.19)	7.88 (1.16)	2.76 [-0.50; 6.02]	0.097

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 3 - < 12 months				
N'/ N	81 / 81	88 / 88		
Baseline Mean (SD)	74.79 (22.07)	71.40 (23.57)		
Week 52 Mean (SD)	84.51 (20.16)	79.85 (20.85)		
Week 100 Mean (SD)	84.05 (18.51)	80.71 (21.43)		
Week 28: Adjusted Mean Change (SE)	5.24 (1.82)	5.22 (1.75)		
Week 52: Adjusted Mean Change (SE)	9.20 (1.74)	6.31 (1.63)	2.89 [-1.78; 7.57]	0.224
Week 100: Adjusted Mean Change (SE)	8.21 (1.84)	6.99 (1.81)	1.21 [-3.86; 6.28]	0.639
≥ 12 months				
N'/ N	81 / 82	78 / 78		
Baseline Mean (SD)	74.13 (23.83)	73.61 (21.45)		
Week 52 Mean (SD)	84.36 (17.82)	84.45 (16.64)		
Week 100 Mean (SD)	81.25 (20.61)	81.07 (18.12)		
Week 28: Adjusted Mean Change (SE)	5.23 (1.82)	5.75 (1.87)		
Week 52: Adjusted Mean Change (SE)	8.45 (1.76)	10.06 (1.71)	-1.61 [-6.42; 3.20]	0.511
Week 100: Adjusted Mean Change (SE)	4.98 (1.89)	5.78 (1.80)	-0.79 [-5.91; 4.33]	0.761
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.023 ***				
KESTREL: Social Functioning				
Interaction test	p=0.574			
≤ 3 months				
N'/ N	120 / 120	110 / 110		
Baseline Mean (SD)	89.38 (19.49)	91.36 (15.31)		
Week 52 Mean (SD)	94.43 (14.52)	93.82 (13.50)		
Week 100 Mean (SD)	91.09 (17.64)	93.31 (14.56)		
Week 28: Adjusted Mean Change (SE)	2.01 (1.13)	5.38 (1.20)		
Week 52: Adjusted Mean Change (SE)	4.06 (1.26)	3.04 (1.31)	1.01 [-2.55; 4.58]	0.576
Week 100: Adjusted Mean Change (SE)	1.55 (1.53)	2.75 (1.60)	-1.20 [-5.55; 3.15]	0.588
> 3 - < 12 months				
N'/ N	30 / 30	39 / 39		
Baseline Mean (SD)	93.33 (10.24)	87.18 (14.48)		
Week 52 Mean (SD)	90.48 (14.74)	94.35 (14.01)		
Week 100 Mean (SD)	92.05 (16.16)	92.13 (13.93)		
Week 28: Adjusted Mean Change (SE)	0.93 (2.34)	4.30 (2.00)		
Week 52: Adjusted Mean Change (SE)	-1.44 (2.72)	5.91 (2.27)	-7.35 [-14.32; -0.38]	0.039 *
Week 100: Adjusted Mean Change (SE)	1.92 (3.17)	3.89 (2.84)	-1.97 [-10.34; 6.40]	0.643

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 12 months				
N'/ N	38 / 39	38 / 38		
Baseline Mean (SD)	83.55 (21.38)	88.16 (17.42)		
Week 52 Mean (SD)	87.04 (15.69)	92.80 (13.27)		
Week 100 Mean (SD)	87.95 (16.13)	87.88 (16.38)		
Week 28: Adjusted Mean Change (SE)	0.77 (2.04)	-0.29 (2.06)		
Week 52: Adjusted Mean Change (SE)	-0.90 (2.42)	4.49 (2.21)	-5.39 [-11.80; 1.03]	0.099
Week 100: Adjusted Mean Change (SE)	1.03 (2.82)	-0.43 (2.61)	1.46 [-6.08; 8.99]	0.704
KITE: Social Functioning				
Interaction test	p=0.480			
≤ 3 months				
N'/ N	84 / 85	92 / 92		
Baseline Mean (SD)	90.48 (15.35)	90.35 (17.10)		
Week 52 Mean (SD)	97.39 (8.01)	93.58 (13.45)		
Week 100 Mean (SD)	96.71 (9.89)	92.47 (14.39)		
Week 28: Adjusted Mean Change (SE)	4.89 (1.55)	3.03 (1.48)		
Week 52: Adjusted Mean Change (SE)	8.57 (1.33)	4.84 (1.26)	3.73 [0.13; 7.33]	0.042 *
Week 100: Adjusted Mean Change (SE)	8.04 (1.75)	3.47 (1.56)	4.57 [-0.04; 9.18]	0.052
> 3 - < 12 months				
N'/ N	51 / 51	49 / 49		
Baseline Mean (SD)	86.76 (18.44)	80.10 (22.81)		
Week 52 Mean (SD)	90.70 (16.61)	86.31 (18.06)		
Week 100 Mean (SD)	91.67 (19.84)	86.51 (22.39)		
Week 28: Adjusted Mean Change (SE)	1.53 (1.95)	4.06 (2.05)		
Week 52: Adjusted Mean Change (SE)	4.42 (1.66)	1.41 (1.69)	3.01 [-1.63; 7.66]	0.203
Week 100: Adjusted Mean Change (SE)	4.47 (2.06)	2.21 (2.17)	2.26 [-3.61; 8.13]	0.450
≥ 12 months				
N'/ N	43 / 43	40 / 40		
Baseline Mean (SD)	86.34 (19.44)	85.00 (20.65)		
Week 52 Mean (SD)	96.32 (9.99)	93.75 (11.20)		
Week 100 Mean (SD)	96.48 (9.11)	93.57 (14.02)		
Week 28: Adjusted Mean Change (SE)	4.10 (2.16)	5.48 (2.25)		
Week 52: Adjusted Mean Change (SE)	8.76 (1.86)	6.86 (1.87)	1.89 [-3.30; 7.08]	0.474
Week 100: Adjusted Mean Change (SE)	7.48 (2.35)	6.05 (2.27)	1.43 [-4.99; 7.85]	0.661

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Social Functioning				
Interaction test	p=0.322			
≤ 3 months				
N'/ N	204 / 205	202 / 202		
Baseline Mean (SD)	89.83 (17.87)	90.90 (16.11)		
Week 52 Mean (SD)	95.61 (12.40)	93.71 (13.43)		
Week 100 Mean (SD)	93.21 (15.39)	92.92 (14.45)		
Week 28: Adjusted Mean Change (SE)	3.64 (0.94)	4.23 (0.95)		
Week 52: Adjusted Mean Change (SE)	6.40 (0.92)	3.80 (0.92)	2.60 [0.06; 5.14]	0.045 *
Week 100: Adjusted Mean Change (SE)	4.56 (1.15)	3.01 (1.12)	1.55 [-1.59; 4.70]	0.332
> 3 - < 12 months				
N'/ N	81 / 81	88 / 88		
Baseline Mean (SD)	89.20 (16.15)	83.24 (19.78)		
Week 52 Mean (SD)	90.63 (15.91)	89.73 (16.84)		
Week 100 Mean (SD)	91.80 (18.53)	88.85 (19.41)		
Week 28: Adjusted Mean Change (SE)	0.53 (1.50)	4.11 (1.44)		
Week 52: Adjusted Mean Change (SE)	1.68 (1.48)	3.23 (1.39)	-1.55 [-5.54; 2.44]	0.445
Week 100: Adjusted Mean Change (SE)	2.81 (1.77)	2.76 (1.75)	0.05 [-4.84; 4.94]	0.983
≥ 12 months				
N'/ N	81 / 82	78 / 78		
Baseline Mean (SD)	85.03 (20.29)	86.54 (19.09)		
Week 52 Mean (SD)	92.21 (13.53)	93.28 (12.18)		
Week 100 Mean (SD)	92.50 (13.46)	90.81 (15.37)		
Week 28: Adjusted Mean Change (SE)	2.36 (1.49)	2.74 (1.53)		
Week 52: Adjusted Mean Change (SE)	4.19 (1.51)	5.78 (1.45)	-1.60 [-5.70; 2.51]	0.446
Week 100: Adjusted Mean Change (SE)	4.34 (1.82)	2.90 (1.73)	1.44 [-3.48; 6.36]	0.565

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Mental Health				
Test of heterogeneity in main analysis: **p_H=0.200**				
KESTREL: Mental Health				
Interaction test	p=0.616			
≤ 3 months				
N'/ N	120 / 120	110 / 110		
Baseline Mean (SD)	65.47 (25.61)	68.86 (23.32)		
Week 52 Mean (SD)	78.47 (21.39)	81.85 (17.17)		
Week 100 Mean (SD)	74.93 (22.48)	79.14 (23.06)		
Week 28: Adjusted Mean Change (SE)	8.31 (1.59)	11.39 (1.69)		
Week 52: Adjusted Mean Change (SE)	10.73 (1.61)	13.51 (1.67)	-2.78 [-7.35; 1.78]	0.231
Week 100: Adjusted Mean Change (SE)	9.33 (1.88)	11.49 (1.96)	-2.16 [-7.50; 3.17]	0.425
> 3 - < 12 months				
N'/ N	30 / 30	39 / 39		
Baseline Mean (SD)	65.42 (22.19)	64.74 (24.14)		
Week 52 Mean (SD)	81.25 (10.46)	74.60 (20.60)		
Week 100 Mean (SD)	75.57 (16.36)	75.69 (19.02)		
Week 28: Adjusted Mean Change (SE)	6.29 (3.28)	8.15 (2.81)		
Week 52: Adjusted Mean Change (SE)	14.59 (3.48)	9.35 (2.90)	5.23 [-3.68; 14.15]	0.249
Week 100: Adjusted Mean Change (SE)	10.35 (3.88)	11.11 (3.47)	-0.76 [-10.99; 9.48]	0.885
≥ 12 months				
N'/ N	38 / 39	38 / 38		
Baseline Mean (SD)	65.79 (25.41)	70.07 (21.17)		
Week 52 Mean (SD)	75.69 (20.31)	73.48 (15.47)		
Week 100 Mean (SD)	74.11 (22.16)	75.19 (18.85)		
Week 28: Adjusted Mean Change (SE)	5.47 (2.85)	4.35 (2.89)		
Week 52: Adjusted Mean Change (SE)	6.62 (3.08)	5.94 (2.83)	0.68 [-7.54; 8.89]	0.872
Week 100: Adjusted Mean Change (SE)	5.43 (3.45)	7.96 (3.21)	-2.53 [-11.77; 6.72]	0.591

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Mental Health				
Interaction test	p=0.242			
≤ 3 months				
N'/ N	84 / 85	92 / 92		
Baseline Mean (SD)	69.20 (22.46)	68.21 (26.22)		
Week 52 Mean (SD)	83.96 (18.05)	78.46 (22.86)		
Week 100 Mean (SD)	86.62 (13.59)	79.88 (23.06)		
Week 28: Adjusted Mean Change (SE)	10.10 (1.89)	8.27 (1.80)		
Week 52: Adjusted Mean Change (SE)	15.12 (2.27)	10.09 (2.16)	5.03 [-1.14; 11.21]	0.110
Week 100: Adjusted Mean Change (SE)	15.55 (2.35)	10.52 (2.12)	5.02 [-1.21; 11.26]	0.114
> 3 - < 12 months				
N'/ N	51 / 51	49 / 49		
Baseline Mean (SD)	66.05 (21.15)	55.99 (25.96)		
Week 52 Mean (SD)	75.44 (25.93)	72.32 (26.63)		
Week 100 Mean (SD)	79.91 (19.30)	78.13 (21.88)		
Week 28: Adjusted Mean Change (SE)	7.44 (2.38)	10.38 (2.53)		
Week 52: Adjusted Mean Change (SE)	8.36 (2.85)	9.33 (2.93)	-0.97 [-8.99; 7.06]	0.813
Week 100: Adjusted Mean Change (SE)	11.71 (2.80)	15.62 (2.96)	-3.91 [-11.92; 4.09]	0.337
≥ 12 months				
N'/ N	43 / 43	40 / 40		
Baseline Mean (SD)	71.80 (20.29)	72.19 (22.64)		
Week 52 Mean (SD)	83.82 (16.93)	78.31 (21.00)		
Week 100 Mean (SD)	85.55 (14.93)	80.71 (21.46)		
Week 28: Adjusted Mean Change (SE)	6.09 (2.64)	8.68 (2.76)		
Week 52: Adjusted Mean Change (SE)	13.19 (3.20)	7.00 (3.24)	6.19 [-2.75; 15.12]	0.174
Week 100: Adjusted Mean Change (SE)	12.63 (3.19)	8.43 (3.13)	4.20 [-4.57; 12.97]	0.347
Pooled Analysis: Mental Health				
Interaction test	p=0.660			
≤ 3 months				
N'/ N	204 / 205	202 / 202		
Baseline Mean (SD)	67.00 (24.37)	68.56 (24.62)		
Week 52 Mean (SD)	80.65 (20.25)	80.36 (19.89)		
Week 100 Mean (SD)	79.35 (20.36)	79.48 (22.99)		
Week 28: Adjusted Mean Change (SE)	9.36 (1.22)	9.92 (1.23)		
Week 52: Adjusted Mean Change (SE)	12.78 (1.35)	11.89 (1.35)	0.89 [-2.86; 4.65]	0.640
Week 100: Adjusted Mean Change (SE)	12.10 (1.47)	10.98 (1.44)	1.12 [-2.92; 5.15]	0.587

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 3 - < 12 months				
N'/ N	81 / 81	88 / 88		
Baseline Mean (SD)	65.82 (21.40)	59.87 (25.40)		
Week 52 Mean (SD)	77.34 (22.15)	73.29 (24.12)		
Week 100 Mean (SD)	78.42 (18.33)	77.12 (20.62)		
Week 28: Adjusted Mean Change (SE)	6.62 (1.94)	9.30 (1.87)		
Week 52: Adjusted Mean Change (SE)	9.95 (2.19)	9.33 (2.06)	0.62 [-5.28; 6.52]	0.836
Week 100: Adjusted Mean Change (SE)	10.85 (2.28)	13.66 (2.25)	-2.81 [-9.09; 3.47]	0.380
≥ 12 months				
N'/ N	81 / 82	78 / 78		
Baseline Mean (SD)	68.98 (22.89)	71.15 (21.82)		
Week 52 Mean (SD)	80.23 (18.79)	75.93 (18.50)		
Week 100 Mean (SD)	80.21 (19.36)	78.03 (20.27)		
Week 28: Adjusted Mean Change (SE)	5.67 (1.94)	6.63 (1.99)		
Week 52: Adjusted Mean Change (SE)	10.14 (2.23)	6.49 (2.15)	3.65 [-2.42; 9.72]	0.238
Week 100: Adjusted Mean Change (SE)	9.33 (2.34)	8.26 (2.23)	1.07 [-5.27; 7.42]	0.740
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.132**				
KESTREL: Role Difficulties				
Interaction test	p=0.095			
≤ 3 months				
N'/ N	120 / 120	110 / 110		
Baseline Mean (SD)	73.33 (28.80)	71.14 (28.87)		
Week 52 Mean (SD)	79.83 (26.22)	85.51 (22.25)		
Week 100 Mean (SD)	82.45 (25.94)	82.56 (24.65)		
Week 28: Adjusted Mean Change (SE)	5.25 (1.99)	10.01 (2.12)		
Week 52: Adjusted Mean Change (SE)	4.44 (2.16)	13.29 (2.24)	-8.85 [-14.97; -2.73]	0.005 *
Week 100: Adjusted Mean Change (SE)	8.72 (2.25)	10.54 (2.35)	-1.83 [-8.21; 4.56]	0.575
> 3 - < 12 months				
N'/ N	30 / 30	39 / 39		
Baseline Mean (SD)	73.33 (27.61)	71.15 (22.43)		
Week 52 Mean (SD)	82.74 (25.76)	80.65 (26.58)		
Week 100 Mean (SD)	82.95 (24.56)	77.78 (26.48)		
Week 28: Adjusted Mean Change (SE)	3.59 (4.12)	9.45 (3.53)		
Week 52: Adjusted Mean Change (SE)	9.36 (4.65)	8.54 (3.89)	0.82 [-11.10; 12.74]	0.893
Week 100: Adjusted Mean Change (SE)	11.68 (4.64)	5.60 (4.14)	6.08 [-6.15; 18.31]	0.329

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 12 months				
N'/ N	38 / 39	38 / 38		
Baseline Mean (SD)	66.78 (28.96)	74.34 (24.31)		
Week 52 Mean (SD)	82.41 (22.00)	78.79 (20.37)		
Week 100 Mean (SD)	77.23 (26.36)	73.86 (25.65)		
Week 28: Adjusted Mean Change (SE)	9.17 (3.60)	5.63 (3.63)		
Week 52: Adjusted Mean Change (SE)	11.96 (4.13)	6.19 (3.80)	5.77 [-5.23; 16.77]	0.303
Week 100: Adjusted Mean Change (SE)	8.31 (4.13)	1.64 (3.86)	6.67 [-4.43; 17.77]	0.238
KITE: Role Difficulties				
Interaction test	p=0.458			
≤ 3 months				
N'/ N	84 / 85	92 / 92		
Baseline Mean (SD)	74.70 (25.37)	70.65 (28.01)		
Week 52 Mean (SD)	86.75 (19.81)	79.22 (26.84)		
Week 100 Mean (SD)	87.94 (19.90)	82.53 (23.73)		
Week 28: Adjusted Mean Change (SE)	6.62 (2.32)	8.63 (2.20)		
Week 52: Adjusted Mean Change (SE)	14.48 (2.47)	7.73 (2.34)	6.75 [0.06; 13.44]	0.048 *
Week 100: Adjusted Mean Change (SE)	12.75 (2.80)	10.13 (2.53)	2.62 [-4.80; 10.04]	0.488
> 3 - < 12 months				
N'/ N	51 / 51	49 / 49		
Baseline Mean (SD)	64.71 (27.58)	58.93 (31.15)		
Week 52 Mean (SD)	76.45 (25.47)	71.13 (25.53)		
Week 100 Mean (SD)	78.57 (27.65)	73.03 (28.99)		
Week 28: Adjusted Mean Change (SE)	7.75 (2.91)	3.09 (3.06)		
Week 52: Adjusted Mean Change (SE)	10.29 (3.09)	4.87 (3.15)	5.42 [-3.22; 14.05]	0.218
Week 100: Adjusted Mean Change (SE)	9.55 (3.34)	7.45 (3.51)	2.10 [-7.40; 11.60]	0.664
≥ 12 months				
N'/ N	43 / 43	40 / 40		
Baseline Mean (SD)	71.51 (29.67)	69.38 (28.72)		
Week 52 Mean (SD)	83.46 (19.88)	84.56 (19.23)		
Week 100 Mean (SD)	88.28 (19.56)	83.57 (23.24)		
Week 28: Adjusted Mean Change (SE)	8.31 (3.23)	13.08 (3.37)		
Week 52: Adjusted Mean Change (SE)	10.67 (3.46)	14.26 (3.48)	-3.59 [-13.25; 6.06]	0.465
Week 100: Adjusted Mean Change (SE)	13.20 (3.79)	11.89 (3.71)	1.31 [-9.12; 11.75]	0.804

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Role Difficulties				
Interaction test	p=0.464			
≤ 3 months				
N'/ N	204 / 205	202 / 202		
Baseline Mean (SD)	73.90 (27.39)	70.92 (28.41)		
Week 52 Mean (SD)	82.59 (24.05)	82.74 (24.50)		
Week 100 Mean (SD)	84.52 (23.92)	82.55 (24.16)		
Week 28: Adjusted Mean Change (SE)	6.14 (1.52)	9.41 (1.53)		
Week 52: Adjusted Mean Change (SE)	8.75 (1.63)	10.87 (1.62)	-2.12 [-6.63; 2.40]	0.357
Week 100: Adjusted Mean Change (SE)	10.68 (1.76)	10.40 (1.72)	0.28 [-4.54; 5.10]	0.909
> 3 - < 12 months				
N'/ N	81 / 81	88 / 88		
Baseline Mean (SD)	67.90 (27.74)	64.35 (28.15)		
Week 52 Mean (SD)	78.52 (25.54)	75.17 (26.23)		
Week 100 Mean (SD)	80.08 (26.51)	75.00 (27.86)		
Week 28: Adjusted Mean Change (SE)	5.71 (2.42)	5.73 (2.32)		
Week 52: Adjusted Mean Change (SE)	9.32 (2.63)	6.30 (2.47)	3.02 [-4.07; 10.10]	0.403
Week 100: Adjusted Mean Change (SE)	9.69 (2.73)	6.60 (2.67)	3.09 [-4.40; 10.58]	0.418
≥ 12 months				
N'/ N	81 / 82	78 / 78		
Baseline Mean (SD)	69.29 (29.25)	71.79 (26.61)		
Week 52 Mean (SD)	82.99 (20.67)	81.72 (19.86)		
Week 100 Mean (SD)	83.13 (23.45)	78.86 (24.74)		
Week 28: Adjusted Mean Change (SE)	8.65 (2.41)	9.47 (2.48)		
Week 52: Adjusted Mean Change (SE)	11.14 (2.68)	10.35 (2.58)	0.79 [-6.51; 8.09]	0.832
Week 100: Adjusted Mean Change (SE)	10.93 (2.79)	6.92 (2.67)	4.01 [-3.57; 11.59]	0.299

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Dependency				
Test of heterogeneity in main analysis: **p_H=0.019 ***				
KESTREL: Dependency				
Interaction test	p=0.963			
≤ 3 months				
N'/ N	120 / 120	110 / 110		
Baseline Mean (SD)	83.82 (24.78)	82.88 (23.57)		
Week 52 Mean (SD)	89.69 (22.58)	93.17 (17.28)		
Week 100 Mean (SD)	87.23 (21.40)	88.47 (22.62)		
Week 28: Adjusted Mean Change (SE)	6.21 (1.71)	7.39 (1.82)		
Week 52: Adjusted Mean Change (SE)	5.23 (1.76)	9.79 (1.82)	-4.56 [-9.54; 0.42]	0.072
Week 100: Adjusted Mean Change (SE)	3.84 (1.99)	5.23 (2.08)	-1.38 [-7.05; 4.28]	0.631
> 3 - < 12 months				
N'/ N	30 / 30	39 / 39		
Baseline Mean (SD)	78.33 (28.25)	80.98 (25.07)		
Week 52 Mean (SD)	90.48 (23.02)	93.82 (12.17)		
Week 100 Mean (SD)	86.36 (24.87)	87.96 (19.38)		
Week 28: Adjusted Mean Change (SE)	3.85 (3.55)	7.61 (3.03)		
Week 52: Adjusted Mean Change (SE)	9.77 (3.79)	10.42 (3.16)	-0.65 [-10.35; 9.06]	0.896
Week 100: Adjusted Mean Change (SE)	7.13 (4.12)	6.29 (3.69)	0.83 [-10.04; 11.71]	0.880
≥ 12 months				
N'/ N	38 / 39	38 / 38		
Baseline Mean (SD)	76.75 (29.46)	84.21 (23.63)		
Week 52 Mean (SD)	85.19 (18.39)	87.12 (19.55)		
Week 100 Mean (SD)	82.44 (24.46)	88.64 (18.14)		
Week 28: Adjusted Mean Change (SE)	4.97 (3.09)	4.39 (3.12)		
Week 52: Adjusted Mean Change (SE)	3.20 (3.36)	4.19 (3.09)	-0.99 [-9.94; 7.96]	0.828
Week 100: Adjusted Mean Change (SE)	0.35 (3.67)	5.62 (3.40)	-5.26 [-15.09; 4.56]	0.293

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Dependency				
Interaction test	p=0.632			
≤ 3 months				
N'/ N	84 / 85	92 / 92		
Baseline Mean (SD)	83.73 (24.37)	84.51 (25.15)		
Week 52 Mean (SD)	93.66 (16.55)	89.30 (20.06)		
Week 100 Mean (SD)	94.59 (12.55)	88.01 (22.44)		
Week 28: Adjusted Mean Change (SE)	6.92 (1.89)	2.97 (1.80)		
Week 52: Adjusted Mean Change (SE)	9.50 (2.04)	4.03 (1.95)	5.47 [-0.09; 11.03]	0.054
Week 100: Adjusted Mean Change (SE)	7.38 (2.31)	2.18 (2.08)	5.19 [-0.93; 11.31]	0.096
> 3 - < 12 months				
N'/ N	51 / 51	49 / 49		
Baseline Mean (SD)	80.88 (24.57)	73.13 (29.48)		
Week 52 Mean (SD)	85.47 (24.27)	79.37 (28.17)		
Week 100 Mean (SD)	90.48 (16.83)	82.89 (26.98)		
Week 28: Adjusted Mean Change (SE)	2.20 (2.38)	1.17 (2.51)		
Week 52: Adjusted Mean Change (SE)	3.91 (2.56)	0.11 (2.63)	3.80 [-3.41; 11.00]	0.300
Week 100: Adjusted Mean Change (SE)	6.57 (2.75)	3.46 (2.89)	3.11 [-4.73; 10.95]	0.435
≥ 12 months				
N'/ N	43 / 43	40 / 40		
Baseline Mean (SD)	85.85 (20.78)	86.67 (26.07)		
Week 52 Mean (SD)	93.14 (15.55)	90.20 (18.86)		
Week 100 Mean (SD)	93.75 (14.66)	90.95 (18.78)		
Week 28: Adjusted Mean Change (SE)	5.68 (2.64)	5.47 (2.76)		
Week 52: Adjusted Mean Change (SE)	6.98 (2.87)	4.47 (2.91)	2.51 [-5.53; 10.54]	0.540
Week 100: Adjusted Mean Change (SE)	4.83 (3.13)	3.96 (3.06)	0.86 [-7.74; 9.46]	0.844
Pooled Analysis: Dependency				
Interaction test	p=0.910			
≤ 3 months				
N'/ N	204 / 205	202 / 202		
Baseline Mean (SD)	83.78 (24.55)	83.62 (24.25)		
Week 52 Mean (SD)	91.27 (20.43)	91.47 (18.60)		
Week 100 Mean (SD)	90.01 (18.86)	88.26 (22.47)		
Week 28: Adjusted Mean Change (SE)	6.64 (1.28)	5.27 (1.29)		
Week 52: Adjusted Mean Change (SE)	7.03 (1.35)	7.10 (1.34)	-0.07 [-3.80; 3.66]	0.972
Week 100: Adjusted Mean Change (SE)	5.43 (1.50)	3.74 (1.47)	1.70 [-2.42; 5.82]	0.419

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 3 - < 12 months				
N'/ N	81 / 81	88 / 88		
Baseline Mean (SD)	79.94 (25.85)	76.61 (27.74)		
Week 52 Mean (SD)	87.11 (23.80)	85.50 (23.78)		
Week 100 Mean (SD)	89.06 (19.86)	85.00 (24.08)		
Week 28: Adjusted Mean Change (SE)	2.51 (2.04)	3.88 (1.96)		
Week 52: Adjusted Mean Change (SE)	5.57 (2.17)	4.44 (2.05)	1.12 [-4.73; 6.98]	0.706
Week 100: Adjusted Mean Change (SE)	6.67 (2.33)	4.68 (2.29)	1.99 [-4.41; 8.40]	0.542
≥ 12 months				
N'/ N	81 / 82	78 / 78		
Baseline Mean (SD)	81.58 (25.47)	85.47 (24.78)		
Week 52 Mean (SD)	89.62 (17.19)	88.68 (19.12)		
Week 100 Mean (SD)	88.47 (20.48)	89.83 (18.37)		
Week 28: Adjusted Mean Change (SE)	5.51 (2.03)	5.22 (2.09)		
Week 52: Adjusted Mean Change (SE)	5.48 (2.21)	4.58 (2.14)	0.90 [-5.12; 6.93]	0.769
Week 100: Adjusted Mean Change (SE)	3.11 (2.39)	5.07 (2.28)	-1.96 [-8.43; 4.51]	0.553
Driving				
Test of heterogeneity in main analysis: **p_H=0.792**				
KESTREL: Driving				
Interaction test	p=0.334			
≤ 3 months				
N'/ N	85 / 120	70 / 110		
Baseline Mean (SD)	82.35 (17.74)	77.08 (21.04)		
Week 52 Mean (SD)	87.21 (16.67)	88.12 (14.80)		
Week 100 Mean (SD)	83.46 (19.25)	80.87 (22.37)		
Week 28: Adjusted Mean Change (SE)	2.11 (1.66)	5.63 (1.87)		
Week 52: Adjusted Mean Change (SE)	4.41 (1.83)	8.12 (2.09)	-3.72 [-9.19; 1.76]	0.182
Week 100: Adjusted Mean Change (SE)	1.17 (2.09)	2.43 (2.40)	-1.26 [-7.53; 5.01]	0.693
> 3 - < 12 months				
N'/ N	13 / 30	26 / 39		
Baseline Mean (SD)	68.59 (22.35)	77.56 (19.26)		
Week 52 Mean (SD)	82.50 (23.39)	77.78 (23.62)		
Week 100 Mean (SD)	80.83 (17.15)	77.94 (24.99)		
Week 28: Adjusted Mean Change (SE)	3.66 (4.08)	5.65 (2.98)		
Week 52: Adjusted Mean Change (SE)	7.79 (4.79)	0.70 (3.38)	7.08 [-4.47; 18.64]	0.228
Week 100: Adjusted Mean Change (SE)	9.56 (5.36)	0.23 (4.02)	9.32 [-3.89; 22.54]	0.166

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 12 months				
N'/ N	22 / 39	24 / 38		
Baseline Mean (SD)	77.27 (17.48)	76.91 (16.57)		
Week 52 Mean (SD)	71.88 (27.70)	80.39 (17.42)		
Week 100 Mean (SD)	82.05 (22.27)	79.41 (15.62)		
Week 28: Adjusted Mean Change (SE)	0.08 (3.45)	4.72 (3.51)		
Week 52: Adjusted Mean Change (SE)	-3.38 (3.87)	5.03 (3.80)	-8.41 [-19.07; 2.25]	0.122
Week 100: Adjusted Mean Change (SE)	2.72 (4.59)	0.83 (4.19)	1.89 [-10.35; 14.13]	0.761
KITE: Driving				
Interaction test	p=0.369			
≤ 3 months				
N'/ N	49 / 85	46 / 92		
Baseline Mean (SD)	80.44 (19.14)	84.51 (19.14)		
Week 52 Mean (SD)	88.03 (17.40)	89.05 (14.54)		
Week 100 Mean (SD)	87.86 (13.76)	89.29 (13.03)		
Week 28: Adjusted Mean Change (SE)	-2.17 (2.10)	5.96 (2.16)		
Week 52: Adjusted Mean Change (SE)	6.13 (1.87)	4.81 (1.95)	1.32 [-4.01; 6.65]	0.625
Week 100: Adjusted Mean Change (SE)	4.22 (2.11)	4.47 (2.12)	-0.25 [-6.16; 5.66]	0.934
> 3 - < 12 months				
N'/ N	31 / 51	24 / 49		
Baseline Mean (SD)	76.21 (22.18)	78.12 (23.67)		
Week 52 Mean (SD)	85.67 (18.56)	84.17 (17.02)		
Week 100 Mean (SD)	82.20 (18.42)	84.80 (18.22)		
Week 28: Adjusted Mean Change (SE)	0.77 (2.65)	7.48 (3.05)		
Week 52: Adjusted Mean Change (SE)	6.06 (2.35)	2.81 (2.63)	3.25 [-3.71; 10.20]	0.358
Week 100: Adjusted Mean Change (SE)	2.03 (2.67)	2.80 (3.02)	-0.77 [-8.71; 7.17]	0.849
≥ 12 months				
N'/ N	23 / 43	26 / 40		
Baseline Mean (SD)	79.71 (20.84)	81.41 (24.44)		
Week 52 Mean (SD)	86.25 (15.83)	89.29 (16.70)		
Week 100 Mean (SD)	87.90 (12.90)	85.51 (13.81)		
Week 28: Adjusted Mean Change (SE)	6.42 (2.98)	2.38 (2.87)		
Week 52: Adjusted Mean Change (SE)	5.15 (2.61)	6.51 (2.54)	-1.36 [-8.55; 5.83]	0.710
Week 100: Adjusted Mean Change (SE)	6.84 (2.79)	0.23 (2.68)	6.61 [-1.03; 14.26]	0.089

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Driving				
Interaction test	p=0.532			
≤ 3 months				
N'/ N	134 / 205	116 / 202		
Baseline Mean (SD)	81.65 (18.22)	80.03 (20.55)		
Week 52 Mean (SD)	87.50 (16.85)	88.48 (14.62)		
Week 100 Mean (SD)	84.98 (17.60)	84.38 (19.40)		
Week 28: Adjusted Mean Change (SE)	0.66 (1.31)	5.67 (1.42)		
Week 52: Adjusted Mean Change (SE)	5.20 (1.33)	6.82 (1.45)	-1.62 [-5.48; 2.24]	0.410
Week 100: Adjusted Mean Change (SE)	2.34 (1.52)	3.25 (1.65)	-0.91 [-5.31; 3.48]	0.683
> 3 - < 12 months				
N'/ N	44 / 81	50 / 88		
Baseline Mean (SD)	73.96 (22.25)	77.83 (21.27)		
Week 52 Mean (SD)	84.76 (19.75)	80.89 (20.67)		
Week 100 Mean (SD)	81.77 (17.76)	81.37 (21.81)		
Week 28: Adjusted Mean Change (SE)	1.65 (2.28)	6.71 (2.14)		
Week 52: Adjusted Mean Change (SE)	6.71 (2.37)	1.89 (2.17)	4.82 [-1.48; 11.12]	0.134
Week 100: Adjusted Mean Change (SE)	4.30 (2.70)	1.68 (2.56)	2.62 [-4.69; 9.93]	0.481
≥ 12 months				
N'/ N	45 / 82	50 / 78		
Baseline Mean (SD)	78.52 (19.09)	79.25 (20.95)		
Week 52 Mean (SD)	79.86 (22.75)	85.31 (17.38)		
Week 100 Mean (SD)	85.66 (17.02)	82.92 (14.73)		
Week 28: Adjusted Mean Change (SE)	3.31 (2.27)	3.27 (2.25)		
Week 52: Adjusted Mean Change (SE)	1.08 (2.31)	5.80 (2.25)	-4.71 [-11.05; 1.62]	0.144
Week 100: Adjusted Mean Change (SE)	4.77 (2.61)	0.39 (2.46)	4.38 [-2.66; 11.43]	0.222

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Color Vision				
Test of heterogeneity in main analysis: **p_H=0.477**				
KESTREL: Color Vision				
Interaction test	p=0.698			
≤ 3 months				
N'/ N	119 / 120	109 / 110		
Baseline Mean (SD)	93.49 (16.74)	94.04 (15.18)		
Week 52 Mean (SD)	97.28 (10.55)	96.47 (11.47)		
Week 100 Mean (SD)	95.38 (12.80)	96.73 (10.82)		
Week 28: Adjusted Mean Change (SE)	2.91 (1.04)	1.80 (1.10)		
Week 52: Adjusted Mean Change (SE)	2.84 (1.05)	2.36 (1.10)	0.49 [-2.50; 3.48]	0.748
Week 100: Adjusted Mean Change (SE)	1.27 (1.25)	2.21 (1.31)	-0.94 [-4.51; 2.63]	0.603
> 3 - < 12 months				
N'/ N	30 / 30	37 / 39		
Baseline Mean (SD)	95.00 (12.11)	94.59 (14.60)		
Week 52 Mean (SD)	98.81 (5.46)	96.43 (13.11)		
Week 100 Mean (SD)	96.59 (8.78)	92.00 (15.68)		
Week 28: Adjusted Mean Change (SE)	-1.16 (2.14)	2.92 (1.88)		
Week 52: Adjusted Mean Change (SE)	4.11 (2.27)	1.47 (1.98)	2.64 [-3.28; 8.57]	0.381
Week 100: Adjusted Mean Change (SE)	2.78 (2.57)	-2.36 (2.39)	5.14 [-1.77; 12.06]	0.144
≥ 12 months				
N'/ N	37 / 39	38 / 38		
Baseline Mean (SD)	89.86 (19.06)	93.42 (15.03)		
Week 52 Mean (SD)	92.31 (15.44)	93.94 (12.55)		
Week 100 Mean (SD)	90.74 (15.73)	93.18 (12.92)		
Week 28: Adjusted Mean Change (SE)	1.70 (1.89)	0.52 (1.88)		
Week 52: Adjusted Mean Change (SE)	-1.87 (2.05)	0.49 (1.84)	-2.36 [-7.77; 3.05]	0.391
Week 100: Adjusted Mean Change (SE)	-3.19 (2.33)	-0.30 (2.12)	-2.89 [-9.06; 3.29]	0.359

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Color Vision				
Interaction test	p=0.321			
≤ 3 months				
N'/ N	84 / 85	91 / 92		
Baseline Mean (SD)	92.86 (15.80)	94.51 (13.85)		
Week 52 Mean (SD)	98.48 (7.44)	96.23 (12.27)		
Week 100 Mean (SD)	97.32 (9.14)	96.13 (12.43)		
Week 28: Adjusted Mean Change (SE)	3.42 (1.22)	3.44 (1.16)		
Week 52: Adjusted Mean Change (SE)	6.31 (1.10)	3.75 (1.05)	2.56 [-0.42; 5.54]	0.092
Week 100: Adjusted Mean Change (SE)	5.10 (1.39)	3.40 (1.24)	1.70 [-1.95; 5.36]	0.360
> 3 - < 12 months				
N'/ N	51 / 51	48 / 49		
Baseline Mean (SD)	90.69 (18.00)	85.42 (19.18)		
Week 52 Mean (SD)	95.93 (10.82)	90.24 (14.66)		
Week 100 Mean (SD)	97.02 (8.19)	91.89 (15.65)		
Week 28: Adjusted Mean Change (SE)	4.60 (1.53)	5.12 (1.62)		
Week 52: Adjusted Mean Change (SE)	5.14 (1.36)	0.69 (1.41)	4.45 [0.60; 8.29]	0.024 *
Week 100: Adjusted Mean Change (SE)	5.71 (1.61)	2.49 (1.72)	3.22 [-1.41; 7.84]	0.172
≥ 12 months				
N'/ N	43 / 43	40 / 40		
Baseline Mean (SD)	92.44 (17.71)	93.13 (14.97)		
Week 52 Mean (SD)	97.79 (7.20)	97.73 (7.30)		
Week 100 Mean (SD)	97.66 (9.75)	96.32 (12.51)		
Week 28: Adjusted Mean Change (SE)	2.04 (1.69)	4.18 (1.76)		
Week 52: Adjusted Mean Change (SE)	4.83 (1.53)	5.41 (1.56)	-0.58 [-4.88; 3.72]	0.792
Week 100: Adjusted Mean Change (SE)	3.71 (1.84)	3.91 (1.79)	-0.20 [-5.25; 4.85]	0.939
Pooled Analysis: Color Vision				
Interaction test	p=0.255			
≤ 3 months				
N'/ N	203 / 205	200 / 202		
Baseline Mean (SD)	93.23 (16.32)	94.25 (14.55)		
Week 52 Mean (SD)	97.75 (9.44)	96.36 (11.80)		
Week 100 Mean (SD)	96.11 (11.56)	96.45 (11.55)		
Week 28: Adjusted Mean Change (SE)	3.43 (0.80)	2.66 (0.81)		
Week 52: Adjusted Mean Change (SE)	4.53 (0.76)	3.12 (0.76)	1.41 [-0.70; 3.51]	0.190
Week 100: Adjusted Mean Change (SE)	3.05 (0.93)	2.88 (0.91)	0.18 [-2.38; 2.73]	0.892

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 3 - < 12 months				
N'/ N	81 / 81	85 / 88		
Baseline Mean (SD)	92.28 (16.13)	89.41 (17.84)		
Week 52 Mean (SD)	96.88 (9.45)	92.75 (14.29)		
Week 100 Mean (SD)	96.88 (8.33)	91.94 (15.53)		
Week 28: Adjusted Mean Change (SE)	2.05 (1.27)	3.76 (1.24)		
Week 52: Adjusted Mean Change (SE)	4.08 (1.22)	0.47 (1.18)	3.60 [0.27; 6.93]	0.034 *
Week 100: Adjusted Mean Change (SE)	4.27 (1.42)	-0.30 (1.44)	4.57 [0.60; 8.54]	0.024 *
≥ 12 months				
N'/ N	80 / 82	78 / 78		
Baseline Mean (SD)	91.25 (18.27)	93.27 (14.90)		
Week 52 Mean (SD)	95.42 (11.73)	95.83 (10.36)		
Week 100 Mean (SD)	94.49 (13.19)	94.78 (12.72)		
Week 28: Adjusted Mean Change (SE)	1.86 (1.28)	2.42 (1.30)		
Week 52: Adjusted Mean Change (SE)	1.86 (1.25)	3.02 (1.21)	-1.17 [-4.57; 2.24]	0.502
Week 100: Adjusted Mean Change (SE)	0.65 (1.47)	1.87 (1.39)	-1.22 [-5.20; 2.75]	0.547
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.003 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.935			
≤ 3 months				
N'/ N	119 / 120	110 / 110		
Baseline Mean (SD)	85.71 (20.73)	82.27 (23.30)		
Week 52 Mean (SD)	91.58 (17.78)	89.25 (18.58)		
Week 100 Mean (SD)	84.95 (23.06)	89.24 (19.38)		
Week 28: Adjusted Mean Change (SE)	3.16 (1.68)	8.99 (1.77)		
Week 52: Adjusted Mean Change (SE)	7.33 (1.68)	6.89 (1.75)	0.44 [-4.33; 5.21]	0.857
Week 100: Adjusted Mean Change (SE)	0.67 (2.05)	5.99 (2.12)	-5.32 [-11.12; 0.48]	0.072
> 3 - < 12 months				
N'/ N	30 / 30	38 / 39		
Baseline Mean (SD)	83.33 (21.10)	80.26 (21.87)		
Week 52 Mean (SD)	86.90 (20.34)	93.55 (12.86)		
Week 100 Mean (SD)	86.36 (18.46)	87.96 (18.82)		
Week 28: Adjusted Mean Change (SE)	2.07 (3.52)	7.53 (2.95)		
Week 52: Adjusted Mean Change (SE)	3.95 (3.65)	11.79 (3.02)	-7.84 [-17.16; 1.48]	0.099
Week 100: Adjusted Mean Change (SE)	4.88 (4.20)	6.56 (3.77)	-1.68 [-12.78; 9.42]	0.766

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 12 months				
N'/ N	38 / 39	38 / 38		
Baseline Mean (SD)	78.95 (25.02)	73.68 (23.93)		
Week 52 Mean (SD)	82.41 (23.83)	81.82 (17.98)		
Week 100 Mean (SD)	80.36 (21.90)	82.58 (25.38)		
Week 28: Adjusted Mean Change (SE)	1.36 (3.00)	3.74 (3.06)		
Week 52: Adjusted Mean Change (SE)	0.34 (3.22)	3.02 (2.96)	-2.68 [-11.26; 5.90]	0.539
Week 100: Adjusted Mean Change (SE)	-0.79 (3.73)	4.45 (3.48)	-5.25 [-15.25; 4.76]	0.303
KITE: Peripheral Vision				
Interaction test	p=0.115			
≤ 3 months				
N'/ N	84 / 85	91 / 92		
Baseline Mean (SD)	83.93 (20.77)	88.46 (20.52)		
Week 52 Mean (SD)	92.91 (13.63)	89.73 (18.56)		
Week 100 Mean (SD)	93.86 (13.60)	88.54 (19.20)		
Week 28: Adjusted Mean Change (SE)	4.50 (1.76)	4.76 (1.69)		
Week 52: Adjusted Mean Change (SE)	8.81 (1.85)	4.04 (1.78)	4.77 [-0.29; 9.83]	0.065
Week 100: Adjusted Mean Change (SE)	8.46 (1.96)	2.03 (1.77)	6.42 [1.23; 11.61]	0.016 *
> 3 - < 12 months				
N'/ N	51 / 51	49 / 49		
Baseline Mean (SD)	82.35 (18.90)	79.59 (22.05)		
Week 52 Mean (SD)	86.05 (20.63)	80.95 (23.30)		
Week 100 Mean (SD)	91.07 (16.40)	85.53 (18.95)		
Week 28: Adjusted Mean Change (SE)	5.93 (2.21)	2.25 (2.31)		
Week 52: Adjusted Mean Change (SE)	4.15 (2.32)	-1.75 (2.36)	5.90 [-0.60; 12.40]	0.075
Week 100: Adjusted Mean Change (SE)	7.85 (2.31)	3.22 (2.43)	4.63 [-1.95; 11.22]	0.167
≥ 12 months				
N'/ N	43 / 43	40 / 40		
Baseline Mean (SD)	82.56 (20.80)	82.50 (21.33)		
Week 52 Mean (SD)	88.24 (17.66)	91.91 (13.37)		
Week 100 Mean (SD)	91.41 (16.33)	88.57 (17.51)		
Week 28: Adjusted Mean Change (SE)	2.90 (2.45)	6.56 (2.56)		
Week 52: Adjusted Mean Change (SE)	4.16 (2.60)	8.76 (2.63)	-4.59 [-11.87; 2.69]	0.215
Week 100: Adjusted Mean Change (SE)	5.63 (2.63)	4.51 (2.56)	1.12 [-6.10; 8.34]	0.760

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.457			
≤ 3 months				
N'/ N	203 / 205	201 / 202		
Baseline Mean (SD)	84.98 (20.71)	85.07 (22.25)		
Week 52 Mean (SD)	92.11 (16.22)	89.46 (18.51)		
Week 100 Mean (SD)	88.33 (20.41)	88.92 (19.24)		
Week 28: Adjusted Mean Change (SE)	3.88 (1.22)	7.02 (1.23)		
Week 52: Adjusted Mean Change (SE)	8.12 (1.26)	5.59 (1.26)	2.54 [-0.96; 6.03]	0.155
Week 100: Adjusted Mean Change (SE)	3.82 (1.43)	4.13 (1.40)	-0.31 [-4.23; 3.62]	0.877
> 3 - < 12 months				
N'/ N	81 / 81	87 / 88		
Baseline Mean (SD)	82.72 (19.62)	79.89 (21.85)		
Week 52 Mean (SD)	86.33 (20.38)	86.30 (20.43)		
Week 100 Mean (SD)	89.45 (17.14)	86.54 (18.79)		
Week 28: Adjusted Mean Change (SE)	4.00 (1.95)	4.71 (1.86)		
Week 52: Adjusted Mean Change (SE)	3.29 (2.04)	4.26 (1.91)	-0.96 [-6.44; 4.51]	0.730
Week 100: Adjusted Mean Change (SE)	6.11 (2.20)	4.71 (2.17)	1.40 [-4.67; 7.48]	0.650
≥ 12 months				
N'/ N	81 / 82	78 / 78		
Baseline Mean (SD)	80.86 (22.80)	78.21 (22.92)		
Week 52 Mean (SD)	85.66 (20.65)	86.94 (16.49)		
Week 100 Mean (SD)	86.25 (19.76)	85.66 (21.73)		
Week 28: Adjusted Mean Change (SE)	2.02 (1.93)	5.59 (1.99)		
Week 52: Adjusted Mean Change (SE)	2.30 (2.07)	6.35 (2.00)	-4.05 [-9.69; 1.59]	0.159
Week 100: Adjusted Mean Change (SE)	2.54 (2.26)	4.83 (2.15)	-2.29 [-8.42; 3.83]	0.463

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
General Health				
Test of heterogeneity in main analysis: **p_H=0.834**				
KESTREL: General Health				
Interaction test	p=0.693			
≤ 3 months				
N'/ N	120 / 120	110 / 110		
Baseline Mean (SD)	46.67 (22.44)	38.86 (20.20)		
Week 52 Mean (SD)	54.70 (25.91)	47.34 (22.74)		
Week 100 Mean (SD)	52.39 (22.62)	49.13 (21.51)		
Week 28: Adjusted Mean Change (SE)	6.19 (1.72)	5.73 (1.82)		
Week 52: Adjusted Mean Change (SE)	10.51 (2.06)	6.78 (2.13)	3.73 [-2.10; 9.57]	0.209
Week 100: Adjusted Mean Change (SE)	9.65 (2.07)	8.36 (2.16)	1.30 [-4.60; 7.19]	0.666
> 3 - < 12 months				
N'/ N	30 / 30	39 / 39		
Baseline Mean (SD)	40.83 (16.72)	38.46 (20.56)		
Week 52 Mean (SD)	47.62 (19.21)	44.35 (23.01)		
Week 100 Mean (SD)	43.18 (23.38)	49.07 (23.49)		
Week 28: Adjusted Mean Change (SE)	0.77 (3.54)	2.39 (3.02)		
Week 52: Adjusted Mean Change (SE)	5.67 (4.44)	3.73 (3.69)	1.94 [-9.43; 13.30]	0.738
Week 100: Adjusted Mean Change (SE)	3.12 (4.27)	7.77 (3.83)	-4.65 [-15.94; 6.64]	0.418
≥ 12 months				
N'/ N	38 / 39	38 / 38		
Baseline Mean (SD)	38.82 (19.01)	37.50 (19.92)		
Week 52 Mean (SD)	44.44 (18.78)	42.42 (15.92)		
Week 100 Mean (SD)	46.43 (24.26)	45.45 (19.22)		
Week 28: Adjusted Mean Change (SE)	1.82 (3.07)	4.53 (3.11)		
Week 52: Adjusted Mean Change (SE)	3.08 (3.93)	2.55 (3.60)	0.52 [-9.94; 10.98]	0.922
Week 100: Adjusted Mean Change (SE)	5.19 (3.80)	5.18 (3.52)	0.01 [-10.16; 10.18]	0.999

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Health				
Interaction test	p=0.646			
≤ 3 months				
N'/ N	84 / 85	92 / 92		
Baseline Mean (SD)	42.86 (18.02)	45.92 (23.81)		
Week 52 Mean (SD)	46.64 (21.27)	51.01 (25.99)		
Week 100 Mean (SD)	52.19 (21.28)	54.79 (24.17)		
Week 28: Adjusted Mean Change (SE)	5.59 (2.04)	6.09 (1.93)		
Week 52: Adjusted Mean Change (SE)	3.32 (2.42)	4.98 (2.30)	-1.67 [-8.25; 4.91]	0.619
Week 100: Adjusted Mean Change (SE)	7.70 (2.31)	8.14 (2.08)	-0.44 [-6.56; 5.68]	0.888
> 3 - < 12 months				
N'/ N	51 / 51	49 / 49		
Baseline Mean (SD)	46.57 (24.50)	39.29 (21.65)		
Week 52 Mean (SD)	54.07 (24.35)	44.05 (21.95)		
Week 100 Mean (SD)	51.79 (20.95)	45.39 (23.14)		
Week 28: Adjusted Mean Change (SE)	1.83 (2.55)	2.54 (2.67)		
Week 52: Adjusted Mean Change (SE)	9.11 (3.02)	2.96 (3.07)	6.16 [-2.33; 14.65]	0.154
Week 100: Adjusted Mean Change (SE)	5.90 (2.74)	3.74 (2.87)	2.17 [-5.64; 9.97]	0.586
≥ 12 months				
N'/ N	43 / 43	40 / 40		
Baseline Mean (SD)	43.02 (19.15)	48.13 (21.47)		
Week 52 Mean (SD)	49.26 (18.95)	55.88 (17.47)		
Week 100 Mean (SD)	46.88 (15.23)	50.00 (16.04)		
Week 28: Adjusted Mean Change (SE)	1.53 (2.83)	2.44 (2.96)		
Week 52: Adjusted Mean Change (SE)	5.39 (3.40)	7.61 (3.42)	-2.21 [-11.69; 7.27]	0.646
Week 100: Adjusted Mean Change (SE)	3.67 (3.12)	2.34 (3.03)	1.32 [-7.23; 9.88]	0.761
Pooled Analysis: General Health				
Interaction test	p=0.828			
≤ 3 months				
N'/ N	204 / 205	202 / 202		
Baseline Mean (SD)	45.10 (20.77)	42.08 (22.15)		
Week 52 Mean (SD)	51.49 (24.42)	48.96 (24.22)		
Week 100 Mean (SD)	52.32 (22.05)	51.73 (22.87)		
Week 28: Adjusted Mean Change (SE)	5.63 (1.31)	5.97 (1.32)		
Week 52: Adjusted Mean Change (SE)	7.30 (1.57)	6.05 (1.56)	1.25 [-3.09; 5.59]	0.571
Week 100: Adjusted Mean Change (SE)	8.61 (1.53)	8.37 (1.50)	0.24 [-3.96; 4.45]	0.911

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 3 - < 12 months				
N'/ N	81 / 81	88 / 88		
Baseline Mean (SD)	44.44 (22.01)	38.92 (21.06)		
Week 52 Mean (SD)	51.95 (22.85)	44.18 (22.25)		
Week 100 Mean (SD)	48.83 (22.02)	46.92 (23.18)		
Week 28: Adjusted Mean Change (SE)	1.65 (2.09)	2.44 (2.01)		
Week 52: Adjusted Mean Change (SE)	8.10 (2.53)	3.19 (2.38)	4.92 [-1.90; 11.74]	0.157
Week 100: Adjusted Mean Change (SE)	5.15 (2.37)	5.39 (2.34)	-0.24 [-6.78; 6.30]	0.942
≥ 12 months				
N'/ N	81 / 82	78 / 78		
Baseline Mean (SD)	41.05 (19.08)	42.95 (21.28)		
Week 52 Mean (SD)	47.13 (18.87)	49.25 (17.93)		
Week 100 Mean (SD)	46.67 (19.78)	47.79 (17.67)		
Week 28: Adjusted Mean Change (SE)	1.71 (2.08)	3.69 (2.14)		
Week 52: Adjusted Mean Change (SE)	4.51 (2.58)	5.42 (2.48)	-0.92 [-7.94; 6.10]	0.798
Week 100: Adjusted Mean Change (SE)	4.40 (2.43)	3.95 (2.31)	0.45 [-6.13; 7.03]	0.893

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + duration of DME + treatment * duration of DME + visit * duration of DME + treatment * duration of DME * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + study + treatment * study + duration of DME + treatment * duration of DME + visit * duration of DME + treatment * duration of DME * visit.

Table 8.9 VFQ by DME type (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Composite Score				
Test of heterogeneity in main analysis: **p_H=0.049 ***				
KESTREL: Composite Score				
Interaction test	p=0.599			
focal				
N'/ N	59 / 59	48 / 48		
Baseline Mean (SD)	77.65 (16.27)	80.21 (13.63)		
Week 52 Mean (SD)	85.78 (14.74)	86.50 (13.72)		
Week 100 Mean (SD)	83.17 (13.45)	88.18 (9.64)		
Week 28: Adjusted Mean Change (SE)	5.33 (1.40)	6.62 (1.57)		
Week 52: Adjusted Mean Change (SE)	7.05 (1.45)	8.31 (1.62)	-1.26 [-5.53; 3.01]	0.562
Week 100: Adjusted Mean Change (SE)	5.81 (1.60)	10.00 (1.88)	-4.19 [-9.05; 0.67]	0.091
diffuse				
N'/ N	127 / 127	134 / 134		
Baseline Mean (SD)	76.57 (17.71)	75.67 (14.83)		
Week 52 Mean (SD)	84.71 (13.66)	84.96 (11.71)		
Week 100 Mean (SD)	83.18 (15.87)	82.00 (15.48)		
Week 28: Adjusted Mean Change (SE)	6.09 (0.97)	8.13 (0.95)		
Week 52: Adjusted Mean Change (SE)	6.63 (1.03)	8.31 (0.97)	-1.68 [-4.46; 1.10]	0.236
Week 100: Adjusted Mean Change (SE)	6.07 (1.16)	5.57 (1.09)	0.50 [-2.64; 3.64]	0.754
KITE: Composite Score				
Interaction test	p=0.192			
focal				
N'/ N	63 / 63	66 / 66		
Baseline Mean (SD)	78.36 (13.96)	80.23 (15.17)		
Week 52 Mean (SD)	88.03 (10.25)	85.93 (14.03)		
Week 100 Mean (SD)	89.32 (10.26)	84.96 (16.12)		
Week 28: Adjusted Mean Change (SE)	6.84 (1.29)	5.17 (1.24)		
Week 52: Adjusted Mean Change (SE)	9.94 (1.41)	6.43 (1.36)	3.50 [-0.33; 7.34]	0.073
Week 100: Adjusted Mean Change (SE)	10.44 (1.64)	5.47 (1.53)	4.97 [0.57; 9.36]	0.027 *

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
diffuse				
N'/ N	114 / 115	109 / 109		
Baseline Mean (SD)	77.53 (15.64)	74.90 (18.58)		
Week 52 Mean (SD)	85.71 (14.08)	82.41 (16.40)		
Week 100 Mean (SD)	87.41 (13.12)	84.22 (14.12)		
Week 28: Adjusted Mean Change (SE)	4.87 (0.95)	5.99 (0.98)		
Week 52: Adjusted Mean Change (SE)	8.11 (1.01)	6.03 (1.02)	2.07 [-0.75; 4.90]	0.150
Week 100: Adjusted Mean Change (SE)	8.02 (1.20)	6.90 (1.20)	1.12 [-2.22; 4.47]	0.509
Pooled Analysis: Composite Score				
Interaction test	p=0.705			
focal				
N'/ N	122 / 122	114 / 114		
Baseline Mean (SD)	78.02 (15.06)	80.22 (14.48)		
Week 52 Mean (SD)	86.88 (12.73)	86.18 (13.82)		
Week 100 Mean (SD)	86.12 (12.36)	86.23 (13.96)		
Week 28: Adjusted Mean Change (SE)	6.10 (0.97)	6.04 (1.00)		
Week 52: Adjusted Mean Change (SE)	8.48 (1.01)	7.51 (1.05)	0.97 [-1.89; 3.83]	0.507
Week 100: Adjusted Mean Change (SE)	8.10 (1.14)	7.56 (1.19)	0.54 [-2.69; 3.77]	0.743

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
diffuse				
N'/ N	241 / 242	243 / 243		
Baseline Mean (SD)	77.02 (16.74)	75.32 (16.59)		
Week 52 Mean (SD)	85.21 (13.84)	83.80 (14.06)		
Week 100 Mean (SD)	85.20 (14.74)	83.00 (14.88)		
Week 28: Adjusted Mean Change (SE)	5.54 (0.69)	7.00 (0.69)		
Week 52: Adjusted Mean Change (SE)	7.38 (0.72)	7.13 (0.71)	0.25 [-1.74; 2.23]	0.806
Week 100: Adjusted Mean Change (SE)	7.06 (0.83)	6.00 (0.81)	1.06 [-1.22; 3.34]	0.361
General Vision				
Test of heterogeneity in main analysis: **p_H=0.762**				
KESTREL: General Vision				
Interaction test	p=0.415			
focal				
N'/ N	59 / 59	48 / 48		
Baseline Mean (SD)	64.75 (16.75)	63.33 (13.26)		
Week 52 Mean (SD)	75.60 (14.17)	74.00 (14.46)		
Week 100 Mean (SD)	74.40 (14.59)	75.43 (10.94)		
Week 28: Adjusted Mean Change (SE)	10.74 (1.72)	11.31 (1.92)		
Week 52: Adjusted Mean Change (SE)	12.82 (1.78)	12.52 (1.99)	0.30 [-4.94; 5.55]	0.910
Week 100: Adjusted Mean Change (SE)	12.57 (1.75)	13.88 (2.07)	-1.31 [-6.65; 4.03]	0.629
diffuse				
N'/ N	127 / 127	134 / 134		
Baseline Mean (SD)	60.16 (17.00)	59.25 (15.20)		
Week 52 Mean (SD)	71.75 (14.07)	70.18 (12.26)		
Week 100 Mean (SD)	73.26 (15.20)	71.21 (12.34)		
Week 28: Adjusted Mean Change (SE)	11.60 (1.18)	10.50 (1.16)		
Week 52: Adjusted Mean Change (SE)	10.77 (1.27)	9.76 (1.18)	1.02 [-2.40; 4.43]	0.558
Week 100: Adjusted Mean Change (SE)	12.84 (1.28)	10.75 (1.20)	2.09 [-1.36; 5.54]	0.233

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Vision				
Interaction test	p=0.833			
focal				
N'/ N	63 / 63	66 / 66		
Baseline Mean (SD)	63.49 (14.16)	62.12 (19.57)		
Week 52 Mean (SD)	72.92 (15.15)	72.94 (17.35)		
Week 100 Mean (SD)	73.04 (14.12)	73.33 (17.37)		
Week 28: Adjusted Mean Change (SE)	10.18 (1.75)	7.57 (1.68)		
Week 52: Adjusted Mean Change (SE)	11.45 (1.96)	11.75 (1.90)	-0.30 [-5.67; 5.06]	0.911
Week 100: Adjusted Mean Change (SE)	11.68 (2.01)	11.40 (1.86)	0.28 [-5.09; 5.65]	0.918
diffuse				
N'/ N	114 / 115	109 / 109		
Baseline Mean (SD)	60.88 (17.12)	59.27 (17.41)		
Week 52 Mean (SD)	72.63 (14.31)	69.47 (16.97)		
Week 100 Mean (SD)	74.05 (13.81)	69.55 (15.46)		
Week 28: Adjusted Mean Change (SE)	8.63 (1.29)	10.47 (1.33)		
Week 52: Adjusted Mean Change (SE)	11.58 (1.40)	9.22 (1.42)	2.36 [-1.56; 6.28]	0.237
Week 100: Adjusted Mean Change (SE)	12.25 (1.48)	8.58 (1.46)	3.67 [-0.42; 7.75]	0.079
Pooled Analysis: General Vision				
Interaction test	p=0.439			
focal				
N'/ N	122 / 122	114 / 114		
Baseline Mean (SD)	64.10 (15.41)	62.63 (17.14)		
Week 52 Mean (SD)	74.29 (14.64)	73.41 (16.07)		
Week 100 Mean (SD)	73.75 (14.31)	74.16 (15.14)		
Week 28: Adjusted Mean Change (SE)	10.40 (1.24)	9.23 (1.27)		
Week 52: Adjusted Mean Change (SE)	12.02 (1.33)	12.20 (1.37)	-0.18 [-3.93; 3.57]	0.926
Week 100: Adjusted Mean Change (SE)	12.03 (1.32)	12.60 (1.37)	-0.57 [-4.31; 3.17]	0.765
diffuse				
N'/ N	241 / 242	243 / 243		
Baseline Mean (SD)	60.50 (17.02)	59.26 (16.19)		
Week 52 Mean (SD)	72.19 (14.16)	69.86 (14.56)		
Week 100 Mean (SD)	73.64 (14.52)	70.46 (13.82)		
Week 28: Adjusted Mean Change (SE)	10.18 (0.88)	10.44 (0.88)		
Week 52: Adjusted Mean Change (SE)	11.22 (0.95)	9.45 (0.92)	1.77 [-0.82; 4.35]	0.181
Week 100: Adjusted Mean Change (SE)	12.65 (0.97)	9.72 (0.93)	2.93 [0.30; 5.56]	0.029 *

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Ocular Pain				
Test of heterogeneity in main analysis: **p_H=0.664**				
KESTREL: Ocular Pain				
Interaction test	p=0.466			
focal				
N'/ N	59 / 59	48 / 48		
Baseline Mean (SD)	81.78 (19.74)	84.11 (18.73)		
Week 52 Mean (SD)	86.00 (17.25)	85.63 (17.58)		
Week 100 Mean (SD)	84.25 (16.52)	88.93 (13.14)		
Week 28: Adjusted Mean Change (SE)	1.84 (2.33)	1.80 (2.61)		
Week 52: Adjusted Mean Change (SE)	3.15 (2.12)	3.02 (2.37)	0.13 [-6.12; 6.38]	0.968
Week 100: Adjusted Mean Change (SE)	1.66 (2.27)	6.44 (2.68)	-4.78 [-11.70; 2.14]	0.175
diffuse				
N'/ N	127 / 127	134 / 134		
Baseline Mean (SD)	84.45 (19.97)	81.53 (21.22)		
Week 52 Mean (SD)	89.95 (15.06)	87.17 (15.82)		
Week 100 Mean (SD)	87.64 (17.53)	82.59 (22.11)		
Week 28: Adjusted Mean Change (SE)	3.25 (1.61)	5.35 (1.58)		
Week 52: Adjusted Mean Change (SE)	5.58 (1.51)	4.86 (1.41)	0.72 [-3.35; 4.80]	0.728
Week 100: Adjusted Mean Change (SE)	4.05 (1.66)	0.46 (1.55)	3.59 [-0.89; 8.07]	0.115
KITE: Ocular Pain				
Interaction test	p=0.712			
focal				
N'/ N	63 / 63	66 / 66		
Baseline Mean (SD)	82.14 (17.78)	82.01 (19.99)		
Week 52 Mean (SD)	89.06 (15.17)	87.75 (15.91)		
Week 100 Mean (SD)	89.95 (14.34)	89.12 (17.85)		
Week 28: Adjusted Mean Change (SE)	4.91 (2.00)	3.33 (1.92)		
Week 52: Adjusted Mean Change (SE)	5.68 (2.13)	4.15 (2.06)	1.53 [-4.29; 7.36]	0.604
Week 100: Adjusted Mean Change (SE)	6.44 (2.14)	5.37 (1.98)	1.07 [-4.65; 6.80]	0.712

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
diffuse				
N'/ N	114 / 115	109 / 109		
Baseline Mean (SD)	85.53 (18.11)	82.80 (21.23)		
Week 52 Mean (SD)	88.95 (17.19)	87.37 (18.64)		
Week 100 Mean (SD)	90.77 (16.01)	89.49 (15.15)		
Week 28: Adjusted Mean Change (SE)	3.84 (1.47)	3.89 (1.52)		
Week 52: Adjusted Mean Change (SE)	4.41 (1.52)	3.52 (1.53)	0.89 [-3.35; 5.12]	0.680
Week 100: Adjusted Mean Change (SE)	5.78 (1.58)	5.31 (1.55)	0.47 [-3.88; 4.82]	0.831
Pooled Analysis: Ocular Pain				
Interaction test	p=0.744			
focal				
N'/ N	122 / 122	114 / 114		
Baseline Mean (SD)	81.97 (18.68)	82.89 (19.41)		
Week 52 Mean (SD)	87.50 (16.25)	86.81 (16.60)		
Week 100 Mean (SD)	86.98 (15.70)	89.04 (16.08)		
Week 28: Adjusted Mean Change (SE)	3.37 (1.54)	2.66 (1.58)		
Week 52: Adjusted Mean Change (SE)	4.45 (1.50)	3.63 (1.56)	0.81 [-3.44; 5.07]	0.707
Week 100: Adjusted Mean Change (SE)	4.09 (1.56)	5.69 (1.62)	-1.61 [-6.01; 2.80]	0.474
diffuse				
N'/ N	241 / 242	243 / 243		
Baseline Mean (SD)	84.96 (19.08)	82.10 (21.19)		
Week 52 Mean (SD)	89.45 (16.11)	87.26 (17.11)		
Week 100 Mean (SD)	89.13 (16.85)	85.71 (19.54)		
Week 28: Adjusted Mean Change (SE)	3.55 (1.09)	4.68 (1.10)		
Week 52: Adjusted Mean Change (SE)	5.01 (1.07)	4.25 (1.04)	0.76 [-2.17; 3.70]	0.610
Week 100: Adjusted Mean Change (SE)	4.91 (1.14)	2.65 (1.09)	2.25 [-0.86; 5.36]	0.155

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.450**				
KESTREL: Near Activities				
Interaction test	p=0.929			
focal				
N'/ N	59 / 59	48 / 48		
Baseline Mean (SD)	65.11 (24.20)	70.23 (18.61)		
Week 52 Mean (SD)	83.17 (18.25)	81.04 (20.50)		
Week 100 Mean (SD)	79.50 (21.11)	83.33 (17.03)		
Week 28: Adjusted Mean Change (SE)	12.62 (2.41)	13.05 (2.70)		
Week 52: Adjusted Mean Change (SE)	16.09 (2.60)	14.43 (2.92)	1.67 [-6.02; 9.36]	0.670
Week 100: Adjusted Mean Change (SE)	13.74 (2.50)	16.10 (2.95)	-2.36 [-9.97; 5.25]	0.542
diffuse				
N'/ N	127 / 127	134 / 134		
Baseline Mean (SD)	63.22 (26.93)	63.99 (22.90)		
Week 52 Mean (SD)	77.53 (22.67)	78.29 (20.15)		
Week 100 Mean (SD)	79.98 (20.63)	75.39 (22.13)		
Week 28: Adjusted Mean Change (SE)	12.30 (1.66)	14.96 (1.64)		
Week 52: Adjusted Mean Change (SE)	11.71 (1.86)	13.48 (1.74)	-1.77 [-6.78; 3.23]	0.487
Week 100: Adjusted Mean Change (SE)	14.81 (1.82)	10.53 (1.71)	4.28 [-0.64; 9.20]	0.088
KITE: Near Activities				
Interaction test	p=0.613			
focal				
N'/ N	62 / 63	66 / 66		
Baseline Mean (SD)	72.31 (21.43)	74.37 (22.35)		
Week 52 Mean (SD)	83.85 (16.79)	82.68 (20.59)		
Week 100 Mean (SD)	86.68 (16.52)	81.17 (23.41)		
Week 28: Adjusted Mean Change (SE)	6.86 (2.37)	6.64 (2.26)		
Week 52: Adjusted Mean Change (SE)	12.84 (2.40)	9.74 (2.32)	3.10 [-3.45; 9.65]	0.352
Week 100: Adjusted Mean Change (SE)	14.55 (2.55)	8.40 (2.38)	6.16 [-0.69; 13.00]	0.078

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
diffuse				
N'/ N	114 / 115	109 / 109		
Baseline Mean (SD)	69.08 (22.98)	67.09 (24.41)		
Week 52 Mean (SD)	78.16 (22.29)	76.62 (22.88)		
Week 100 Mean (SD)	82.44 (19.78)	76.80 (22.19)		
Week 28: Adjusted Mean Change (SE)	5.77 (1.73)	5.17 (1.78)		
Week 52: Adjusted Mean Change (SE)	8.66 (1.72)	8.26 (1.74)	0.40 [-4.41; 5.20]	0.871
Week 100: Adjusted Mean Change (SE)	10.60 (1.88)	7.25 (1.86)	3.35 [-1.85; 8.55]	0.206
Pooled Analysis: Near Activities				
Interaction test	p=0.882			
focal				
N'/ N	121 / 122	114 / 114		
Baseline Mean (SD)	68.80 (23.01)	72.62 (20.87)		
Week 52 Mean (SD)	83.50 (17.46)	81.96 (20.45)		
Week 100 Mean (SD)	82.94 (19.29)	82.02 (21.06)		
Week 28: Adjusted Mean Change (SE)	9.93 (1.71)	10.02 (1.76)		
Week 52: Adjusted Mean Change (SE)	14.54 (1.79)	12.46 (1.85)	2.08 [-2.97; 7.13]	0.419
Week 100: Adjusted Mean Change (SE)	14.16 (1.79)	12.32 (1.86)	1.84 [-3.22; 6.89]	0.476
diffuse				
N'/ N	241 / 242	243 / 243		
Baseline Mean (SD)	65.99 (25.26)	65.38 (23.59)		
Week 52 Mean (SD)	77.84 (22.42)	77.53 (21.40)		
Week 100 Mean (SD)	81.16 (20.21)	76.03 (22.11)		
Week 28: Adjusted Mean Change (SE)	9.17 (1.21)	10.10 (1.22)		
Week 52: Adjusted Mean Change (SE)	10.23 (1.28)	10.73 (1.24)	-0.51 [-4.00; 2.98]	0.776
Week 100: Adjusted Mean Change (SE)	12.81 (1.31)	8.65 (1.26)	4.16 [0.61; 7.72]	0.022 *

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Distance Activities				
Test of heterogeneity in main analysis: **p_H=0.046 ***				
KESTREL: Distance Activities				
Interaction test	p=0.228			
focal				
N'/ N	59 / 59	48 / 48		
Baseline Mean (SD)	78.32 (23.66)	78.99 (18.29)		
Week 52 Mean (SD)	86.83 (17.64)	87.50 (18.66)		
Week 100 Mean (SD)	80.83 (19.49)	88.45 (13.56)		
Week 28: Adjusted Mean Change (SE)	4.67 (2.09)	8.34 (2.34)		
Week 52: Adjusted Mean Change (SE)	8.79 (1.99)	10.18 (2.22)	-1.38 [-7.25; 4.48]	0.642
Week 100: Adjusted Mean Change (SE)	4.32 (2.14)	10.60 (2.53)	-6.28 [-12.80; 0.23]	0.059
diffuse				
N'/ N	127 / 127	134 / 134		
Baseline Mean (SD)	74.31 (23.66)	73.82 (22.15)		
Week 52 Mean (SD)	85.05 (16.84)	84.72 (16.41)		
Week 100 Mean (SD)	82.74 (20.16)	82.09 (19.73)		
Week 28: Adjusted Mean Change (SE)	9.10 (1.44)	9.38 (1.42)		
Week 52: Adjusted Mean Change (SE)	8.99 (1.41)	9.71 (1.33)	-0.72 [-4.54; 3.09]	0.710
Week 100: Adjusted Mean Change (SE)	7.74 (1.56)	7.19 (1.46)	0.55 [-3.66; 4.76]	0.797
KITE: Distance Activities				
Interaction test	p=0.805			
focal				
N'/ N	63 / 63	66 / 66		
Baseline Mean (SD)	78.44 (19.61)	79.80 (21.61)		
Week 52 Mean (SD)	89.76 (15.35)	87.17 (15.52)		
Week 100 Mean (SD)	91.76 (12.00)	84.41 (19.16)		
Week 28: Adjusted Mean Change (SE)	6.06 (2.05)	6.06 (1.96)		
Week 52: Adjusted Mean Change (SE)	11.58 (1.95)	8.89 (1.88)	2.69 [-2.62; 8.00]	0.320
Week 100: Adjusted Mean Change (SE)	13.38 (2.10)	6.27 (1.95)	7.11 [1.47; 12.75]	0.014 *

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
diffuse				
N'/ N	114 / 115	109 / 109		
Baseline Mean (SD)	76.06 (22.56)	74.73 (22.81)		
Week 52 Mean (SD)	86.97 (18.57)	82.94 (20.26)		
Week 100 Mean (SD)	87.65 (17.64)	84.14 (18.32)		
Week 28: Adjusted Mean Change (SE)	5.96 (1.50)	4.56 (1.55)		
Week 52: Adjusted Mean Change (SE)	10.96 (1.39)	7.11 (1.40)	3.86 [-0.03; 7.74]	0.052
Week 100: Adjusted Mean Change (SE)	9.85 (1.55)	7.35 (1.53)	2.49 [-1.79; 6.78]	0.253
Pooled Analysis: Distance Activities				
Interaction test	p=0.406			
focal				
N'/ N	122 / 122	114 / 114		
Baseline Mean (SD)	78.38 (21.57)	79.46 (20.20)		
Week 52 Mean (SD)	88.27 (16.54)	87.32 (16.87)		
Week 100 Mean (SD)	86.07 (17.15)	86.00 (17.21)		
Week 28: Adjusted Mean Change (SE)	5.30 (1.48)	7.34 (1.52)		
Week 52: Adjusted Mean Change (SE)	10.15 (1.39)	9.71 (1.44)	0.43 [-3.50; 4.37]	0.828
Week 100: Adjusted Mean Change (SE)	8.71 (1.50)	8.31 (1.56)	0.40 [-3.85; 4.65]	0.854
diffuse				
N'/ N	241 / 242	243 / 243		
Baseline Mean (SD)	75.14 (23.11)	74.23 (22.40)		
Week 52 Mean (SD)	86.00 (17.69)	83.91 (18.24)		
Week 100 Mean (SD)	85.09 (19.10)	83.01 (19.08)		
Week 28: Adjusted Mean Change (SE)	7.65 (1.05)	7.03 (1.06)		
Week 52: Adjusted Mean Change (SE)	10.01 (0.99)	8.41 (0.97)	1.60 [-1.12; 4.32]	0.248
Week 100: Adjusted Mean Change (SE)	8.79 (1.10)	7.13 (1.06)	1.67 [-1.33; 4.66]	0.275

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.023 ***				
KESTREL: Social Functioning				
Interaction test	p=0.396			
focal				
N'/ N	59 / 59	48 / 48		
Baseline Mean (SD)	88.77 (19.38)	90.63 (16.81)		
Week 52 Mean (SD)	94.00 (13.89)	94.23 (12.45)		
Week 100 Mean (SD)	90.75 (18.18)	95.71 (10.91)		
Week 28: Adjusted Mean Change (SE)	-0.16 (1.58)	2.91 (1.77)		
Week 52: Adjusted Mean Change (SE)	2.97 (1.80)	3.93 (2.04)	-0.96 [-6.31; 4.39]	0.724
Week 100: Adjusted Mean Change (SE)	1.12 (2.08)	6.27 (2.46)	-5.16 [-11.50; 1.19]	0.111
diffuse				
N'/ N	127 / 127	134 / 134		
Baseline Mean (SD)	89.17 (18.59)	89.65 (15.22)		
Week 52 Mean (SD)	92.14 (15.45)	93.53 (13.94)		
Week 100 Mean (SD)	90.49 (16.72)	90.77 (15.58)		
Week 28: Adjusted Mean Change (SE)	2.77 (1.09)	4.21 (1.07)		
Week 52: Adjusted Mean Change (SE)	2.11 (1.29)	3.81 (1.20)	-1.70 [-5.16; 1.77]	0.336
Week 100: Adjusted Mean Change (SE)	1.31 (1.52)	1.06 (1.42)	0.25 [-3.85; 4.35]	0.905
KITE: Social Functioning				
Interaction test	p=0.479			
focal				
N'/ N	63 / 63	66 / 66		
Baseline Mean (SD)	88.89 (16.82)	88.83 (17.83)		
Week 52 Mean (SD)	96.09 (10.68)	93.14 (13.30)		
Week 100 Mean (SD)	95.65 (11.25)	91.90 (15.39)		
Week 28: Adjusted Mean Change (SE)	5.48 (1.79)	4.56 (1.72)		
Week 52: Adjusted Mean Change (SE)	8.22 (1.57)	4.77 (1.52)	3.46 [-0.83; 7.75]	0.114
Week 100: Adjusted Mean Change (SE)	7.97 (1.94)	3.45 (1.79)	4.52 [-0.67; 9.71]	0.087

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
diffuse				
N'/ N	114 / 115	109 / 109		
Baseline Mean (SD)	88.16 (17.74)	85.67 (20.89)		
Week 52 Mean (SD)	94.61 (12.59)	90.79 (15.39)		
Week 100 Mean (SD)	94.64 (15.19)	91.62 (16.92)		
Week 28: Adjusted Mean Change (SE)	2.56 (1.32)	2.90 (1.36)		
Week 52: Adjusted Mean Change (SE)	6.78 (1.12)	3.86 (1.13)	2.92 [-0.20; 6.04]	0.067
Week 100: Adjusted Mean Change (SE)	6.01 (1.43)	4.49 (1.41)	1.52 [-2.42; 5.47]	0.448
Pooled Analysis: Social Functioning				
Interaction test	p=0.791			
focal				
N'/ N	122 / 122	114 / 114		
Baseline Mean (SD)	88.83 (18.03)	89.58 (17.36)		
Week 52 Mean (SD)	95.03 (12.40)	93.61 (12.88)		
Week 100 Mean (SD)	93.10 (15.38)	93.40 (13.86)		
Week 28: Adjusted Mean Change (SE)	2.68 (1.20)	3.94 (1.24)		
Week 52: Adjusted Mean Change (SE)	5.64 (1.20)	4.50 (1.25)	1.14 [-2.26; 4.54]	0.510
Week 100: Adjusted Mean Change (SE)	4.52 (1.43)	4.61 (1.48)	-0.10 [-4.13; 3.94]	0.963
diffuse				
N'/ N	241 / 242	243 / 243		
Baseline Mean (SD)	88.69 (18.16)	87.86 (18.05)		
Week 52 Mean (SD)	93.36 (14.12)	92.28 (14.64)		
Week 100 Mean (SD)	92.47 (16.10)	91.15 (16.16)		
Week 28: Adjusted Mean Change (SE)	2.76 (0.86)	3.53 (0.86)		
Week 52: Adjusted Mean Change (SE)	4.47 (0.86)	3.75 (0.83)	0.72 [-1.62; 3.06]	0.545
Week 100: Adjusted Mean Change (SE)	3.65 (1.05)	2.49 (1.00)	1.17 [-1.68; 4.01]	0.420

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Mental Health				
Test of heterogeneity in main analysis: **p_H=0.200**				
KESTREL: Mental Health				
Interaction test	p=0.512			
focal				
N'/ N	59 / 59	48 / 48		
Baseline Mean (SD)	66.63 (24.77)	73.05 (20.55)		
Week 52 Mean (SD)	78.88 (22.01)	79.53 (18.83)		
Week 100 Mean (SD)	74.50 (19.47)	87.50 (13.13)		
Week 28: Adjusted Mean Change (SE)	8.16 (2.27)	7.79 (2.55)		
Week 52: Adjusted Mean Change (SE)	10.41 (2.25)	10.69 (2.53)	-0.29 [-6.96; 6.38]	0.932
Week 100: Adjusted Mean Change (SE)	8.19 (2.55)	18.72 (3.01)	-10.52 [-18.30; -2.75]	0.008 *
diffuse				
N'/ N	127 / 127	134 / 134		
Baseline Mean (SD)	65.26 (25.16)	66.84 (23.79)		
Week 52 Mean (SD)	77.71 (18.96)	78.89 (16.99)		
Week 100 Mean (SD)	75.00 (22.79)	74.82 (22.66)		
Week 28: Adjusted Mean Change (SE)	7.05 (1.56)	9.80 (1.54)		
Week 52: Adjusted Mean Change (SE)	9.80 (1.61)	11.44 (1.50)	-1.64 [-5.98; 2.70]	0.457
Week 100: Adjusted Mean Change (SE)	8.64 (1.86)	8.19 (1.74)	0.45 [-4.57; 5.47]	0.860
KITE: Mental Health				
Interaction test	p=0.143			
focal				
N'/ N	63 / 63	66 / 66		
Baseline Mean (SD)	69.05 (22.60)	71.69 (22.95)		
Week 52 Mean (SD)	83.85 (16.60)	80.39 (21.54)		
Week 100 Mean (SD)	86.82 (13.45)	79.75 (22.97)		
Week 28: Adjusted Mean Change (SE)	12.12 (2.18)	7.61 (2.09)		
Week 52: Adjusted Mean Change (SE)	14.97 (2.68)	10.77 (2.58)	4.20 [-3.10; 11.50]	0.259
Week 100: Adjusted Mean Change (SE)	16.18 (2.65)	9.72 (2.46)	6.46 [-0.64; 13.56]	0.074

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
diffuse				
N'/ N	114 / 115	109 / 109		
Baseline Mean (SD)	68.80 (21.16)	62.96 (27.35)		
Week 52 Mean (SD)	80.13 (22.59)	74.80 (24.61)		
Week 100 Mean (SD)	82.74 (17.37)	80.11 (21.41)		
Week 28: Adjusted Mean Change (SE)	6.12 (1.60)	9.33 (1.66)		
Week 52: Adjusted Mean Change (SE)	11.36 (1.92)	8.13 (1.94)	3.23 [-2.13; 8.60]	0.237
Week 100: Adjusted Mean Change (SE)	12.28 (1.94)	12.60 (1.94)	-0.32 [-5.72; 5.08]	0.907
Pooled Analysis: Mental Health				
Interaction test	p=0.561			
focal				
N'/ N	122 / 122	114 / 114		
Baseline Mean (SD)	67.88 (23.61)	72.26 (21.89)		
Week 52 Mean (SD)	81.31 (19.61)	80.01 (20.29)		
Week 100 Mean (SD)	80.40 (17.88)	82.79 (19.97)		
Week 28: Adjusted Mean Change (SE)	10.14 (1.57)	7.84 (1.62)		
Week 52: Adjusted Mean Change (SE)	12.62 (1.75)	10.84 (1.81)	1.78 [-3.17; 6.73]	0.480
Week 100: Adjusted Mean Change (SE)	12.14 (1.85)	13.43 (1.93)	-1.29 [-6.53; 3.96]	0.629
diffuse				
N'/ N	241 / 242	243 / 243		
Baseline Mean (SD)	66.93 (23.37)	65.10 (25.46)		
Week 52 Mean (SD)	78.91 (20.82)	77.03 (20.85)		
Week 100 Mean (SD)	78.69 (20.69)	77.21 (22.20)		
Week 28: Adjusted Mean Change (SE)	6.69 (1.12)	9.47 (1.13)		
Week 52: Adjusted Mean Change (SE)	10.68 (1.25)	9.78 (1.21)	0.89 [-2.53; 4.31]	0.608
Week 100: Adjusted Mean Change (SE)	10.53 (1.36)	10.05 (1.31)	0.48 [-3.21; 4.18]	0.798

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.132**				
KESTREL: Role Difficulties				
Interaction test	p=0.840			
focal				
N'/ N	59 / 59	48 / 48		
Baseline Mean (SD)	74.15 (28.70)	79.69 (23.86)		
Week 52 Mean (SD)	80.00 (25.13)	86.56 (21.81)		
Week 100 Mean (SD)	84.25 (23.26)	87.14 (17.54)		
Week 28: Adjusted Mean Change (SE)	6.58 (2.81)	9.13 (3.15)		
Week 52: Adjusted Mean Change (SE)	5.56 (3.05)	11.47 (3.42)	-5.91 [-14.93; 3.10]	0.198
Week 100: Adjusted Mean Change (SE)	11.58 (3.10)	11.98 (3.63)	-0.40 [-9.79; 8.99]	0.934
diffuse				
N'/ N	127 / 127	134 / 134		
Baseline Mean (SD)	71.56 (28.51)	69.03 (27.41)		
Week 52 Mean (SD)	81.06 (25.65)	82.35 (22.85)		
Week 100 Mean (SD)	80.16 (26.99)	77.10 (27.12)		
Week 28: Adjusted Mean Change (SE)	5.86 (1.94)	8.93 (1.91)		
Week 52: Adjusted Mean Change (SE)	6.44 (2.18)	10.85 (2.04)	-4.41 [-10.28; 1.46]	0.141
Week 100: Adjusted Mean Change (SE)	7.13 (2.25)	5.87 (2.12)	1.25 [-4.82; 7.33]	0.685
KITE: Role Difficulties				
Interaction test	p=0.923			
focal				
N'/ N	63 / 63	66 / 66		
Baseline Mean (SD)	73.02 (25.42)	74.43 (26.80)		
Week 52 Mean (SD)	84.90 (20.30)	81.13 (22.55)		
Week 100 Mean (SD)	86.68 (20.65)	84.03 (23.09)		
Week 28: Adjusted Mean Change (SE)	7.09 (2.71)	8.29 (2.59)		
Week 52: Adjusted Mean Change (SE)	12.83 (2.91)	7.79 (2.81)	5.04 [-2.90; 12.99]	0.213
Week 100: Adjusted Mean Change (SE)	13.08 (3.13)	11.30 (2.92)	1.78 [-6.62; 10.18]	0.677

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
diffuse				
N'/ N	114 / 115	109 / 109		
Baseline Mean (SD)	69.96 (28.40)	64.33 (29.99)		
Week 52 Mean (SD)	82.11 (22.82)	77.37 (26.25)		
Week 100 Mean (SD)	84.38 (24.07)	79.40 (25.15)		
Week 28: Adjusted Mean Change (SE)	7.07 (1.99)	7.84 (2.06)		
Week 52: Adjusted Mean Change (SE)	12.03 (2.08)	8.69 (2.10)	3.34 [-2.47; 9.15]	0.259
Week 100: Adjusted Mean Change (SE)	11.19 (2.30)	9.29 (2.29)	1.91 [-4.48; 8.29]	0.558
Pooled Analysis: Role Difficulties				
Interaction test	p=0.919			
focal				
N'/ N	122 / 122	114 / 114		
Baseline Mean (SD)	73.57 (26.95)	76.64 (25.63)		
Week 52 Mean (SD)	82.40 (22.90)	83.52 (22.27)		
Week 100 Mean (SD)	85.42 (21.96)	85.25 (21.03)		
Week 28: Adjusted Mean Change (SE)	6.83 (1.95)	8.73 (2.02)		
Week 52: Adjusted Mean Change (SE)	9.11 (2.11)	9.49 (2.18)	-0.38 [-6.33; 5.57]	0.900
Week 100: Adjusted Mean Change (SE)	12.35 (2.19)	11.71 (2.28)	0.64 [-5.57; 6.84]	0.840
diffuse				
N'/ N	241 / 242	243 / 243		
Baseline Mean (SD)	70.80 (28.41)	66.92 (28.63)		
Week 52 Mean (SD)	81.58 (24.23)	80.08 (24.52)		
Week 100 Mean (SD)	82.17 (25.65)	78.14 (26.21)		
Week 28: Adjusted Mean Change (SE)	6.48 (1.39)	8.38 (1.40)		
Week 52: Adjusted Mean Change (SE)	9.20 (1.50)	9.82 (1.46)	-0.62 [-4.74; 3.49]	0.766
Week 100: Adjusted Mean Change (SE)	9.12 (1.60)	7.36 (1.55)	1.77 [-2.61; 6.14]	0.428

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Dependency				
Test of heterogeneity in main analysis: **p_H=0.019 ***				
KESTREL: Dependency				
Interaction test	p=0.689			
focal				
N'/ N	59 / 59	48 / 48		
Baseline Mean (SD)	82.49 (24.74)	87.33 (21.26)		
Week 52 Mean (SD)	87.83 (24.98)	92.71 (14.40)		
Week 100 Mean (SD)	85.83 (22.67)	94.05 (13.64)		
Week 28: Adjusted Mean Change (SE)	7.54 (2.43)	5.66 (2.72)		
Week 52: Adjusted Mean Change (SE)	3.79 (2.45)	8.62 (2.75)	-4.82 [-12.07; 2.42]	0.191
Week 100: Adjusted Mean Change (SE)	3.47 (2.75)	10.44 (3.25)	-6.97 [-15.35; 1.41]	0.103
diffuse				
N'/ N	127 / 127	134 / 134		
Baseline Mean (SD)	81.36 (27.04)	81.28 (24.13)		
Week 52 Mean (SD)	89.52 (20.42)	92.25 (17.02)		
Week 100 Mean (SD)	86.50 (22.64)	86.29 (22.87)		
Week 28: Adjusted Mean Change (SE)	4.92 (1.67)	7.30 (1.65)		
Week 52: Adjusted Mean Change (SE)	6.05 (1.75)	9.29 (1.63)	-3.24 [-7.96; 1.47]	0.177
Week 100: Adjusted Mean Change (SE)	3.77 (2.01)	3.75 (1.88)	0.01 [-5.40; 5.43]	0.996
KITE: Dependency				
Interaction test	p=0.196			
focal				
N'/ N	63 / 63	66 / 66		
Baseline Mean (SD)	83.33 (23.99)	88.51 (19.49)		
Week 52 Mean (SD)	94.10 (16.48)	89.22 (21.49)		
Week 100 Mean (SD)	94.38 (11.66)	86.73 (22.75)		
Week 28: Adjusted Mean Change (SE)	7.02 (2.19)	2.33 (2.10)		
Week 52: Adjusted Mean Change (SE)	9.84 (2.41)	2.49 (2.32)	7.34 [0.77; 13.92]	0.029 *
Week 100: Adjusted Mean Change (SE)	7.19 (2.58)	0.36 (2.41)	6.83 [-0.11; 13.77]	0.054

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
diffuse				
N'/ N	114 / 115	109 / 109		
Baseline Mean (SD)	83.33 (23.47)	78.90 (29.34)		
Week 52 Mean (SD)	89.47 (20.42)	85.35 (23.72)		
Week 100 Mean (SD)	92.26 (15.99)	88.45 (22.05)		
Week 28: Adjusted Mean Change (SE)	4.11 (1.61)	2.76 (1.67)		
Week 52: Adjusted Mean Change (SE)	5.77 (1.72)	2.81 (1.74)	2.97 [-1.85; 7.79]	0.227
Week 100: Adjusted Mean Change (SE)	6.06 (1.90)	4.51 (1.89)	1.55 [-3.72; 6.82]	0.563
Pooled Analysis: Dependency				
Interaction test	p=0.608			
focal				
N'/ N	122 / 122	114 / 114		
Baseline Mean (SD)	82.92 (24.26)	88.01 (20.17)		
Week 52 Mean (SD)	90.90 (21.37)	90.75 (18.69)		
Week 100 Mean (SD)	89.93 (18.65)	89.61 (19.91)		
Week 28: Adjusted Mean Change (SE)	7.26 (1.64)	4.29 (1.70)		
Week 52: Adjusted Mean Change (SE)	6.75 (1.73)	5.67 (1.80)	1.07 [-3.82; 5.97]	0.667
Week 100: Adjusted Mean Change (SE)	5.44 (1.90)	5.04 (1.97)	0.40 [-4.97; 5.77]	0.885
diffuse				
N'/ N	241 / 242	243 / 243		
Baseline Mean (SD)	82.30 (25.38)	80.21 (26.56)		
Week 52 Mean (SD)	89.50 (20.37)	89.11 (20.58)		
Week 100 Mean (SD)	89.25 (19.90)	87.26 (22.47)		
Week 28: Adjusted Mean Change (SE)	4.58 (1.17)	4.95 (1.18)		
Week 52: Adjusted Mean Change (SE)	5.93 (1.24)	6.05 (1.20)	-0.13 [-3.51; 3.26]	0.941
Week 100: Adjusted Mean Change (SE)	4.98 (1.39)	3.81 (1.34)	1.17 [-2.61; 4.95]	0.544

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Driving				
Test of heterogeneity in main analysis: **p_H=0.792**				
KESTREL: Driving				
Interaction test	p=0.864			
focal				
N'/ N	39 / 59	31 / 48		
Baseline Mean (SD)	79.49 (17.19)	80.51 (20.51)		
Week 52 Mean (SD)	86.67 (18.21)	90.28 (13.38)		
Week 100 Mean (SD)	84.37 (14.78)	84.85 (23.09)		
Week 28: Adjusted Mean Change (SE)	6.17 (2.40)	8.64 (2.75)		
Week 52: Adjusted Mean Change (SE)	7.07 (2.72)	9.10 (3.22)	-2.03 [-10.34; 6.28]	0.630
Week 100: Adjusted Mean Change (SE)	5.53 (3.02)	6.05 (3.59)	-0.52 [-9.78; 8.74]	0.912
diffuse				
N'/ N	80 / 127	87 / 134		
Baseline Mean (SD)	80.10 (19.46)	76.01 (19.23)		
Week 52 Mean (SD)	82.94 (21.24)	82.58 (19.10)		
Week 100 Mean (SD)	81.99 (21.66)	78.46 (21.05)		
Week 28: Adjusted Mean Change (SE)	-0.08 (1.68)	4.15 (1.68)		
Week 52: Adjusted Mean Change (SE)	1.72 (1.98)	5.01 (1.95)	-3.29 [-8.78; 2.19]	0.238
Week 100: Adjusted Mean Change (SE)	0.52 (2.24)	0.17 (2.20)	0.35 [-5.84; 6.54]	0.911
KITE: Driving				
Interaction test	p=0.141			
focal				
N'/ N	38 / 63	42 / 66		
Baseline Mean (SD)	77.52 (21.69)	83.63 (21.15)		
Week 52 Mean (SD)	88.06 (15.58)	86.52 (19.68)		
Week 100 Mean (SD)	86.78 (13.27)	87.27 (14.84)		
Week 28: Adjusted Mean Change (SE)	3.51 (2.45)	4.37 (2.21)		
Week 52: Adjusted Mean Change (SE)	8.70 (2.14)	4.59 (2.00)	4.11 [-1.67; 9.89]	0.162
Week 100: Adjusted Mean Change (SE)	6.86 (2.36)	3.37 (2.13)	3.49 [-2.80; 9.78]	0.275

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
diffuse				
N'/ N	64 / 115	53 / 109		
Baseline Mean (SD)	80.08 (19.73)	80.82 (22.55)		
Week 52 Mean (SD)	86.32 (18.35)	88.82 (11.98)		
Week 100 Mean (SD)	86.02 (16.27)	87.06 (14.59)		
Week 28: Adjusted Mean Change (SE)	-1.09 (1.79)	6.56 (2.05)		
Week 52: Adjusted Mean Change (SE)	4.11 (1.61)	4.68 (1.82)	-0.57 [-5.37; 4.22]	0.814
Week 100: Adjusted Mean Change (SE)	2.54 (1.82)	2.13 (2.04)	0.41 [-4.98; 5.80]	0.881
Pooled Analysis: Driving				
Interaction test	p=0.344			
focal				
N'/ N	77 / 122	73 / 114		
Baseline Mean (SD)	78.52 (19.44)	82.31 (20.80)		
Week 52 Mean (SD)	87.31 (16.93)	88.07 (17.32)		
Week 100 Mean (SD)	85.52 (14.02)	86.35 (18.25)		
Week 28: Adjusted Mean Change (SE)	4.81 (1.72)	6.39 (1.75)		
Week 52: Adjusted Mean Change (SE)	7.88 (1.75)	6.72 (1.83)	1.15 [-3.83; 6.13]	0.650
Week 100: Adjusted Mean Change (SE)	6.19 (1.95)	4.79 (2.01)	1.40 [-4.11; 6.91]	0.619
diffuse				
N'/ N	144 / 242	140 / 243		
Baseline Mean (SD)	80.09 (19.52)	77.83 (20.60)		
Week 52 Mean (SD)	84.48 (19.96)	84.97 (16.95)		
Week 100 Mean (SD)	83.85 (19.38)	81.83 (19.17)		
Week 28: Adjusted Mean Change (SE)	-0.52 (1.23)	4.90 (1.31)		
Week 52: Adjusted Mean Change (SE)	2.92 (1.29)	4.77 (1.36)	-1.85 [-5.54; 1.84]	0.324
Week 100: Adjusted Mean Change (SE)	1.44 (1.47)	0.79 (1.54)	0.64 [-3.54; 4.82]	0.762

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Color Vision				
Test of heterogeneity in main analysis: **p_H=0.477**				
KESTREL: Color Vision				
Interaction test	p=0.949			
focal				
N'/ N	59 / 59	48 / 48		
Baseline Mean (SD)	91.53 (19.48)	94.79 (13.60)		
Week 52 Mean (SD)	97.00 (9.64)	95.51 (12.66)		
Week 100 Mean (SD)	94.90 (12.48)	95.71 (11.32)		
Week 28: Adjusted Mean Change (SE)	2.40 (1.49)	2.45 (1.66)		
Week 52: Adjusted Mean Change (SE)	2.72 (1.50)	1.60 (1.69)	1.12 [-3.33; 5.57]	0.621
Week 100: Adjusted Mean Change (SE)	1.34 (1.74)	2.12 (2.04)	-0.78 [-6.06; 4.51]	0.773
diffuse				
N'/ N	126 / 127	131 / 134		
Baseline Mean (SD)	93.65 (15.14)	93.89 (15.22)		
Week 52 Mean (SD)	96.39 (11.96)	95.91 (11.99)		
Week 100 Mean (SD)	94.51 (13.33)	94.90 (12.80)		
Week 28: Adjusted Mean Change (SE)	1.82 (1.03)	1.24 (1.02)		
Week 52: Adjusted Mean Change (SE)	1.81 (1.07)	1.59 (1.01)	0.23 [-2.68; 3.13]	0.878
Week 100: Adjusted Mean Change (SE)	0.22 (1.27)	0.33 (1.20)	-0.12 [-3.56; 3.33]	0.948
KITE: Color Vision				
Interaction test	p=0.988			
focal				
N'/ N	63 / 63	64 / 66		
Baseline Mean (SD)	92.46 (15.96)	94.53 (12.17)		
Week 52 Mean (SD)	98.44 (8.00)	96.88 (9.82)		
Week 100 Mean (SD)	97.28 (9.47)	96.50 (10.11)		
Week 28: Adjusted Mean Change (SE)	4.27 (1.40)	4.70 (1.37)		
Week 52: Adjusted Mean Change (SE)	6.52 (1.28)	4.20 (1.28)	2.32 [-1.25; 5.88]	0.202
Week 100: Adjusted Mean Change (SE)	5.19 (1.51)	3.62 (1.45)	1.58 [-2.54; 5.70]	0.452

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
diffuse				
N'/ N	114 / 115	109 / 109		
Baseline Mean (SD)	91.89 (17.44)	90.60 (17.61)		
Week 52 Mean (SD)	97.07 (8.87)	93.95 (13.51)		
Week 100 Mean (SD)	97.29 (8.74)	94.89 (14.26)		
Week 28: Adjusted Mean Change (SE)	2.86 (1.04)	3.21 (1.06)		
Week 52: Adjusted Mean Change (SE)	5.02 (0.92)	2.55 (0.92)	2.47 [-0.09; 5.03]	0.058
Week 100: Adjusted Mean Change (SE)	4.71 (1.12)	3.44 (1.10)	1.27 [-1.82; 4.36]	0.421
Pooled Analysis: Color Vision				
Interaction test	p=0.870			
focal				
N'/ N	122 / 122	112 / 114		
Baseline Mean (SD)	92.01 (17.68)	94.64 (12.75)		
Week 52 Mean (SD)	97.70 (8.86)	96.26 (11.13)		
Week 100 Mean (SD)	96.05 (11.13)	96.18 (10.57)		
Week 28: Adjusted Mean Change (SE)	3.39 (1.03)	3.63 (1.07)		
Week 52: Adjusted Mean Change (SE)	4.65 (0.98)	3.00 (1.04)	1.64 [-1.17; 4.45]	0.251
Week 100: Adjusted Mean Change (SE)	3.29 (1.16)	2.92 (1.22)	0.37 [-2.94; 3.68]	0.826
diffuse				
N'/ N	240 / 242	240 / 243		
Baseline Mean (SD)	92.81 (16.26)	92.40 (16.40)		
Week 52 Mean (SD)	96.73 (10.53)	95.00 (12.72)		
Week 100 Mean (SD)	95.83 (11.43)	94.90 (13.46)		
Week 28: Adjusted Mean Change (SE)	2.37 (0.74)	2.16 (0.74)		
Week 52: Adjusted Mean Change (SE)	3.38 (0.70)	2.01 (0.68)	1.37 [-0.56; 3.30]	0.163
Week 100: Adjusted Mean Change (SE)	2.47 (0.85)	1.61 (0.82)	0.86 [-1.46; 3.18]	0.465

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.003 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.770			
focal				
N'/ N	59 / 59	48 / 48		
Baseline Mean (SD)	84.75 (21.28)	80.73 (24.86)		
Week 52 Mean (SD)	90.00 (19.56)	88.75 (20.37)		
Week 100 Mean (SD)	85.00 (18.90)	88.57 (17.51)		
Week 28: Adjusted Mean Change (SE)	0.42 (2.32)	4.98 (2.60)		
Week 52: Adjusted Mean Change (SE)	5.88 (2.39)	6.98 (2.68)	-1.10 [-8.18; 5.98]	0.760
Week 100: Adjusted Mean Change (SE)	1.49 (2.74)	5.80 (3.24)	-4.30 [-12.65; 4.05]	0.312
diffuse				
N'/ N	126 / 127	133 / 134		
Baseline Mean (SD)	84.13 (21.59)	79.89 (22.92)		
Week 52 Mean (SD)	88.92 (19.75)	88.72 (16.70)		
Week 100 Mean (SD)	84.34 (23.76)	88.32 (20.69)		
Week 28: Adjusted Mean Change (SE)	4.16 (1.61)	8.59 (1.58)		
Week 52: Adjusted Mean Change (SE)	4.95 (1.72)	7.24 (1.60)	-2.29 [-6.92; 2.33]	0.330
Week 100: Adjusted Mean Change (SE)	0.74 (2.02)	6.87 (1.87)	-6.13 [-11.55; -0.71]	0.027 *
KITE: Peripheral Vision				
Interaction test	p=0.614			
focal				
N'/ N	63 / 63	66 / 66		
Baseline Mean (SD)	82.94 (19.99)	87.50 (20.22)		
Week 52 Mean (SD)	89.58 (16.17)	91.18 (15.67)		
Week 100 Mean (SD)	94.02 (13.11)	87.96 (19.27)		
Week 28: Adjusted Mean Change (SE)	5.56 (2.04)	5.11 (1.96)		
Week 52: Adjusted Mean Change (SE)	6.68 (2.23)	5.71 (2.16)	0.97 [-5.13; 7.07]	0.755
Week 100: Adjusted Mean Change (SE)	10.50 (2.17)	2.26 (2.02)	8.25 [2.42; 14.07]	0.006 *

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
diffuse				
N'/ N	114 / 115	108 / 109		
Baseline Mean (SD)	83.33 (20.41)	83.56 (21.93)		
Week 52 Mean (SD)	89.74 (17.68)	85.90 (21.24)		
Week 100 Mean (SD)	91.37 (16.23)	88.51 (17.80)		
Week 28: Adjusted Mean Change (SE)	3.84 (1.50)	3.97 (1.56)		
Week 52: Adjusted Mean Change (SE)	5.93 (1.59)	2.14 (1.61)	3.80 [-0.65; 8.24]	0.094
Week 100: Adjusted Mean Change (SE)	5.81 (1.60)	4.02 (1.59)	1.79 [-2.64; 6.23]	0.427
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.750			
focal				
N'/ N	122 / 122	114 / 114		
Baseline Mean (SD)	83.81 (20.56)	84.65 (22.44)		
Week 52 Mean (SD)	89.80 (17.89)	90.11 (17.83)		
Week 100 Mean (SD)	89.32 (16.91)	88.20 (18.50)		
Week 28: Adjusted Mean Change (SE)	2.89 (1.56)	5.67 (1.60)		
Week 52: Adjusted Mean Change (SE)	6.08 (1.65)	6.90 (1.71)	-0.81 [-5.47; 3.84]	0.732
Week 100: Adjusted Mean Change (SE)	5.76 (1.76)	4.23 (1.83)	1.53 [-3.45; 6.52]	0.546
diffuse				
N'/ N	240 / 242	241 / 243		
Baseline Mean (SD)	83.75 (21.00)	81.54 (22.51)		
Week 52 Mean (SD)	89.32 (18.71)	87.44 (18.90)		
Week 100 Mean (SD)	87.71 (20.74)	88.40 (19.40)		
Week 28: Adjusted Mean Change (SE)	3.95 (1.11)	6.36 (1.12)		
Week 52: Adjusted Mean Change (SE)	5.41 (1.18)	4.82 (1.14)	0.58 [-2.63; 3.80]	0.722
Week 100: Adjusted Mean Change (SE)	3.10 (1.30)	5.39 (1.24)	-2.30 [-5.82; 1.23]	0.201

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
General Health				
Test of heterogeneity in main analysis: **p_H=0.834**				
KESTREL: General Health				
Interaction test	p=0.768			
focal				
N'/ N	59 / 59	48 / 48		
Baseline Mean (SD)	45.34 (19.41)	42.19 (20.08)		
Week 52 Mean (SD)	53.50 (23.15)	47.50 (23.20)		
Week 100 Mean (SD)	53.00 (24.03)	52.14 (17.54)		
Week 28: Adjusted Mean Change (SE)	4.25 (2.43)	3.85 (2.71)		
Week 52: Adjusted Mean Change (SE)	9.78 (2.93)	5.40 (3.27)	4.38 [-4.26; 13.02]	0.319
Week 100: Adjusted Mean Change (SE)	10.50 (2.85)	9.13 (3.37)	1.38 [-7.30; 10.05]	0.755
diffuse				
N'/ N	127 / 127	134 / 134		
Baseline Mean (SD)	44.09 (21.70)	37.50 (20.28)		
Week 52 Mean (SD)	51.29 (24.84)	44.74 (21.16)		
Week 100 Mean (SD)	48.64 (22.35)	46.96 (22.70)		
Week 28: Adjusted Mean Change (SE)	4.83 (1.67)	4.33 (1.65)		
Week 52: Adjusted Mean Change (SE)	7.31 (2.10)	4.52 (1.95)	2.79 [-2.86; 8.45]	0.332
Week 100: Adjusted Mean Change (SE)	6.22 (2.08)	6.60 (1.95)	-0.38 [-6.01; 5.24]	0.893
KITE: General Health				
Interaction test	p=0.135			
focal				
N'/ N	63 / 63	66 / 66		
Baseline Mean (SD)	44.44 (23.09)	46.97 (25.01)		
Week 52 Mean (SD)	50.00 (23.63)	55.39 (24.14)		
Week 100 Mean (SD)	52.17 (20.97)	57.41 (24.10)		
Week 28: Adjusted Mean Change (SE)	4.20 (2.35)	6.93 (2.26)		
Week 52: Adjusted Mean Change (SE)	5.68 (2.82)	8.89 (2.73)	-3.21 [-10.92; 4.50]	0.413
Week 100: Adjusted Mean Change (SE)	6.76 (2.59)	10.53 (2.41)	-3.77 [-10.73; 3.19]	0.287

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
diffuse				
N'/ N	114 / 115	109 / 109		
Baseline Mean (SD)	43.64 (18.76)	43.58 (21.62)		
Week 52 Mean (SD)	48.68 (20.42)	47.37 (22.91)		
Week 100 Mean (SD)	49.70 (19.21)	48.01 (20.84)		
Week 28: Adjusted Mean Change (SE)	2.80 (1.73)	3.00 (1.78)		
Week 52: Adjusted Mean Change (SE)	4.89 (2.01)	2.41 (2.02)	2.49 [-3.11; 8.09]	0.382
Week 100: Adjusted Mean Change (SE)	5.53 (1.91)	2.69 (1.89)	2.85 [-2.44; 8.13]	0.290
Pooled Analysis: General Health				
Interaction test	p=0.410			
focal				
N'/ N	122 / 122	114 / 114		
Baseline Mean (SD)	44.88 (21.31)	44.96 (23.09)		
Week 52 Mean (SD)	51.79 (23.33)	51.92 (23.93)		
Week 100 Mean (SD)	52.60 (22.50)	55.34 (21.80)		
Week 28: Adjusted Mean Change (SE)	4.16 (1.69)	5.80 (1.74)		
Week 52: Adjusted Mean Change (SE)	7.68 (2.03)	7.47 (2.10)	0.21 [-5.52; 5.95]	0.941
Week 100: Adjusted Mean Change (SE)	8.62 (1.93)	10.08 (2.00)	-1.47 [-6.92; 3.99]	0.598
diffuse				
N'/ N	241 / 242	243 / 243		
Baseline Mean (SD)	43.88 (20.32)	40.23 (21.07)		
Week 52 Mean (SD)	50.00 (22.74)	45.93 (21.96)		
Week 100 Mean (SD)	49.15 (20.86)	47.44 (21.83)		
Week 28: Adjusted Mean Change (SE)	3.74 (1.20)	3.77 (1.21)		
Week 52: Adjusted Mean Change (SE)	6.00 (1.45)	3.61 (1.40)	2.39 [-1.57; 6.35]	0.236
Week 100: Adjusted Mean Change (SE)	5.76 (1.42)	4.92 (1.36)	0.84 [-3.01; 4.69]	0.667

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + DME type + treatment * DME type + visit * DME type + treatment * DME type * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + study + treatment * study + DME type + treatment * DME type + visit * DME type + treatment * DME type * visit.

Table 8.10 VFQ by CSFT (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Composite Score				
Test of heterogeneity in main analysis: **p_H=0.049 ***				
KESTREL: Composite Score				
Interaction test	p=0.330			
< 450 µm				
N'/ N	107 / 107	96 / 96		
Baseline Mean (SD)	78.64 (17.75)	80.03 (12.83)		
Week 52 Mean (SD)	86.84 (13.69)	86.68 (10.74)		
Week 100 Mean (SD)	84.72 (14.93)	86.32 (11.71)		
Week 28: Adjusted Mean Change (SE)	6.93 (1.05)	6.96 (1.12)		
Week 52: Adjusted Mean Change (SE)	8.15 (1.11)	8.11 (1.16)	0.04 [-3.12; 3.19]	0.981
Week 100: Adjusted Mean Change (SE)	6.99 (1.24)	8.24 (1.29)	-1.25 [-4.76; 2.27]	0.486
≥ 450 - < 650 µm				
N'/ N	69 / 70	71 / 71		
Baseline Mean (SD)	74.53 (16.31)	75.38 (14.61)		
Week 52 Mean (SD)	83.37 (12.63)	84.31 (13.17)		
Week 100 Mean (SD)	81.55 (13.94)	80.78 (16.03)		
Week 28: Adjusted Mean Change (SE)	5.02 (1.29)	8.31 (1.30)		
Week 52: Adjusted Mean Change (SE)	6.08 (1.38)	8.35 (1.34)	-2.27 [-6.05; 1.50]	0.237
Week 100: Adjusted Mean Change (SE)	5.48 (1.51)	4.80 (1.52)	0.68 [-3.54; 4.90]	0.751
≥ 650 µm				
N'/ N	12 / 12	20 / 20		
Baseline Mean (SD)	70.95 (20.01)	66.47 (17.36)		
Week 52 Mean (SD)	78.09 (20.61)	80.65 (15.12)		
Week 100 Mean (SD)	75.29 (21.07)	77.72 (17.57)		
Week 28: Adjusted Mean Change (SE)	-0.48 (3.16)	9.49 (2.47)		
Week 52: Adjusted Mean Change (SE)	2.26 (3.43)	8.07 (2.59)	-5.81 [-14.23; 2.61]	0.175
Week 100: Adjusted Mean Change (SE)	2.00 (4.10)	4.58 (2.84)	-2.59 [-12.36; 7.19]	0.603

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Composite Score				
Interaction test	p=0.854			
< 450 µm				
N'/ N	84 / 85	82 / 82		
Baseline Mean (SD)	79.85 (14.40)	79.07 (16.77)		
Week 52 Mean (SD)	86.48 (14.15)	84.73 (15.34)		
Week 100 Mean (SD)	87.96 (12.13)	84.80 (14.75)		
Week 28: Adjusted Mean Change (SE)	5.02 (1.13)	5.13 (1.17)		
Week 52: Adjusted Mean Change (SE)	7.10 (1.24)	5.47 (1.26)	1.63 [-1.84; 5.11]	0.356
Week 100: Adjusted Mean Change (SE)	7.28 (1.42)	5.00 (1.41)	2.28 [-1.65; 6.21]	0.255
≥ 450 - < 650 µm				
N'/ N	74 / 74	79 / 79		
Baseline Mean (SD)	77.13 (15.68)	74.39 (17.97)		
Week 52 Mean (SD)	86.79 (12.00)	82.04 (16.29)		
Week 100 Mean (SD)	88.36 (12.72)	84.33 (15.62)		
Week 28: Adjusted Mean Change (SE)	6.28 (1.18)	6.11 (1.13)		
Week 52: Adjusted Mean Change (SE)	9.89 (1.24)	6.52 (1.19)	3.37 [-0.01; 6.75]	0.050
Week 100: Adjusted Mean Change (SE)	10.13 (1.48)	8.05 (1.37)	2.09 [-1.88; 6.05]	0.301
≥ 650 µm				
N'/ N	20 / 20	19 / 19		
Baseline Mean (SD)	71.86 (13.56)	73.13 (19.61)		
Week 52 Mean (SD)	85.13 (11.76)	84.92 (14.31)		
Week 100 Mean (SD)	87.56 (10.54)	78.72 (16.41)		
Week 28: Adjusted Mean Change (SE)	6.40 (2.23)	7.92 (2.41)		
Week 52: Adjusted Mean Change (SE)	11.35 (2.52)	8.94 (2.52)	2.41 [-4.59; 9.42]	0.498
Week 100: Adjusted Mean Change (SE)	11.25 (2.85)	2.90 (2.90)	8.36 [0.37; 16.34]	0.040 *
Pooled Analysis: Composite Score				
Interaction test	p=0.789			
< 450 µm				
N'/ N	191 / 192	178 / 178		
Baseline Mean (SD)	79.17 (16.34)	79.58 (14.74)		
Week 52 Mean (SD)	86.69 (13.84)	85.84 (12.91)		
Week 100 Mean (SD)	86.09 (13.86)	85.63 (13.15)		
Week 28: Adjusted Mean Change (SE)	6.17 (0.78)	6.02 (0.82)		
Week 52: Adjusted Mean Change (SE)	7.76 (0.84)	6.85 (0.86)	0.91 [-1.44; 3.26]	0.446
Week 100: Adjusted Mean Change (SE)	7.21 (0.94)	6.65 (0.95)	0.56 [-2.06; 3.18]	0.675

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 450 - < 650 µm				
N'/ N	143 / 144	150 / 150		
Baseline Mean (SD)	75.88 (15.98)	74.86 (16.42)		
Week 52 Mean (SD)	85.24 (12.36)	83.08 (14.93)		
Week 100 Mean (SD)	84.99 (13.71)	82.74 (15.84)		
Week 28: Adjusted Mean Change (SE)	5.77 (0.89)	7.06 (0.87)		
Week 52: Adjusted Mean Change (SE)	8.19 (0.93)	7.31 (0.90)	0.87 [-1.66; 3.41]	0.499
Week 100: Adjusted Mean Change (SE)	7.98 (1.06)	6.54 (1.02)	1.44 [-1.44; 4.32]	0.326
≥ 650 µm				
N'/ N	32 / 32	39 / 39		
Baseline Mean (SD)	71.52 (15.97)	69.71 (18.55)		
Week 52 Mean (SD)	82.49 (15.62)	82.78 (14.65)		
Week 100 Mean (SD)	83.65 (15.33)	78.21 (16.74)		
Week 28: Adjusted Mean Change (SE)	3.55 (1.87)	9.13 (1.74)		
Week 52: Adjusted Mean Change (SE)	7.61 (2.06)	8.99 (1.82)	-1.38 [-6.76; 4.00]	0.614
Week 100: Adjusted Mean Change (SE)	7.62 (2.35)	4.21 (2.03)	3.41 [-2.67; 9.50]	0.271
General Vision				
Test of heterogeneity in main analysis: **p_H=0.762**				
KESTREL: General Vision				
Interaction test	p=0.234			
< 450 µm				
N'/ N	107 / 107	96 / 96		
Baseline Mean (SD)	62.99 (17.76)	64.79 (14.14)		
Week 52 Mean (SD)	74.59 (14.60)	72.84 (12.77)		
Week 100 Mean (SD)	74.39 (16.11)	73.95 (12.23)		
Week 28: Adjusted Mean Change (SE)	12.31 (1.29)	10.26 (1.37)		
Week 52: Adjusted Mean Change (SE)	13.03 (1.35)	11.04 (1.40)	1.99 [-1.83; 5.81]	0.306
Week 100: Adjusted Mean Change (SE)	13.39 (1.36)	12.21 (1.42)	1.18 [-2.69; 5.05]	0.549
≥ 450 - < 650 µm				
N'/ N	69 / 70	71 / 71		
Baseline Mean (SD)	59.71 (16.62)	56.06 (14.59)		
Week 52 Mean (SD)	72.36 (11.86)	69.18 (12.42)		
Week 100 Mean (SD)	73.09 (12.30)	70.74 (12.11)		
Week 28: Adjusted Mean Change (SE)	10.96 (1.58)	11.09 (1.60)		
Week 52: Adjusted Mean Change (SE)	11.31 (1.67)	10.02 (1.62)	1.29 [-3.29; 5.86]	0.580
Week 100: Adjusted Mean Change (SE)	12.93 (1.67)	11.57 (1.68)	1.36 [-3.30; 6.01]	0.567

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 650 µm				
N'/ N	12 / 12	20 / 20		
Baseline Mean (SD)	55.00 (15.08)	53.00 (9.79)		
Week 52 Mean (SD)	62.22 (18.56)	70.00 (14.61)		
Week 100 Mean (SD)	68.57 (19.52)	70.00 (10.33)		
Week 28: Adjusted Mean Change (SE)	5.32 (3.86)	11.82 (3.01)		
Week 52: Adjusted Mean Change (SE)	2.75 (4.16)	11.00 (3.12)	-8.26 [-18.46; 1.94]	0.112
Week 100: Adjusted Mean Change (SE)	9.84 (4.61)	10.89 (3.10)	-1.05 [-11.95; 9.86]	0.851
KITE: General Vision				
Interaction test	p=0.752			
< 450 µm				
N'/ N	84 / 85	82 / 82		
Baseline Mean (SD)	63.33 (15.47)	62.93 (16.67)		
Week 52 Mean (SD)	73.02 (17.29)	72.13 (16.44)		
Week 100 Mean (SD)	74.00 (15.32)	71.43 (16.35)		
Week 28: Adjusted Mean Change (SE)	8.92 (1.53)	8.63 (1.57)		
Week 52: Adjusted Mean Change (SE)	11.02 (1.72)	10.54 (1.76)	0.48 [-4.36; 5.32]	0.845
Week 100: Adjusted Mean Change (SE)	11.54 (1.76)	8.83 (1.73)	2.71 [-2.13; 7.56]	0.271
≥ 450 - < 650 µm				
N'/ N	74 / 74	79 / 79		
Baseline Mean (SD)	61.89 (16.61)	58.23 (18.73)		
Week 52 Mean (SD)	73.64 (11.72)	68.89 (17.41)		
Week 100 Mean (SD)	74.29 (12.48)	71.64 (16.39)		
Week 28: Adjusted Mean Change (SE)	10.39 (1.60)	10.03 (1.52)		
Week 52: Adjusted Mean Change (SE)	13.03 (1.71)	9.18 (1.64)	3.85 [-0.82; 8.52]	0.106
Week 100: Adjusted Mean Change (SE)	13.26 (1.82)	11.20 (1.68)	2.07 [-2.81; 6.95]	0.406
≥ 650 µm				
N'/ N	20 / 20	19 / 19		
Baseline Mean (SD)	55.00 (15.73)	52.63 (21.30)		
Week 52 Mean (SD)	68.00 (12.65)	71.25 (19.28)		
Week 100 Mean (SD)	70.67 (12.80)	61.33 (15.98)		
Week 28: Adjusted Mean Change (SE)	7.61 (2.99)	11.44 (3.25)		
Week 52: Adjusted Mean Change (SE)	9.48 (3.52)	14.36 (3.49)	-4.88 [-14.60; 4.84]	0.324
Week 100: Adjusted Mean Change (SE)	11.15 (3.52)	5.31 (3.56)	5.84 [-3.99; 15.67]	0.243

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: General Vision				
Interaction test	p=0.302			
< 450 µm				
N'/ N	191 / 192	178 / 178		
Baseline Mean (SD)	63.14 (16.75)	63.93 (15.34)		
Week 52 Mean (SD)	73.92 (15.76)	72.54 (14.41)		
Week 100 Mean (SD)	74.23 (15.72)	72.81 (14.25)		
Week 28: Adjusted Mean Change (SE)	10.74 (1.00)	9.37 (1.04)		
Week 52: Adjusted Mean Change (SE)	12.09 (1.08)	10.64 (1.11)	1.45 [-1.59; 4.49]	0.350
Week 100: Adjusted Mean Change (SE)	12.58 (1.09)	10.57 (1.11)	2.01 [-1.03; 5.06]	0.194
≥ 450 - < 650 µm				
N'/ N	143 / 144	150 / 150		
Baseline Mean (SD)	60.84 (16.59)	57.20 (16.87)		
Week 52 Mean (SD)	73.06 (11.75)	69.02 (15.27)		
Week 100 Mean (SD)	73.69 (12.35)	71.24 (14.58)		
Week 28: Adjusted Mean Change (SE)	10.77 (1.13)	10.65 (1.10)		
Week 52: Adjusted Mean Change (SE)	12.32 (1.20)	9.72 (1.15)	2.60 [-0.67; 5.87]	0.119
Week 100: Adjusted Mean Change (SE)	13.22 (1.23)	11.53 (1.18)	1.68 [-1.66; 5.03]	0.324
≥ 650 µm				
N'/ N	32 / 32	39 / 39		
Baseline Mean (SD)	55.00 (15.24)	52.82 (16.21)		
Week 52 Mean (SD)	65.83 (15.01)	70.63 (16.84)		
Week 100 Mean (SD)	70.00 (14.80)	65.81 (13.85)		
Week 28: Adjusted Mean Change (SE)	6.77 (2.37)	11.65 (2.22)		
Week 52: Adjusted Mean Change (SE)	6.96 (2.68)	12.77 (2.35)	-5.80 [-12.77; 1.17]	0.103
Week 100: Adjusted Mean Change (SE)	10.70 (2.75)	8.16 (2.34)	2.54 [-4.54; 9.62]	0.482

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Ocular Pain				
Test of heterogeneity in main analysis: **p_H=0.664**				
KESTREL: Ocular Pain				
Interaction test	p=0.263			
< 450 µm				
N'/ N	107 / 107	96 / 96		
Baseline Mean (SD)	84.00 (20.66)	82.29 (18.02)		
Week 52 Mean (SD)	88.82 (16.02)	87.04 (16.35)		
Week 100 Mean (SD)	85.67 (18.33)	86.68 (18.63)		
Week 28: Adjusted Mean Change (SE)	3.25 (1.74)	2.22 (1.85)		
Week 52: Adjusted Mean Change (SE)	5.39 (1.62)	4.25 (1.67)	1.14 [-3.43; 5.70]	0.624
Week 100: Adjusted Mean Change (SE)	2.75 (1.77)	4.30 (1.85)	-1.56 [-6.59; 3.48]	0.543
≥ 450 - < 650 µm				
N'/ N	69 / 70	71 / 71		
Baseline Mean (SD)	83.15 (18.79)	81.69 (21.63)		
Week 52 Mean (SD)	88.41 (15.38)	84.84 (16.63)		
Week 100 Mean (SD)	86.36 (16.89)	79.86 (20.38)		
Week 28: Adjusted Mean Change (SE)	3.46 (2.14)	5.18 (2.15)		
Week 52: Adjusted Mean Change (SE)	4.51 (2.00)	3.12 (1.93)	1.39 [-4.08; 6.85]	0.618
Week 100: Adjusted Mean Change (SE)	3.21 (2.17)	-1.82 (2.18)	5.03 [-1.03; 11.08]	0.103
≥ 650 µm				
N'/ N	12 / 12	20 / 20		
Baseline Mean (SD)	79.17 (20.87)	83.13 (27.59)		
Week 52 Mean (SD)	87.50 (18.75)	92.19 (12.81)		
Week 100 Mean (SD)	87.50 (12.50)	85.16 (25.91)		
Week 28: Adjusted Mean Change (SE)	-5.47 (5.22)	12.79 (4.05)		
Week 52: Adjusted Mean Change (SE)	4.32 (4.97)	10.40 (3.72)	-6.07 [-18.26; 6.11]	0.328
Week 100: Adjusted Mean Change (SE)	4.49 (5.97)	2.78 (4.03)	1.71 [-12.44; 15.85]	0.812

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Ocular Pain				
Interaction test	p=0.895			
< 450 µm				
N'/ N	84 / 85	82 / 82		
Baseline Mean (SD)	85.42 (17.34)	83.38 (21.70)		
Week 52 Mean (SD)	88.89 (15.89)	85.86 (18.47)		
Week 100 Mean (SD)	89.79 (16.51)	89.09 (16.11)		
Week 28: Adjusted Mean Change (SE)	4.00 (1.75)	4.08 (1.80)		
Week 52: Adjusted Mean Change (SE)	3.71 (1.87)	2.01 (1.89)	1.69 [-3.54; 6.93]	0.524
Week 100: Adjusted Mean Change (SE)	4.70 (1.88)	4.77 (1.84)	-0.07 [-5.24; 5.10]	0.979
≥ 450 - < 650 µm				
N'/ N	74 / 74	79 / 79		
Baseline Mean (SD)	82.09 (18.74)	81.33 (20.89)		
Week 52 Mean (SD)	88.26 (17.52)	88.37 (16.43)		
Week 100 Mean (SD)	90.40 (15.63)	88.81 (17.43)		
Week 28: Adjusted Mean Change (SE)	3.69 (1.83)	3.33 (1.73)		
Week 52: Adjusted Mean Change (SE)	5.52 (1.84)	5.23 (1.76)	0.29 [-4.72; 5.30]	0.909
Week 100: Adjusted Mean Change (SE)	7.04 (1.94)	5.59 (1.79)	1.45 [-3.75; 6.65]	0.585
≥ 650 µm				
N'/ N	20 / 20	19 / 19		
Baseline Mean (SD)	87.50 (17.68)	82.89 (14.56)		
Week 52 Mean (SD)	90.83 (16.00)	87.50 (21.89)		
Week 100 Mean (SD)	92.50 (9.21)	90.83 (12.91)		
Week 28: Adjusted Mean Change (SE)	8.43 (3.42)	4.10 (3.70)		
Week 52: Adjusted Mean Change (SE)	5.68 (3.81)	3.24 (3.74)	2.45 [-8.05; 12.94]	0.647
Week 100: Adjusted Mean Change (SE)	7.35 (3.76)	6.68 (3.77)	0.67 [-9.81; 11.14]	0.900
Pooled Analysis: Ocular Pain				
Interaction test	p=0.646			
< 450 µm				
N'/ N	191 / 192	178 / 178		
Baseline Mean (SD)	84.62 (19.23)	82.79 (19.75)		
Week 52 Mean (SD)	88.85 (15.91)	86.53 (17.24)		
Week 100 Mean (SD)	87.41 (17.65)	87.77 (17.51)		
Week 28: Adjusted Mean Change (SE)	3.64 (1.24)	3.10 (1.30)		
Week 52: Adjusted Mean Change (SE)	4.77 (1.23)	3.36 (1.26)	1.41 [-2.04; 4.86]	0.424
Week 100: Adjusted Mean Change (SE)	3.70 (1.28)	4.51 (1.30)	-0.80 [-4.39; 2.78]	0.660

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 450 - < 650 µm				
N'/ N	143 / 144	150 / 150		
Baseline Mean (SD)	82.60 (18.71)	81.50 (21.17)		
Week 52 Mean (SD)	88.33 (16.52)	86.75 (16.55)		
Week 100 Mean (SD)	88.40 (16.32)	84.81 (19.24)		
Week 28: Adjusted Mean Change (SE)	3.54 (1.41)	4.05 (1.38)		
Week 52: Adjusted Mean Change (SE)	5.01 (1.36)	4.13 (1.31)	0.88 [-2.83; 4.59]	0.643
Week 100: Adjusted Mean Change (SE)	5.22 (1.45)	2.18 (1.39)	3.04 [-0.91; 6.98]	0.131
≥ 650 µm				
N'/ N	32 / 32	39 / 39		
Baseline Mean (SD)	84.38 (19.05)	83.01 (21.93)		
Week 52 Mean (SD)	89.58 (16.76)	89.84 (17.80)		
Week 100 Mean (SD)	90.91 (10.34)	87.90 (20.54)		
Week 28: Adjusted Mean Change (SE)	3.35 (2.95)	8.67 (2.76)		
Week 52: Adjusted Mean Change (SE)	5.12 (3.04)	7.02 (2.65)	-1.91 [-9.82; 6.01]	0.637
Week 100: Adjusted Mean Change (SE)	6.08 (3.25)	4.93 (2.75)	1.15 [-7.21; 9.51]	0.787
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.450**				
KESTREL: Near Activities				
Interaction test	p=0.538			
< 450 µm				
N'/ N	107 / 107	96 / 96		
Baseline Mean (SD)	67.37 (26.89)	70.53 (20.53)		
Week 52 Mean (SD)	83.24 (20.71)	79.68 (18.86)		
Week 100 Mean (SD)	82.67 (21.45)	80.54 (19.52)		
Week 28: Adjusted Mean Change (SE)	13.82 (1.80)	15.28 (1.92)		
Week 52: Adjusted Mean Change (SE)	15.90 (1.97)	12.74 (2.04)	3.16 [-2.41; 8.72]	0.265
Week 100: Adjusted Mean Change (SE)	16.06 (1.94)	13.71 (2.03)	2.35 [-3.16; 7.85]	0.402
≥ 450 - < 650 µm				
N'/ N	69 / 70	71 / 71		
Baseline Mean (SD)	59.00 (24.10)	63.15 (19.84)		
Week 52 Mean (SD)	75.68 (19.77)	79.30 (20.10)		
Week 100 Mean (SD)	76.29 (18.77)	74.61 (23.04)		
Week 28: Adjusted Mean Change (SE)	11.36 (2.22)	14.78 (2.23)		
Week 52: Adjusted Mean Change (SE)	11.24 (2.44)	15.47 (2.35)	-4.23 [-10.89; 2.44]	0.213
Week 100: Adjusted Mean Change (SE)	12.66 (2.37)	10.37 (2.38)	2.29 [-4.32; 8.90]	0.496

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 650 µm				
N'/ N	12 / 12	20 / 20		
Baseline Mean (SD)	54.86 (26.70)	51.04 (27.10)		
Week 52 Mean (SD)	62.96 (26.72)	71.35 (25.63)		
Week 100 Mean (SD)	67.86 (22.27)	68.23 (19.06)		
Week 28: Adjusted Mean Change (SE)	3.18 (5.41)	8.17 (4.22)		
Week 52: Adjusted Mean Change (SE)	1.17 (6.06)	10.58 (4.56)	-9.41 [-24.28; 5.47]	0.215
Week 100: Adjusted Mean Change (SE)	10.03 (6.44)	6.82 (4.43)	3.21 [-12.12; 18.54]	0.681
KITE: Near Activities				
Interaction test	p=0.377			
< 450 µm				
N'/ N	83 / 85	82 / 82		
Baseline Mean (SD)	72.64 (21.10)	74.03 (23.53)		
Week 52 Mean (SD)	80.95 (21.87)	82.79 (20.33)		
Week 100 Mean (SD)	84.72 (18.21)	80.82 (21.15)		
Week 28: Adjusted Mean Change (SE)	6.80 (2.05)	7.01 (2.10)		
Week 52: Adjusted Mean Change (SE)	9.56 (2.10)	9.93 (2.15)	-0.36 [-6.27; 5.54]	0.904
Week 100: Adjusted Mean Change (SE)	11.37 (2.20)	7.76 (2.17)	3.62 [-2.45; 9.68]	0.241
≥ 450 - < 650 µm				
N'/ N	74 / 74	79 / 79		
Baseline Mean (SD)	70.27 (23.17)	65.30 (22.10)		
Week 52 Mean (SD)	81.44 (19.05)	75.75 (22.80)		
Week 100 Mean (SD)	83.85 (19.94)	78.73 (22.53)		
Week 28: Adjusted Mean Change (SE)	6.51 (2.13)	5.80 (2.03)		
Week 52: Adjusted Mean Change (SE)	11.51 (2.10)	8.75 (2.01)	2.76 [-2.97; 8.50]	0.343
Week 100: Adjusted Mean Change (SE)	12.02 (2.28)	10.53 (2.11)	1.49 [-4.63; 7.61]	0.632
≥ 650 µm				
N'/ N	20 / 20	19 / 19		
Baseline Mean (SD)	59.38 (22.62)	64.91 (29.21)		
Week 52 Mean (SD)	70.56 (21.10)	74.48 (23.86)		
Week 100 Mean (SD)	80.56 (16.27)	61.67 (27.96)		
Week 28: Adjusted Mean Change (SE)	4.26 (4.01)	1.70 (4.33)		
Week 52: Adjusted Mean Change (SE)	7.86 (4.29)	6.53 (4.27)	1.33 [-10.55; 13.22]	0.826
Week 100: Adjusted Mean Change (SE)	15.35 (4.40)	-6.35 (4.46)	21.70 [9.39; 34.02]	<.001 *

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Near Activities				
Interaction test	p=0.897			
< 450 µm				
N'/ N	190 / 192	178 / 178		
Baseline Mean (SD)	69.67 (24.61)	72.14 (21.97)		
Week 52 Mean (SD)	82.26 (21.17)	81.02 (19.50)		
Week 100 Mean (SD)	83.54 (20.10)	80.67 (20.20)		
Week 28: Adjusted Mean Change (SE)	10.55 (1.37)	11.24 (1.43)		
Week 52: Adjusted Mean Change (SE)	12.91 (1.46)	11.16 (1.49)	1.75 [-2.34; 5.84]	0.401
Week 100: Adjusted Mean Change (SE)	13.81 (1.46)	10.75 (1.49)	3.06 [-1.02; 7.15]	0.142
≥ 450 - < 650 µm				
N'/ N	143 / 144	150 / 150		
Baseline Mean (SD)	64.83 (24.21)	64.28 (21.02)		
Week 52 Mean (SD)	78.82 (19.51)	77.38 (21.60)		
Week 100 Mean (SD)	80.11 (19.65)	76.89 (22.76)		
Week 28: Adjusted Mean Change (SE)	9.38 (1.55)	9.91 (1.52)		
Week 52: Adjusted Mean Change (SE)	11.87 (1.62)	11.88 (1.56)	-0.01 [-4.41; 4.39]	0.997
Week 100: Adjusted Mean Change (SE)	12.81 (1.65)	10.58 (1.59)	2.23 [-2.26; 6.72]	0.330
≥ 650 µm				
N'/ N	32 / 32	39 / 39		
Baseline Mean (SD)	57.68 (23.90)	57.80 (28.65)		
Week 52 Mean (SD)	67.71 (23.09)	72.92 (24.41)		
Week 100 Mean (SD)	76.52 (18.83)	65.05 (23.61)		
Week 28: Adjusted Mean Change (SE)	3.98 (3.27)	5.59 (3.05)		
Week 52: Adjusted Mean Change (SE)	5.36 (3.60)	9.36 (3.15)	-4.00 [-13.36; 5.36]	0.402
Week 100: Adjusted Mean Change (SE)	13.54 (3.68)	1.07 (3.15)	12.47 [2.99; 21.94]	0.010 *

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Distance Activities				
Test of heterogeneity in main analysis: **p_H=0.046 ***				
KESTREL: Distance Activities				
Interaction test	p=0.640			
< 450 µm				
N'/ N	107 / 107	96 / 96		
Baseline Mean (SD)	78.00 (24.50)	79.12 (20.07)		
Week 52 Mean (SD)	86.47 (17.06)	87.35 (15.06)		
Week 100 Mean (SD)	83.33 (20.76)	85.75 (16.36)		
Week 28: Adjusted Mean Change (SE)	9.34 (1.58)	6.80 (1.68)		
Week 52: Adjusted Mean Change (SE)	8.97 (1.52)	9.83 (1.57)	-0.86 [-5.15; 3.44]	0.695
Week 100: Adjusted Mean Change (SE)	7.06 (1.67)	8.71 (1.75)	-1.65 [-6.40; 3.11]	0.496
≥ 450 - < 650 µm				
N'/ N	69 / 70	71 / 71		
Baseline Mean (SD)	72.46 (22.47)	73.18 (21.77)		
Week 52 Mean (SD)	83.94 (16.71)	82.58 (19.82)		
Week 100 Mean (SD)	80.30 (17.74)	81.40 (20.54)		
Week 28: Adjusted Mean Change (SE)	4.39 (1.94)	11.23 (1.95)		
Week 52: Adjusted Mean Change (SE)	8.42 (1.88)	8.40 (1.82)	0.02 [-5.11; 5.16]	0.993
Week 100: Adjusted Mean Change (SE)	5.74 (2.05)	6.94 (2.06)	-1.19 [-6.90; 4.52]	0.681
≥ 650 µm				
N'/ N	12 / 12	20 / 20		
Baseline Mean (SD)	67.01 (23.60)	65.00 (20.30)		
Week 52 Mean (SD)	84.26 (22.61)	83.07 (14.47)		
Week 100 Mean (SD)	75.60 (26.83)	77.08 (21.35)		
Week 28: Adjusted Mean Change (SE)	7.30 (4.74)	11.13 (3.69)		
Week 52: Adjusted Mean Change (SE)	12.54 (4.66)	11.81 (3.52)	0.74 [-10.70; 12.18]	0.899
Week 100: Adjusted Mean Change (SE)	6.74 (5.59)	4.32 (3.82)	2.42 [-10.86; 15.70]	0.720

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Distance Activities				
Interaction test	p=0.903			
< 450 µm				
N'/ N	84 / 85	82 / 82		
Baseline Mean (SD)	77.83 (22.23)	79.32 (21.66)		
Week 52 Mean (SD)	87.96 (19.63)	86.27 (17.42)		
Week 100 Mean (SD)	89.37 (14.15)	85.38 (18.45)		
Week 28: Adjusted Mean Change (SE)	6.21 (1.78)	5.75 (1.83)		
Week 52: Adjusted Mean Change (SE)	11.11 (1.71)	7.63 (1.75)	3.48 [-1.33; 8.28]	0.156
Week 100: Adjusted Mean Change (SE)	11.13 (1.83)	6.52 (1.81)	4.60 [-0.46; 9.67]	0.075
≥ 450 - < 650 µm				
N'/ N	74 / 74	79 / 79		
Baseline Mean (SD)	77.36 (21.39)	73.63 (23.02)		
Week 52 Mean (SD)	88.07 (15.49)	83.22 (18.66)		
Week 100 Mean (SD)	89.14 (18.20)	83.83 (18.88)		
Week 28: Adjusted Mean Change (SE)	7.08 (1.86)	4.54 (1.76)		
Week 52: Adjusted Mean Change (SE)	10.97 (1.70)	8.52 (1.63)	2.45 [-2.19; 7.10]	0.299
Week 100: Adjusted Mean Change (SE)	11.21 (1.90)	8.15 (1.76)	3.06 [-2.05; 8.18]	0.240
≥ 650 µm				
N'/ N	20 / 20	19 / 19		
Baseline Mean (SD)	71.25 (18.38)	72.59 (22.92)		
Week 52 Mean (SD)	87.22 (17.43)	81.51 (23.91)		
Week 100 Mean (SD)	88.61 (14.30)	76.11 (19.57)		
Week 28: Adjusted Mean Change (SE)	2.63 (3.48)	6.37 (3.77)		
Week 52: Adjusted Mean Change (SE)	13.72 (3.49)	6.77 (3.45)	6.94 [-2.71; 16.60]	0.158
Week 100: Adjusted Mean Change (SE)	12.55 (3.67)	1.71 (3.73)	10.84 [0.56; 21.12]	0.039 *
Pooled Analysis: Distance Activities				
Interaction test	p=0.819			
< 450 µm				
N'/ N	191 / 192	178 / 178		
Baseline Mean (SD)	77.92 (23.47)	79.21 (20.76)		
Week 52 Mean (SD)	87.11 (18.15)	86.88 (16.06)		
Week 100 Mean (SD)	85.89 (18.45)	85.58 (17.28)		
Week 28: Adjusted Mean Change (SE)	8.03 (1.19)	6.22 (1.25)		
Week 52: Adjusted Mean Change (SE)	9.94 (1.14)	8.79 (1.17)	1.15 [-2.05; 4.36]	0.479
Week 100: Adjusted Mean Change (SE)	8.85 (1.23)	7.62 (1.26)	1.23 [-2.22; 4.68]	0.484

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 450 - < 650 µm				
N'/ N	143 / 144	150 / 150		
Baseline Mean (SD)	75.00 (21.98)	73.42 (22.37)		
Week 52 Mean (SD)	86.19 (16.12)	82.93 (19.13)		
Week 100 Mean (SD)	84.76 (18.43)	82.75 (19.59)		
Week 28: Adjusted Mean Change (SE)	5.87 (1.35)	7.59 (1.32)		
Week 52: Adjusted Mean Change (SE)	9.82 (1.27)	8.46 (1.22)	1.36 [-2.09; 4.82]	0.438
Week 100: Adjusted Mean Change (SE)	8.61 (1.39)	7.64 (1.34)	0.97 [-2.83; 4.77]	0.616
≥ 650 µm				
N'/ N	32 / 32	39 / 39		
Baseline Mean (SD)	69.66 (20.23)	68.70 (21.67)		
Week 52 Mean (SD)	86.11 (19.10)	82.29 (19.46)		
Week 100 Mean (SD)	84.47 (19.51)	76.61 (20.18)		
Week 28: Adjusted Mean Change (SE)	3.91 (2.85)	9.11 (2.66)		
Week 52: Adjusted Mean Change (SE)	12.82 (2.82)	9.69 (2.47)	3.13 [-4.20; 10.47]	0.402
Week 100: Adjusted Mean Change (SE)	10.24 (3.11)	3.41 (2.66)	6.82 [-1.19; 14.84]	0.095
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.023 ***				
KESTREL: Social Functioning				
Interaction test	p=0.875			
< 450 µm				
N'/ N	107 / 107	96 / 96		
Baseline Mean (SD)	91.00 (17.49)	92.32 (14.32)		
Week 52 Mean (SD)	93.68 (13.86)	96.45 (9.93)		
Week 100 Mean (SD)	92.07 (16.49)	95.89 (10.68)		
Week 28: Adjusted Mean Change (SE)	3.42 (1.21)	4.34 (1.29)		
Week 52: Adjusted Mean Change (SE)	3.03 (1.37)	5.65 (1.41)	-2.62 [-6.48; 1.24]	0.183
Week 100: Adjusted Mean Change (SE)	2.24 (1.62)	5.40 (1.69)	-3.17 [-7.77; 1.44]	0.177
≥ 450 - < 650 µm				
N'/ N	69 / 70	71 / 71		
Baseline Mean (SD)	85.69 (20.37)	88.38 (15.72)		
Week 52 Mean (SD)	90.91 (14.72)	91.25 (14.97)		
Week 100 Mean (SD)	89.32 (16.39)	87.73 (17.25)		
Week 28: Adjusted Mean Change (SE)	-1.18 (1.49)	3.54 (1.50)		
Week 52: Adjusted Mean Change (SE)	1.52 (1.70)	2.14 (1.64)	-0.62 [-5.26; 4.02]	0.793
Week 100: Adjusted Mean Change (SE)	1.20 (1.98)	-1.00 (2.00)	2.19 [-3.34; 7.73]	0.436

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 650 µm				
N'/ N	12 / 12	20 / 20		
Baseline Mean (SD)	87.50 (21.32)	83.13 (19.14)		
Week 52 Mean (SD)	91.67 (25.00)	89.06 (19.83)		
Week 100 Mean (SD)	83.93 (27.68)	86.72 (19.08)		
Week 28: Adjusted Mean Change (SE)	1.41 (3.62)	4.13 (2.83)		
Week 52: Adjusted Mean Change (SE)	1.44 (4.22)	1.95 (3.16)	-0.51 [-10.87; 9.85]	0.923
Week 100: Adjusted Mean Change (SE)	-4.53 (5.48)	-1.43 (3.68)	-3.09 [-16.07; 9.88]	0.639
KITE: Social Functioning				
Interaction test	p=0.574			
< 450 µm				
N'/ N	84 / 85	82 / 82		
Baseline Mean (SD)	88.99 (16.62)	89.02 (17.83)		
Week 52 Mean (SD)	95.24 (12.38)	93.03 (11.97)		
Week 100 Mean (SD)	95.00 (13.26)	91.87 (14.75)		
Week 28: Adjusted Mean Change (SE)	4.63 (1.57)	4.04 (1.61)		
Week 52: Adjusted Mean Change (SE)	6.98 (1.38)	4.02 (1.40)	2.96 [-0.91; 6.82]	0.133
Week 100: Adjusted Mean Change (SE)	6.53 (1.72)	3.01 (1.69)	3.52 [-1.23; 8.27]	0.145
≥ 450 - < 650 µm				
N'/ N	74 / 74	79 / 79		
Baseline Mean (SD)	88.51 (18.59)	84.34 (20.85)		
Week 52 Mean (SD)	96.02 (10.55)	89.41 (17.51)		
Week 100 Mean (SD)	94.87 (15.22)	90.67 (18.89)		
Week 28: Adjusted Mean Change (SE)	3.41 (1.63)	2.94 (1.55)		
Week 52: Adjusted Mean Change (SE)	8.19 (1.36)	3.64 (1.30)	4.55 [0.84; 8.26]	0.016 *
Week 100: Adjusted Mean Change (SE)	6.70 (1.78)	4.55 (1.64)	2.15 [-2.64; 6.93]	0.378
≥ 650 µm				
N'/ N	20 / 20	19 / 19		
Baseline Mean (SD)	85.63 (15.85)	82.89 (24.37)		
Week 52 Mean (SD)	90.83 (15.28)	95.31 (8.98)		
Week 100 Mean (SD)	95.83 (11.25)	90.00 (17.17)		
Week 28: Adjusted Mean Change (SE)	1.45 (3.06)	7.25 (3.32)		
Week 52: Adjusted Mean Change (SE)	5.67 (2.82)	8.82 (2.76)	-3.15 [-10.90; 4.60]	0.425
Week 100: Adjusted Mean Change (SE)	8.33 (3.45)	3.26 (3.47)	5.08 [-4.55; 14.71]	0.301

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Social Functioning				
Interaction test	p=0.616			
< 450 µm				
N'/ N	191 / 192	178 / 178		
Baseline Mean (SD)	90.12 (17.10)	90.80 (16.07)		
Week 52 Mean (SD)	94.34 (13.23)	94.98 (10.95)		
Week 100 Mean (SD)	93.31 (15.23)	94.06 (12.80)		
Week 28: Adjusted Mean Change (SE)	4.12 (0.98)	4.19 (1.02)		
Week 52: Adjusted Mean Change (SE)	4.97 (0.98)	4.97 (1.00)	-0.00 [-2.74; 2.74]	0.999
Week 100: Adjusted Mean Change (SE)	4.28 (1.18)	4.26 (1.20)	0.02 [-3.29; 3.32]	0.992
≥ 450 - < 650 µm				
N'/ N	143 / 144	150 / 150		
Baseline Mean (SD)	87.15 (19.45)	86.25 (18.64)		
Week 52 Mean (SD)	93.70 (12.82)	90.25 (16.37)		
Week 100 Mean (SD)	92.12 (15.98)	89.36 (18.16)		
Week 28: Adjusted Mean Change (SE)	1.27 (1.11)	3.05 (1.08)		
Week 52: Adjusted Mean Change (SE)	5.10 (1.08)	2.78 (1.04)	2.32 [-0.62; 5.27]	0.122
Week 100: Adjusted Mean Change (SE)	4.12 (1.33)	1.86 (1.28)	2.26 [-1.37; 5.90]	0.222
≥ 650 µm				
N'/ N	32 / 32	39 / 39		
Baseline Mean (SD)	86.33 (17.78)	83.01 (21.55)		
Week 52 Mean (SD)	91.15 (18.97)	92.19 (15.47)		
Week 100 Mean (SD)	92.05 (18.32)	88.31 (17.95)		
Week 28: Adjusted Mean Change (SE)	0.74 (2.32)	5.87 (2.18)		
Week 52: Adjusted Mean Change (SE)	3.48 (2.42)	5.65 (2.11)	-2.17 [-8.46; 4.12]	0.499
Week 100: Adjusted Mean Change (SE)	3.35 (2.99)	1.14 (2.54)	2.22 [-5.49; 9.92]	0.572

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Mental Health				
Test of heterogeneity in main analysis: **p_H=0.200**				
KESTREL: Mental Health				
Interaction test	p=0.500			
< 450 µm				
N'/ N	107 / 107	96 / 96		
Baseline Mean (SD)	68.34 (25.02)	70.83 (21.18)		
Week 52 Mean (SD)	80.59 (19.07)	78.55 (17.23)		
Week 100 Mean (SD)	76.75 (21.02)	79.85 (19.70)		
Week 28: Adjusted Mean Change (SE)	8.96 (1.70)	8.24 (1.80)		
Week 52: Adjusted Mean Change (SE)	11.02 (1.76)	9.94 (1.82)	1.08 [-3.89; 6.06]	0.668
Week 100: Adjusted Mean Change (SE)	9.36 (2.00)	12.21 (2.09)	-2.85 [-8.53; 2.84]	0.325
≥ 450 - < 650 µm				
N'/ N	69 / 70	71 / 71		
Baseline Mean (SD)	62.50 (23.82)	68.84 (22.45)		
Week 52 Mean (SD)	75.68 (20.68)	81.45 (16.46)		
Week 100 Mean (SD)	73.52 (21.45)	77.31 (22.07)		
Week 28: Adjusted Mean Change (SE)	6.82 (2.09)	10.16 (2.10)		
Week 52: Adjusted Mean Change (SE)	10.21 (2.18)	13.88 (2.10)	-3.67 [-9.63; 2.29]	0.226
Week 100: Adjusted Mean Change (SE)	8.94 (2.45)	9.55 (2.46)	-0.62 [-7.45; 6.22]	0.859
≥ 650 µm				
N'/ N	12 / 12	20 / 20		
Baseline Mean (SD)	57.81 (28.72)	53.75 (28.92)		
Week 52 Mean (SD)	73.61 (23.34)	68.75 (23.27)		
Week 100 Mean (SD)	63.39 (25.62)	67.97 (25.40)		
Week 28: Adjusted Mean Change (SE)	-2.64 (5.09)	11.53 (3.98)		
Week 52: Adjusted Mean Change (SE)	7.41 (5.43)	6.60 (4.08)	0.82 [-12.51; 14.15]	0.904
Week 100: Adjusted Mean Change (SE)	0.68 (6.71)	7.26 (4.57)	-6.58 [-22.52; 9.35]	0.417

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Mental Health				
Interaction test	p=0.904			
< 450 µm				
N'/ N	84 / 85	82 / 82		
Baseline Mean (SD)	71.21 (20.44)	68.14 (24.72)		
Week 52 Mean (SD)	81.55 (22.55)	76.74 (22.65)		
Week 100 Mean (SD)	83.85 (16.96)	79.27 (21.76)		
Week 28: Adjusted Mean Change (SE)	8.36 (1.91)	7.35 (1.96)		
Week 52: Adjusted Mean Change (SE)	11.49 (2.34)	7.72 (2.37)	3.77 [-2.79; 10.33]	0.259
Week 100: Adjusted Mean Change (SE)	12.71 (2.32)	9.62 (2.29)	3.09 [-3.32; 9.50]	0.344
≥ 450 - < 650 µm				
N'/ N	74 / 74	79 / 79		
Baseline Mean (SD)	68.07 (22.94)	63.29 (26.90)		
Week 52 Mean (SD)	81.82 (19.60)	74.83 (25.65)		
Week 100 Mean (SD)	85.04 (15.84)	80.88 (22.71)		
Week 28: Adjusted Mean Change (SE)	7.62 (2.00)	9.58 (1.90)		
Week 52: Adjusted Mean Change (SE)	14.03 (2.33)	8.84 (2.23)	5.20 [-1.15; 11.55]	0.108
Week 100: Adjusted Mean Change (SE)	14.92 (2.40)	14.05 (2.23)	0.87 [-5.59; 7.33]	0.791
≥ 650 µm				
N'/ N	20 / 20	19 / 19		
Baseline Mean (SD)	62.50 (20.38)	65.46 (28.67)		
Week 52 Mean (SD)	78.75 (18.42)	83.98 (16.29)		
Week 100 Mean (SD)	82.50 (14.21)	74.17 (23.01)		
Week 28: Adjusted Mean Change (SE)	11.09 (3.75)	12.00 (4.06)		
Week 52: Adjusted Mean Change (SE)	11.27 (4.76)	15.73 (4.74)	-4.46 [-17.67; 8.75]	0.507
Week 100: Adjusted Mean Change (SE)	12.76 (4.64)	5.92 (4.72)	6.84 [-6.18; 19.86]	0.302
Pooled Analysis: Mental Health				
Interaction test	p=0.648			
< 450 µm				
N'/ N	191 / 192	178 / 178		
Baseline Mean (SD)	69.60 (23.10)	69.59 (22.85)		
Week 52 Mean (SD)	81.00 (20.55)	77.77 (19.69)		
Week 100 Mean (SD)	79.75 (19.66)	79.59 (20.59)		
Week 28: Adjusted Mean Change (SE)	8.84 (1.27)	7.77 (1.33)		
Week 52: Adjusted Mean Change (SE)	11.38 (1.44)	8.89 (1.47)	2.49 [-1.55; 6.53]	0.227
Week 100: Adjusted Mean Change (SE)	10.98 (1.52)	11.00 (1.54)	-0.02 [-4.27; 4.23]	0.992

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 450 - < 650 µm				
N'/ N	143 / 144	150 / 150		
Baseline Mean (SD)	65.38 (23.45)	65.92 (24.96)		
Week 52 Mean (SD)	79.03 (20.25)	77.87 (22.09)		
Week 100 Mean (SD)	79.34 (19.62)	79.29 (22.40)		
Week 28: Adjusted Mean Change (SE)	7.28 (1.44)	9.76 (1.41)		
Week 52: Adjusted Mean Change (SE)	12.26 (1.60)	11.09 (1.54)	1.17 [-3.19; 5.52]	0.599
Week 100: Adjusted Mean Change (SE)	12.10 (1.72)	11.96 (1.65)	0.14 [-4.53; 4.82]	0.952
≥ 650 µm				
N'/ N	32 / 32	39 / 39		
Baseline Mean (SD)	60.74 (23.51)	59.46 (29.03)		
Week 52 Mean (SD)	76.82 (20.06)	76.37 (21.22)		
Week 100 Mean (SD)	76.42 (20.13)	70.97 (24.07)		
Week 28: Adjusted Mean Change (SE)	5.83 (3.03)	12.00 (2.83)		
Week 52: Adjusted Mean Change (SE)	9.63 (3.56)	11.33 (3.11)	-1.69 [-10.97; 7.58]	0.720
Week 100: Adjusted Mean Change (SE)	8.46 (3.83)	6.76 (3.28)	1.70 [-8.19; 11.58]	0.736
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.132**				
KESTREL: Role Difficulties				
Interaction test	p=0.525			
< 450 µm				
N'/ N	107 / 107	96 / 96		
Baseline Mean (SD)	75.23 (28.21)	76.56 (24.95)		
Week 52 Mean (SD)	84.71 (22.69)	84.88 (22.77)		
Week 100 Mean (SD)	85.98 (22.26)	82.73 (23.89)		
Week 28: Adjusted Mean Change (SE)	6.44 (2.13)	9.96 (2.26)		
Week 52: Adjusted Mean Change (SE)	9.80 (2.33)	11.14 (2.40)	-1.34 [-7.90; 5.23]	0.688
Week 100: Adjusted Mean Change (SE)	12.19 (2.40)	9.65 (2.50)	2.54 [-4.28; 9.35]	0.465
≥ 450 - < 650 µm				
N'/ N	69 / 70	71 / 71		
Baseline Mean (SD)	68.30 (29.59)	70.77 (25.44)		
Week 52 Mean (SD)	77.50 (25.16)	84.63 (20.72)		
Week 100 Mean (SD)	76.82 (27.58)	77.55 (25.16)		
Week 28: Adjusted Mean Change (SE)	6.23 (2.62)	9.15 (2.64)		
Week 52: Adjusted Mean Change (SE)	4.04 (2.88)	13.01 (2.77)	-8.97 [-16.83; -1.12]	0.025 *
Week 100: Adjusted Mean Change (SE)	5.99 (2.93)	5.57 (2.95)	0.42 [-7.77; 8.60]	0.920

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 650 µm				
N'/ N	12 / 12	20 / 20		
Baseline Mean (SD)	64.58 (24.33)	52.50 (30.78)		
Week 52 Mean (SD)	62.50 (39.53)	68.75 (27.00)		
Week 100 Mean (SD)	66.07 (38.67)	72.66 (31.36)		
Week 28: Adjusted Mean Change (SE)	-2.82 (6.39)	4.08 (5.00)		
Week 52: Adjusted Mean Change (SE)	-8.91 (7.15)	1.43 (5.39)	-10.35 [-27.93; 7.23]	0.248
Week 100: Adjusted Mean Change (SE)	-2.28 (7.98)	5.32 (5.48)	-7.60 [-26.61; 11.41]	0.432
KITE: Role Difficulties				
Interaction test	p=0.689			
< 450 µm				
N'/ N	84 / 85	82 / 82		
Baseline Mean (SD)	76.64 (24.37)	70.58 (28.08)		
Week 52 Mean (SD)	83.73 (21.14)	79.92 (25.44)		
Week 100 Mean (SD)	84.79 (24.37)	81.15 (24.58)		
Week 28: Adjusted Mean Change (SE)	6.12 (2.35)	7.27 (2.41)		
Week 52: Adjusted Mean Change (SE)	9.99 (2.55)	8.07 (2.58)	1.91 [-5.21; 9.03]	0.597
Week 100: Adjusted Mean Change (SE)	8.19 (2.77)	8.59 (2.72)	-0.41 [-8.03; 7.22]	0.917
≥ 450 - < 650 µm				
N'/ N	74 / 74	79 / 79		
Baseline Mean (SD)	69.93 (27.21)	64.72 (30.01)		
Week 52 Mean (SD)	82.01 (23.42)	76.04 (25.15)		
Week 100 Mean (SD)	85.94 (21.59)	80.60 (25.86)		
Week 28: Adjusted Mean Change (SE)	8.29 (2.45)	7.92 (2.33)		
Week 52: Adjusted Mean Change (SE)	12.81 (2.52)	7.96 (2.41)	4.85 [-2.01; 11.71]	0.166
Week 100: Adjusted Mean Change (SE)	15.12 (2.86)	11.60 (2.65)	3.52 [-4.15; 11.19]	0.368
≥ 650 µm				
N'/ N	20 / 20	19 / 19		
Baseline Mean (SD)	51.88 (30.96)	62.50 (32.27)		
Week 52 Mean (SD)	83.33 (19.86)	79.69 (26.17)		
Week 100 Mean (SD)	82.50 (22.56)	74.17 (26.92)		
Week 28: Adjusted Mean Change (SE)	8.99 (4.63)	12.17 (4.97)		
Week 52: Adjusted Mean Change (SE)	20.14 (5.22)	11.25 (5.12)	8.89 [-5.47; 23.25]	0.224
Week 100: Adjusted Mean Change (SE)	14.33 (5.55)	5.89 (5.61)	8.44 [-7.06; 23.95]	0.285

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Role Difficulties				
Interaction test	p=0.994			
< 450 µm				
N'/ N	191 / 192	178 / 178		
Baseline Mean (SD)	75.85 (26.53)	73.81 (26.53)		
Week 52 Mean (SD)	84.29 (21.97)	82.75 (23.99)		
Week 100 Mean (SD)	85.48 (23.09)	82.01 (24.13)		
Week 28: Adjusted Mean Change (SE)	6.57 (1.59)	8.66 (1.65)		
Week 52: Adjusted Mean Change (SE)	10.16 (1.73)	9.75 (1.77)	0.41 [-4.44; 5.25]	0.868
Week 100: Adjusted Mean Change (SE)	10.83 (1.82)	9.15 (1.84)	1.69 [-3.39; 6.76]	0.515
≥ 450 - < 650 µm				
N'/ N	143 / 144	150 / 150		
Baseline Mean (SD)	69.14 (28.30)	67.58 (28.01)		
Week 52 Mean (SD)	79.96 (24.23)	79.98 (23.53)		
Week 100 Mean (SD)	81.42 (25.05)	79.24 (25.49)		
Week 28: Adjusted Mean Change (SE)	7.28 (1.80)	8.38 (1.75)		
Week 52: Adjusted Mean Change (SE)	8.68 (1.92)	10.19 (1.84)	-1.51 [-6.72; 3.70]	0.569
Week 100: Adjusted Mean Change (SE)	10.71 (2.05)	8.82 (1.97)	1.89 [-3.69; 7.48]	0.506
≥ 650 µm				
N'/ N	32 / 32	39 / 39		
Baseline Mean (SD)	56.64 (28.92)	57.37 (31.51)		
Week 52 Mean (SD)	75.52 (29.83)	74.22 (26.74)		
Week 100 Mean (SD)	77.27 (28.77)	73.39 (28.82)		
Week 28: Adjusted Mean Change (SE)	3.70 (3.78)	8.33 (3.53)		
Week 52: Adjusted Mean Change (SE)	8.23 (4.28)	6.72 (3.74)	1.51 [-9.61; 12.63]	0.790
Week 100: Adjusted Mean Change (SE)	7.52 (4.57)	5.83 (3.92)	1.69 [-10.11; 13.48]	0.779

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Dependency				
Test of heterogeneity in main analysis: **p_H=0.019 ***				
KESTREL: Dependency				
Interaction test	p=0.147			
< 450 µm				
N'/ N	107 / 107	96 / 96		
Baseline Mean (SD)	82.94 (25.63)	87.33 (20.94)		
Week 52 Mean (SD)	90.39 (20.63)	93.52 (15.98)		
Week 100 Mean (SD)	87.91 (22.19)	94.08 (13.25)		
Week 28: Adjusted Mean Change (SE)	6.99 (1.82)	5.04 (1.93)		
Week 52: Adjusted Mean Change (SE)	6.44 (1.90)	8.98 (1.97)	-2.54 [-7.92; 2.84]	0.354
Week 100: Adjusted Mean Change (SE)	5.08 (2.09)	9.67 (2.18)	-4.59 [-10.53; 1.36]	0.130
≥ 450 - < 650 µm				
N'/ N	69 / 70	71 / 71		
Baseline Mean (SD)	80.43 (26.11)	80.63 (23.64)		
Week 52 Mean (SD)	88.79 (20.36)	91.67 (18.51)		
Week 100 Mean (SD)	85.91 (20.59)	82.87 (25.20)		
Week 28: Adjusted Mean Change (SE)	5.70 (2.23)	9.18 (2.25)		
Week 52: Adjusted Mean Change (SE)	5.94 (2.36)	9.10 (2.27)	-3.15 [-9.59; 3.29]	0.336
Week 100: Adjusted Mean Change (SE)	3.66 (2.56)	1.13 (2.58)	2.53 [-4.61; 9.66]	0.487
≥ 650 µm				
N'/ N	12 / 12	20 / 20		
Baseline Mean (SD)	75.00 (34.82)	68.33 (30.78)		
Week 52 Mean (SD)	76.85 (37.45)	85.94 (15.73)		
Week 100 Mean (SD)	67.86 (33.83)	80.21 (28.03)		
Week 28: Adjusted Mean Change (SE)	-7.44 (5.44)	7.23 (4.26)		
Week 52: Adjusted Mean Change (SE)	-6.55 (5.86)	6.43 (4.41)	-12.98 [-27.40; 1.45]	0.078
Week 100: Adjusted Mean Change (SE)	-11.54 (7.02)	1.07 (4.77)	-12.62 [-29.31; 4.07]	0.138

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Dependency				
Interaction test	p=0.944			
< 450 µm				
N'/ N	84 / 85	82 / 82		
Baseline Mean (SD)	86.51 (21.25)	85.98 (22.10)		
Week 52 Mean (SD)	92.20 (18.98)	87.16 (20.95)		
Week 100 Mean (SD)	91.94 (16.02)	87.43 (21.73)		
Week 28: Adjusted Mean Change (SE)	5.02 (1.92)	1.60 (1.97)		
Week 52: Adjusted Mean Change (SE)	6.09 (2.11)	0.90 (2.15)	5.19 [-0.73; 11.10]	0.085
Week 100: Adjusted Mean Change (SE)	4.33 (2.27)	0.77 (2.24)	3.56 [-2.70; 9.82]	0.264
≥ 450 - < 650 µm				
N'/ N	74 / 74	79 / 79		
Baseline Mean (SD)	81.76 (25.61)	79.22 (29.86)		
Week 52 Mean (SD)	90.53 (19.71)	86.23 (24.11)		
Week 100 Mean (SD)	93.90 (14.08)	88.43 (22.56)		
Week 28: Adjusted Mean Change (SE)	5.70 (2.00)	3.55 (1.90)		
Week 52: Adjusted Mean Change (SE)	8.30 (2.10)	4.42 (2.01)	3.87 [-1.86; 9.60]	0.184
Week 100: Adjusted Mean Change (SE)	8.18 (2.35)	5.47 (2.17)	2.71 [-3.59; 9.01]	0.398
≥ 650 µm				
N'/ N	20 / 20	19 / 19		
Baseline Mean (SD)	76.67 (23.97)	74.56 (32.21)		
Week 52 Mean (SD)	88.89 (18.81)	86.46 (24.51)		
Week 100 Mean (SD)	94.44 (9.79)	81.67 (30.24)		
Week 28: Adjusted Mean Change (SE)	4.87 (3.76)	6.95 (4.07)		
Week 52: Adjusted Mean Change (SE)	7.94 (4.30)	5.37 (4.28)	2.56 [-9.35; 14.47]	0.672
Week 100: Adjusted Mean Change (SE)	10.01 (4.54)	0.58 (4.61)	9.43 [-3.28; 22.14]	0.146
Pooled Analysis: Dependency				
Interaction test	p=0.491			
< 450 µm				
N'/ N	191 / 192	178 / 178		
Baseline Mean (SD)	84.51 (23.81)	86.70 (21.43)		
Week 52 Mean (SD)	91.16 (19.90)	90.79 (18.48)		
Week 100 Mean (SD)	89.61 (19.85)	91.07 (17.85)		
Week 28: Adjusted Mean Change (SE)	6.29 (1.33)	3.26 (1.39)		
Week 52: Adjusted Mean Change (SE)	6.48 (1.42)	5.19 (1.46)	1.29 [-2.71; 5.29]	0.528
Week 100: Adjusted Mean Change (SE)	5.05 (1.55)	5.46 (1.58)	-0.41 [-4.75; 3.93]	0.853

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 450 - < 650 µm				
N'/ N	143 / 144	150 / 150		
Baseline Mean (SD)	81.12 (25.77)	79.89 (27.02)		
Week 52 Mean (SD)	89.74 (19.95)	88.72 (21.81)		
Week 100 Mean (SD)	89.94 (17.98)	85.95 (23.84)		
Week 28: Adjusted Mean Change (SE)	5.75 (1.51)	6.15 (1.47)		
Week 52: Adjusted Mean Change (SE)	7.18 (1.58)	6.63 (1.52)	0.55 [-3.76; 4.86]	0.803
Week 100: Adjusted Mean Change (SE)	6.07 (1.75)	3.66 (1.69)	2.41 [-2.36; 7.18]	0.321
≥ 650 µm				
N'/ N	32 / 32	39 / 39		
Baseline Mean (SD)	76.04 (27.98)	71.37 (31.23)		
Week 52 Mean (SD)	84.37 (27.18)	86.20 (20.26)		
Week 100 Mean (SD)	85.98 (23.48)	80.91 (28.64)		
Week 28: Adjusted Mean Change (SE)	-0.07 (3.16)	7.59 (2.96)		
Week 52: Adjusted Mean Change (SE)	2.14 (3.52)	6.30 (3.09)	-4.15 [-13.33; 5.03]	0.375
Week 100: Adjusted Mean Change (SE)	2.51 (3.91)	1.19 (3.34)	1.32 [-8.77; 11.41]	0.797
Driving				
Test of heterogeneity in main analysis: **p_H=0.792**				
KESTREL: Driving				
Interaction test	p=0.979			
< 450 µm				
N'/ N	69 / 107	61 / 96		
Baseline Mean (SD)	82.25 (17.85)	80.12 (19.16)		
Week 52 Mean (SD)	85.88 (18.65)	86.05 (16.26)		
Week 100 Mean (SD)	82.69 (20.67)	81.16 (21.09)		
Week 28: Adjusted Mean Change (SE)	3.10 (1.82)	6.19 (1.98)		
Week 52: Adjusted Mean Change (SE)	4.84 (2.08)	6.96 (2.27)	-2.12 [-8.19; 3.95]	0.492
Week 100: Adjusted Mean Change (SE)	1.68 (2.35)	2.53 (2.48)	-0.84 [-7.58; 5.89]	0.805
≥ 450 - < 650 µm				
N'/ N	45 / 70	47 / 71		
Baseline Mean (SD)	76.48 (19.89)	75.62 (20.49)		
Week 52 Mean (SD)	81.19 (22.36)	84.56 (17.42)		
Week 100 Mean (SD)	82.60 (17.93)	80.06 (19.95)		
Week 28: Adjusted Mean Change (SE)	0.76 (2.30)	3.13 (2.34)		
Week 52: Adjusted Mean Change (SE)	1.13 (2.65)	6.03 (2.72)	-4.91 [-12.40; 2.59]	0.198
Week 100: Adjusted Mean Change (SE)	3.02 (2.92)	1.42 (3.15)	1.60 [-6.87; 10.08]	0.710

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 650 µm				
N'/ N	6 / 12	12 / 20		
Baseline Mean (SD)	79.17 (15.59)	68.06 (16.98)		
Week 52 Mean (SD)	86.67 (21.73)	74.07 (26.82)		
Week 100 Mean (SD)	91.67 (8.33)	71.43 (31.13)		
Week 28: Adjusted Mean Change (SE)	-1.81 (5.94)	11.05 (4.52)		
Week 52: Adjusted Mean Change (SE)	4.12 (7.05)	-0.58 (5.22)	4.70 [-12.58; 21.99]	0.592
Week 100: Adjusted Mean Change (SE)	4.57 (9.19)	-2.39 (6.21)	6.97 [-14.88; 28.82]	0.530
KITE: Driving				
Interaction test	p=0.213			
< 450 µm				
N'/ N	53 / 85	51 / 82		
Baseline Mean (SD)	83.57 (18.17)	82.84 (23.37)		
Week 52 Mean (SD)	87.40 (15.15)	88.29 (18.58)		
Week 100 Mean (SD)	86.62 (12.34)	88.46 (14.26)		
Week 28: Adjusted Mean Change (SE)	-0.51 (2.02)	4.61 (2.16)		
Week 52: Adjusted Mean Change (SE)	3.37 (1.82)	5.05 (1.90)	-1.68 [-6.85; 3.50]	0.523
Week 100: Adjusted Mean Change (SE)	0.44 (2.00)	3.04 (2.00)	-2.61 [-8.18; 2.97]	0.358
≥ 450 - < 650 µm				
N'/ N	37 / 74	39 / 79		
Baseline Mean (SD)	74.10 (23.06)	79.81 (20.95)		
Week 52 Mean (SD)	85.61 (20.33)	86.52 (13.10)		
Week 100 Mean (SD)	87.08 (17.66)	85.48 (13.94)		
Week 28: Adjusted Mean Change (SE)	2.93 (2.46)	5.62 (2.30)		
Week 52: Adjusted Mean Change (SE)	7.81 (2.07)	4.25 (1.99)	3.56 [-2.10; 9.22]	0.216
Week 100: Adjusted Mean Change (SE)	9.51 (2.29)	3.06 (2.21)	6.45 [0.17; 12.73]	0.044 *
≥ 650 µm				
N'/ N	13 / 20	5 / 19		
Baseline Mean (SD)	74.36 (17.50)	91.67 (8.33)		
Week 52 Mean (SD)	89.17 (15.24)	91.67 (9.62)		
Week 100 Mean (SD)	82.50 (16.87)	83.33 (23.57)		
Week 28: Adjusted Mean Change (SE)	-0.07 (4.12)	6.94 (6.36)		
Week 52: Adjusted Mean Change (SE)	10.07 (3.72)	2.66 (5.82)	7.41 [-6.22; 21.05]	0.285
Week 100: Adjusted Mean Change (SE)	3.44 (3.99)	-5.67 (6.26)	9.11 [-5.54; 23.76]	0.221

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Driving				
Interaction test	p=0.476			
< 450 µm				
N'/ N	122 / 192	112 / 178		
Baseline Mean (SD)	82.82 (17.92)	81.36 (21.13)		
Week 52 Mean (SD)	86.50 (17.24)	87.02 (17.23)		
Week 100 Mean (SD)	84.35 (17.66)	84.43 (18.61)		
Week 28: Adjusted Mean Change (SE)	1.54 (1.36)	5.50 (1.46)		
Week 52: Adjusted Mean Change (SE)	4.15 (1.40)	6.19 (1.50)	-2.04 [-6.08; 2.00]	0.322
Week 100: Adjusted Mean Change (SE)	1.09 (1.59)	2.80 (1.63)	-1.72 [-6.19; 2.76]	0.451
≥ 450 - < 650 µm				
N'/ N	82 / 144	86 / 150		
Baseline Mean (SD)	75.41 (21.27)	77.52 (20.68)		
Week 52 Mean (SD)	83.33 (21.36)	85.54 (15.33)		
Week 100 Mean (SD)	84.70 (17.80)	82.91 (17.12)		
Week 28: Adjusted Mean Change (SE)	1.72 (1.68)	4.39 (1.65)		
Week 52: Adjusted Mean Change (SE)	4.59 (1.70)	5.17 (1.70)	-0.58 [-5.30; 4.15]	0.810
Week 100: Adjusted Mean Change (SE)	6.15 (1.90)	2.26 (1.94)	3.89 [-1.44; 9.22]	0.152
≥ 650 µm				
N'/ N	19 / 32	17 / 39		
Baseline Mean (SD)	75.88 (16.64)	75.00 (18.40)		
Week 52 Mean (SD)	88.33 (16.90)	79.49 (23.96)		
Week 100 Mean (SD)	84.62 (15.53)	75.76 (28.00)		
Week 28: Adjusted Mean Change (SE)	-0.88 (3.43)	9.33 (3.69)		
Week 52: Adjusted Mean Change (SE)	8.31 (3.64)	0.49 (3.85)	7.82 [-2.57; 18.21]	0.140
Week 100: Adjusted Mean Change (SE)	3.39 (4.16)	-3.70 (4.45)	7.09 [-4.87; 19.06]	0.245

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Color Vision				
Test of heterogeneity in main analysis: **p_H=0.477**				
KESTREL: Color Vision				
Interaction test	p=0.581			
< 450 µm				
N'/ N	105 / 107	96 / 96		
Baseline Mean (SD)	93.33 (17.08)	94.53 (15.48)		
Week 52 Mean (SD)	97.02 (10.56)	97.15 (9.80)		
Week 100 Mean (SD)	96.52 (10.39)	97.33 (8.79)		
Week 28: Adjusted Mean Change (SE)	3.52 (1.10)	4.05 (1.16)		
Week 52: Adjusted Mean Change (SE)	3.03 (1.15)	2.97 (1.19)	0.06 [-3.19; 3.32]	0.970
Week 100: Adjusted Mean Change (SE)	2.56 (1.35)	3.13 (1.38)	-0.57 [-4.37; 3.22]	0.766
≥ 450 - < 650 µm				
N'/ N	69 / 70	70 / 71		
Baseline Mean (SD)	92.75 (15.52)	93.21 (15.30)		
Week 52 Mean (SD)	96.36 (11.20)	94.58 (13.88)		
Week 100 Mean (SD)	92.73 (14.96)	91.51 (16.22)		
Week 28: Adjusted Mean Change (SE)	0.85 (1.34)	-0.03 (1.36)		
Week 52: Adjusted Mean Change (SE)	1.44 (1.41)	0.46 (1.37)	0.98 [-2.89; 4.85]	0.619
Week 100: Adjusted Mean Change (SE)	-1.28 (1.62)	-2.32 (1.64)	1.03 [-3.50; 5.56]	0.654
≥ 650 µm				
N'/ N	12 / 12	18 / 20		
Baseline Mean (SD)	91.67 (19.46)	94.44 (10.69)		
Week 52 Mean (SD)	94.44 (16.67)	94.64 (14.47)		
Week 100 Mean (SD)	89.29 (19.67)	96.43 (9.08)		
Week 28: Adjusted Mean Change (SE)	-3.67 (3.26)	-3.05 (2.62)		
Week 52: Adjusted Mean Change (SE)	-1.25 (3.52)	0.73 (2.80)	-1.98 [-10.82; 6.86]	0.660
Week 100: Adjusted Mean Change (SE)	-5.00 (4.47)	0.55 (3.20)	-5.56 [-16.36; 5.24]	0.312

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Color Vision				
Interaction test	p=0.452			
< 450 µm				
N'/ N	84 / 85	82 / 82		
Baseline Mean (SD)	92.56 (16.82)	93.60 (15.12)		
Week 52 Mean (SD)	97.18 (9.17)	95.00 (12.86)		
Week 100 Mean (SD)	98.33 (6.29)	95.49 (14.07)		
Week 28: Adjusted Mean Change (SE)	3.00 (1.23)	3.51 (1.26)		
Week 52: Adjusted Mean Change (SE)	4.77 (1.12)	2.45 (1.15)	2.32 [-0.84; 5.48]	0.150
Week 100: Adjusted Mean Change (SE)	5.78 (1.34)	2.87 (1.33)	2.91 [-0.81; 6.63]	0.125
≥ 450 - < 650 µm				
N'/ N	74 / 74	77 / 79		
Baseline Mean (SD)	91.55 (17.69)	90.58 (16.74)		
Week 52 Mean (SD)	97.73 (8.47)	93.57 (13.25)		
Week 100 Mean (SD)	96.82 (9.69)	95.38 (12.42)		
Week 28: Adjusted Mean Change (SE)	4.80 (1.27)	3.81 (1.22)		
Week 52: Adjusted Mean Change (SE)	6.00 (1.10)	2.65 (1.07)	3.36 [0.33; 6.38]	0.030 *
Week 100: Adjusted Mean Change (SE)	4.42 (1.40)	4.30 (1.30)	0.11 [-3.65; 3.88]	0.953
≥ 650 µm				
N'/ N	20 / 20	19 / 19		
Baseline Mean (SD)	92.50 (14.28)	88.16 (17.42)		
Week 52 Mean (SD)	98.33 (6.45)	100.00 (0.00)		
Week 100 Mean (SD)	95.00 (14.02)	91.67 (15.43)		
Week 28: Adjusted Mean Change (SE)	0.46 (2.38)	7.50 (2.58)		
Week 52: Adjusted Mean Change (SE)	7.76 (2.28)	9.15 (2.23)	-1.40 [-7.67; 4.88]	0.661
Week 100: Adjusted Mean Change (SE)	3.80 (2.68)	0.59 (2.69)	3.21 [-4.26; 10.68]	0.399
Pooled Analysis: Color Vision				
Interaction test	p=0.394			
< 450 µm				
N'/ N	189 / 192	178 / 178		
Baseline Mean (SD)	92.99 (16.92)	94.10 (15.28)		
Week 52 Mean (SD)	97.09 (9.96)	96.22 (11.23)		
Week 100 Mean (SD)	97.30 (8.87)	96.51 (11.46)		
Week 28: Adjusted Mean Change (SE)	3.50 (0.84)	3.89 (0.87)		
Week 52: Adjusted Mean Change (SE)	3.95 (0.81)	2.86 (0.83)	1.08 [-1.19; 3.35]	0.349
Week 100: Adjusted Mean Change (SE)	4.23 (0.96)	3.03 (0.97)	1.20 [-1.48; 3.88]	0.379

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 450 - < 650 µm				
N'/ N	143 / 144	147 / 150		
Baseline Mean (SD)	92.13 (16.63)	91.84 (16.07)		
Week 52 Mean (SD)	97.11 (9.78)	94.04 (13.50)		
Week 100 Mean (SD)	94.77 (12.71)	93.64 (14.32)		
Week 28: Adjusted Mean Change (SE)	2.87 (0.94)	1.89 (0.93)		
Week 52: Adjusted Mean Change (SE)	3.80 (0.89)	1.48 (0.86)	2.32 [-0.11; 4.75]	0.061
Week 100: Adjusted Mean Change (SE)	1.67 (1.08)	0.98 (1.04)	0.69 [-2.26; 3.63]	0.648
≥ 650 µm				
N'/ N	32 / 32	37 / 39		
Baseline Mean (SD)	92.19 (16.11)	91.22 (14.69)		
Week 52 Mean (SD)	96.88 (11.21)	97.50 (10.06)		
Week 100 Mean (SD)	93.18 (15.78)	93.97 (12.77)		
Week 28: Adjusted Mean Change (SE)	-1.50 (1.97)	2.19 (1.88)		
Week 52: Adjusted Mean Change (SE)	3.98 (1.98)	5.06 (1.78)	-1.08 [-6.31; 4.15]	0.685
Week 100: Adjusted Mean Change (SE)	0.02 (2.41)	0.63 (2.10)	-0.61 [-6.88; 5.66]	0.849
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.003 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.849			
< 450 µm				
N'/ N	106 / 107	96 / 96		
Baseline Mean (SD)	85.61 (21.25)	83.07 (22.21)		
Week 52 Mean (SD)	90.88 (18.44)	90.74 (16.51)		
Week 100 Mean (SD)	85.80 (22.34)	91.12 (18.58)		
Week 28: Adjusted Mean Change (SE)	4.05 (1.80)	6.43 (1.89)		
Week 52: Adjusted Mean Change (SE)	6.91 (1.83)	8.00 (1.88)	-1.10 [-6.26; 4.07]	0.677
Week 100: Adjusted Mean Change (SE)	2.26 (2.18)	8.40 (2.26)	-6.14 [-12.31; 0.04]	0.051
≥ 450 - < 650 µm				
N'/ N	69 / 70	70 / 71		
Baseline Mean (SD)	82.25 (21.90)	79.64 (22.64)		
Week 52 Mean (SD)	87.27 (20.34)	85.83 (18.04)		
Week 100 Mean (SD)	82.27 (21.34)	84.72 (21.94)		
Week 28: Adjusted Mean Change (SE)	1.20 (2.19)	8.09 (2.21)		
Week 52: Adjusted Mean Change (SE)	3.66 (2.27)	4.67 (2.19)	-1.00 [-7.21; 5.20]	0.750
Week 100: Adjusted Mean Change (SE)	-0.97 (2.65)	3.46 (2.67)	-4.42 [-11.83; 2.98]	0.241

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 650 µm				
N'/ N	12 / 12	20 / 20		
Baseline Mean (SD)	79.17 (25.75)	67.50 (27.02)		
Week 52 Mean (SD)	86.11 (25.34)	87.50 (22.36)		
Week 100 Mean (SD)	82.14 (27.82)	79.69 (24.53)		
Week 28: Adjusted Mean Change (SE)	-1.42 (5.34)	11.92 (4.19)		
Week 52: Adjusted Mean Change (SE)	4.63 (5.63)	11.53 (4.27)	-6.90 [-20.78; 6.97]	0.329
Week 100: Adjusted Mean Change (SE)	2.64 (7.32)	1.68 (4.95)	0.96 [-16.40; 18.32]	0.913
KITE: Peripheral Vision				
Interaction test	p=0.214			
< 450 µm				
N'/ N	84 / 85	81 / 82		
Baseline Mean (SD)	84.23 (20.45)	85.80 (20.13)		
Week 52 Mean (SD)	87.70 (18.44)	90.00 (16.08)		
Week 100 Mean (SD)	91.67 (15.72)	88.31 (18.51)		
Week 28: Adjusted Mean Change (SE)	4.24 (1.78)	4.96 (1.84)		
Week 52: Adjusted Mean Change (SE)	3.48 (1.92)	4.78 (1.98)	-1.29 [-6.73; 4.14]	0.640
Week 100: Adjusted Mean Change (SE)	6.08 (1.92)	2.50 (1.91)	3.58 [-1.75; 8.90]	0.188
≥ 450 - < 650 µm				
N'/ N	74 / 74	79 / 79		
Baseline Mean (SD)	83.78 (20.03)	83.54 (22.96)		
Week 52 Mean (SD)	90.91 (16.19)	85.42 (22.50)		
Week 100 Mean (SD)	92.41 (15.01)	87.31 (19.16)		
Week 28: Adjusted Mean Change (SE)	3.95 (1.86)	3.73 (1.76)		
Week 52: Adjusted Mean Change (SE)	7.26 (1.90)	2.23 (1.82)	5.04 [-0.15; 10.22]	0.057
Week 100: Adjusted Mean Change (SE)	7.58 (2.00)	3.57 (1.84)	4.01 [-1.34; 9.36]	0.141
≥ 650 µm				
N'/ N	20 / 20	19 / 19		
Baseline Mean (SD)	76.25 (18.98)	84.21 (20.77)		
Week 52 Mean (SD)	93.33 (14.84)	89.06 (15.73)		
Week 100 Mean (SD)	95.00 (14.02)	86.67 (18.58)		
Week 28: Adjusted Mean Change (SE)	8.33 (3.49)	5.78 (3.77)		
Week 52: Adjusted Mean Change (SE)	14.05 (3.94)	4.16 (3.87)	9.89 [-0.97; 20.76]	0.074
Week 100: Adjusted Mean Change (SE)	13.69 (3.85)	1.52 (3.89)	12.16 [1.39; 22.94]	0.027 *

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.805			
< 450 µm				
N'/ N	190 / 192	177 / 178		
Baseline Mean (SD)	85.00 (20.86)	84.32 (21.27)		
Week 52 Mean (SD)	89.53 (18.45)	90.43 (16.27)		
Week 100 Mean (SD)	88.30 (19.94)	89.86 (18.53)		
Week 28: Adjusted Mean Change (SE)	4.10 (1.27)	5.67 (1.33)		
Week 52: Adjusted Mean Change (SE)	5.53 (1.34)	6.55 (1.37)	-1.02 [-4.79; 2.74]	0.593
Week 100: Adjusted Mean Change (SE)	3.90 (1.48)	5.55 (1.50)	-1.65 [-5.78; 2.48]	0.433
≥ 450 - < 650 µm				
N'/ N	143 / 144	149 / 150		
Baseline Mean (SD)	83.04 (20.90)	81.71 (22.82)		
Week 52 Mean (SD)	89.26 (18.21)	85.61 (20.52)		
Week 100 Mean (SD)	87.39 (19.03)	86.16 (20.40)		
Week 28: Adjusted Mean Change (SE)	2.63 (1.44)	5.85 (1.40)		
Week 52: Adjusted Mean Change (SE)	5.46 (1.48)	3.49 (1.42)	1.97 [-2.06; 6.01]	0.337
Week 100: Adjusted Mean Change (SE)	3.38 (1.66)	3.66 (1.60)	-0.28 [-4.81; 4.25]	0.904
≥ 650 µm				
N'/ N	32 / 32	39 / 39		
Baseline Mean (SD)	77.34 (21.40)	75.64 (25.32)		
Week 52 Mean (SD)	90.63 (19.24)	88.28 (19.03)		
Week 100 Mean (SD)	90.91 (19.74)	83.06 (21.78)		
Week 28: Adjusted Mean Change (SE)	4.15 (3.02)	9.64 (2.83)		
Week 52: Adjusted Mean Change (SE)	9.86 (3.31)	8.64 (2.89)	1.22 [-7.39; 9.83]	0.781
Week 100: Adjusted Mean Change (SE)	8.97 (3.72)	2.44 (3.17)	6.53 [-3.05; 16.11]	0.181

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
General Health				
Test of heterogeneity in main analysis: **p_H=0.834**				
KESTREL: General Health				
Interaction test	p=0.850			
< 450 µm				
N'/ N	107 / 107	96 / 96		
Baseline Mean (SD)	43.46 (22.08)	38.28 (19.18)		
Week 52 Mean (SD)	51.76 (26.94)	47.53 (20.39)		
Week 100 Mean (SD)	50.30 (25.61)	50.33 (18.48)		
Week 28: Adjusted Mean Change (SE)	5.71 (1.83)	5.94 (1.94)		
Week 52: Adjusted Mean Change (SE)	8.49 (2.23)	7.56 (2.30)	0.94 [-5.38; 7.25]	0.771
Week 100: Adjusted Mean Change (SE)	8.66 (2.20)	9.73 (2.30)	-1.07 [-7.34; 5.19]	0.737
≥ 450 - < 650 µm				
N'/ N	69 / 70	71 / 71		
Baseline Mean (SD)	44.93 (19.45)	38.38 (19.74)		
Week 52 Mean (SD)	52.27 (20.57)	43.03 (22.88)		
Week 100 Mean (SD)	49.55 (20.12)	47.69 (25.82)		
Week 28: Adjusted Mean Change (SE)	2.97 (2.24)	5.19 (2.26)		
Week 52: Adjusted Mean Change (SE)	8.70 (2.77)	2.61 (2.66)	6.09 [-1.47; 13.65]	0.114
Week 100: Adjusted Mean Change (SE)	7.09 (2.70)	7.46 (2.72)	-0.37 [-7.90; 7.17]	0.923
≥ 650 µm				
N'/ N	12 / 12	20 / 20		
Baseline Mean (SD)	45.83 (23.44)	40.00 (26.16)		
Week 52 Mean (SD)	50.00 (17.68)	46.88 (22.13)		
Week 100 Mean (SD)	46.43 (17.25)	40.63 (15.48)		
Week 28: Adjusted Mean Change (SE)	1.79 (5.47)	-1.83 (4.25)		
Week 52: Adjusted Mean Change (SE)	5.09 (6.87)	4.78 (5.14)	0.32 [-16.55; 17.18]	0.971
Week 100: Adjusted Mean Change (SE)	3.18 (7.45)	-2.29 (5.00)	5.47 [-12.15; 23.10]	0.542

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Health				
Interaction test	p=0.933			
< 450 µm				
N'/ N	84 / 85	82 / 82		
Baseline Mean (SD)	44.35 (20.66)	46.04 (19.83)		
Week 52 Mean (SD)	51.98 (22.59)	52.05 (20.56)		
Week 100 Mean (SD)	52.08 (20.22)	54.76 (19.50)		
Week 28: Adjusted Mean Change (SE)	3.47 (2.05)	3.37 (2.11)		
Week 52: Adjusted Mean Change (SE)	7.10 (2.50)	5.86 (2.54)	1.24 [-5.76; 8.24]	0.728
Week 100: Adjusted Mean Change (SE)	6.36 (2.28)	8.35 (2.24)	-1.99 [-8.27; 4.29]	0.533
≥ 450 - < 650 µm				
N'/ N	74 / 74	79 / 79		
Baseline Mean (SD)	42.91 (20.90)	42.41 (24.79)		
Week 52 Mean (SD)	47.73 (21.81)	48.96 (26.35)		
Week 100 Mean (SD)	49.11 (20.21)	47.76 (24.51)		
Week 28: Adjusted Mean Change (SE)	4.79 (2.15)	5.91 (2.03)		
Week 52: Adjusted Mean Change (SE)	5.45 (2.46)	5.27 (2.35)	0.18 [-6.52; 6.89]	0.957
Week 100: Adjusted Mean Change (SE)	6.47 (2.36)	3.29 (2.17)	3.18 [-3.14; 9.50]	0.323
≥ 650 µm				
N'/ N	20 / 20	19 / 19		
Baseline Mean (SD)	46.25 (16.77)	46.05 (26.70)		
Week 52 Mean (SD)	46.67 (18.58)	48.44 (21.35)		
Week 100 Mean (SD)	51.67 (17.59)	50.00 (23.15)		
Week 28: Adjusted Mean Change (SE)	-0.58 (4.02)	1.09 (4.35)		
Week 52: Adjusted Mean Change (SE)	0.24 (5.11)	2.12 (5.00)	-1.88 [-15.95; 12.19]	0.793
Week 100: Adjusted Mean Change (SE)	4.76 (4.56)	4.19 (4.60)	0.57 [-12.18; 13.31]	0.930
Pooled Analysis: General Health				
Interaction test	p=0.876			
< 450 µm				
N'/ N	191 / 192	178 / 178		
Baseline Mean (SD)	43.85 (21.42)	41.85 (19.81)		
Week 52 Mean (SD)	51.86 (25.10)	49.47 (20.51)		
Week 100 Mean (SD)	51.06 (23.42)	52.34 (19.01)		
Week 28: Adjusted Mean Change (SE)	4.59 (1.37)	4.86 (1.43)		
Week 52: Adjusted Mean Change (SE)	7.71 (1.66)	6.90 (1.70)	0.81 [-3.85; 5.46]	0.734
Week 100: Adjusted Mean Change (SE)	7.57 (1.58)	9.21 (1.60)	-1.64 [-6.06; 2.78]	0.467

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 450 - < 650 µm				
N'/ N	143 / 144	150 / 150		
Baseline Mean (SD)	43.88 (20.17)	40.50 (22.56)		
Week 52 Mean (SD)	49.79 (21.29)	46.24 (24.90)		
Week 100 Mean (SD)	49.32 (20.07)	47.73 (25.00)		
Week 28: Adjusted Mean Change (SE)	3.83 (1.55)	5.64 (1.52)		
Week 52: Adjusted Mean Change (SE)	6.85 (1.84)	4.07 (1.76)	2.79 [-2.22; 7.79]	0.275
Week 100: Adjusted Mean Change (SE)	6.60 (1.79)	5.24 (1.72)	1.36 [-3.51; 6.22]	0.585
≥ 650 µm				
N'/ N	32 / 32	39 / 39		
Baseline Mean (SD)	46.09 (19.17)	42.95 (26.25)		
Week 52 Mean (SD)	47.92 (17.93)	47.66 (21.40)		
Week 100 Mean (SD)	50.00 (17.25)	45.16 (19.81)		
Week 28: Adjusted Mean Change (SE)	0.35 (3.25)	-0.34 (3.04)		
Week 52: Adjusted Mean Change (SE)	2.14 (4.12)	3.39 (3.58)	-1.25 [-11.95; 9.45]	0.818
Week 100: Adjusted Mean Change (SE)	4.45 (4.00)	0.89 (3.40)	3.56 [-6.74; 13.85]	0.498

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + CSFT + treatment * CSFT + visit * CSFT + treatment * CSFT * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + study + treatment * study + CSFT + treatment * CSFT + visit * CSFT + treatment * CSFT * visit.

Table 8.11 VFQ by status of SRF (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Composite Score				
Test of heterogeneity in main analysis: **p_H=0.049 ***				
KESTREL: Composite Score				
Interaction test	p=0.185			
presence				
N'/ N	61 / 62	61 / 61		
Baseline Mean (SD)	73.02 (19.90)	72.72 (16.06)		
Week 52 Mean (SD)	82.45 (16.49)	85.37 (12.20)		
Week 100 Mean (SD)	81.03 (16.94)	80.60 (16.48)		
Week 28: Adjusted Mean Change (SE)	5.16 (1.37)	10.32 (1.39)		
Week 52: Adjusted Mean Change (SE)	5.63 (1.49)	9.68 (1.44)	-4.04 [-8.10; 0.01]	0.051
Week 100: Adjusted Mean Change (SE)	5.26 (1.61)	5.31 (1.62)	-0.04 [-4.51; 4.42]	0.985
absence				
N'/ N	127 / 127	126 / 126		
Baseline Mean (SD)	78.38 (15.95)	78.80 (13.44)		
Week 52 Mean (SD)	86.19 (12.50)	85.05 (12.36)		
Week 100 Mean (SD)	84.12 (13.76)	84.66 (13.15)		
Week 28: Adjusted Mean Change (SE)	6.05 (0.97)	6.42 (0.99)		
Week 52: Adjusted Mean Change (SE)	7.66 (1.02)	7.48 (1.02)	0.18 [-2.63; 3.00]	0.898
Week 100: Adjusted Mean Change (SE)	6.56 (1.15)	7.16 (1.14)	-0.60 [-3.78; 2.58]	0.710
KITE: Composite Score				
Interaction test	p=0.123			
presence				
N'/ N	56 / 56	67 / 67		
Baseline Mean (SD)	74.47 (15.38)	75.11 (17.98)		
Week 52 Mean (SD)	87.42 (12.10)	83.95 (16.15)		
Week 100 Mean (SD)	90.44 (11.30)	83.57 (16.94)		
Week 28: Adjusted Mean Change (SE)	7.02 (1.36)	5.49 (1.23)		
Week 52: Adjusted Mean Change (SE)	11.31 (1.48)	7.42 (1.31)	3.89 [0.02; 7.76]	0.049 *
Week 100: Adjusted Mean Change (SE)	11.93 (1.75)	5.72 (1.52)	6.21 [1.66; 10.76]	0.008 *

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
absence				
N'/ N	122 / 123	114 / 114		
Baseline Mean (SD)	79.36 (14.61)	77.26 (17.51)		
Week 52 Mean (SD)	86.07 (13.25)	83.29 (15.42)		
Week 100 Mean (SD)	87.09 (12.39)	84.33 (14.38)		
Week 28: Adjusted Mean Change (SE)	5.10 (0.93)	6.13 (0.97)		
Week 52: Adjusted Mean Change (SE)	7.65 (0.99)	5.64 (1.03)	2.01 [-0.79; 4.81]	0.160
Week 100: Adjusted Mean Change (SE)	7.65 (1.15)	6.48 (1.16)	1.17 [-2.05; 4.39]	0.474
Pooled Analysis: Composite Score				
Interaction test	p=0.986			
presence				
N'/ N	117 / 118	128 / 128		
Baseline Mean (SD)	73.71 (17.82)	73.97 (17.07)		
Week 52 Mean (SD)	84.88 (14.65)	84.62 (14.37)		
Week 100 Mean (SD)	85.16 (15.39)	82.17 (16.71)		
Week 28: Adjusted Mean Change (SE)	6.13 (0.98)	7.88 (0.94)		
Week 52: Adjusted Mean Change (SE)	8.46 (1.06)	8.62 (0.98)	-0.17 [-2.99; 2.65]	0.908
Week 100: Adjusted Mean Change (SE)	8.42 (1.18)	5.62 (1.11)	2.80 [-0.37; 5.96]	0.083

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
absence				
N'/ N	249 / 250	240 / 240		
Baseline Mean (SD)	78.86 (15.29)	78.06 (15.49)		
Week 52 Mean (SD)	86.13 (12.84)	84.23 (13.85)		
Week 100 Mean (SD)	85.59 (13.15)	84.50 (13.72)		
Week 28: Adjusted Mean Change (SE)	5.59 (0.68)	6.17 (0.70)		
Week 52: Adjusted Mean Change (SE)	7.65 (0.71)	6.53 (0.73)	1.13 [-0.87; 3.13]	0.268
Week 100: Adjusted Mean Change (SE)	7.13 (0.81)	6.73 (0.81)	0.40 [-1.85; 2.66]	0.726
General Vision				
Test of heterogeneity in main analysis: **p_H=0.762**				
KESTREL: General Vision				
Interaction test	p=0.252			
presence				
N'/ N	61 / 62	61 / 61		
Baseline Mean (SD)	57.70 (16.77)	57.05 (14.06)		
Week 52 Mean (SD)	70.00 (14.45)	71.54 (12.11)		
Week 100 Mean (SD)	73.60 (14.25)	72.08 (10.71)		
Week 28: Adjusted Mean Change (SE)	11.10 (1.67)	12.90 (1.70)		
Week 52: Adjusted Mean Change (SE)	9.64 (1.84)	11.66 (1.75)	-2.03 [-6.99; 2.94]	0.422
Week 100: Adjusted Mean Change (SE)	13.50 (1.75)	12.00 (1.78)	1.50 [-3.40; 6.40]	0.547
absence				
N'/ N	127 / 127	126 / 126		
Baseline Mean (SD)	62.99 (17.29)	61.75 (14.76)		
Week 52 Mean (SD)	74.37 (13.84)	70.94 (13.28)		
Week 100 Mean (SD)	73.62 (15.30)	72.45 (12.69)		
Week 28: Adjusted Mean Change (SE)	11.49 (1.19)	9.64 (1.21)		
Week 52: Adjusted Mean Change (SE)	12.71 (1.24)	10.14 (1.23)	2.58 [-0.84; 6.00]	0.139
Week 100: Adjusted Mean Change (SE)	12.72 (1.27)	11.73 (1.25)	0.99 [-2.51; 4.49]	0.579

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Vision				
Interaction test	p=0.796			
presence				
N'/ N	56 / 56	67 / 67		
Baseline Mean (SD)	58.57 (16.56)	55.52 (19.33)		
Week 52 Mean (SD)	72.27 (14.45)	70.00 (19.91)		
Week 100 Mean (SD)	74.87 (10.97)	70.74 (16.81)		
Week 28: Adjusted Mean Change (SE)	10.64 (1.83)	10.35 (1.66)		
Week 52: Adjusted Mean Change (SE)	12.83 (2.07)	11.34 (1.82)	1.49 [-3.90; 6.89]	0.587
Week 100: Adjusted Mean Change (SE)	14.41 (2.17)	10.58 (1.87)	3.83 [-1.77; 9.44]	0.179
absence				
N'/ N	122 / 123	114 / 114		
Baseline Mean (SD)	63.28 (15.72)	62.46 (17.27)		
Week 52 Mean (SD)	73.00 (14.60)	70.87 (15.24)		
Week 100 Mean (SD)	73.26 (14.91)	70.43 (16.37)		
Week 28: Adjusted Mean Change (SE)	8.75 (1.25)	9.04 (1.31)		
Week 52: Adjusted Mean Change (SE)	11.18 (1.38)	9.56 (1.44)	1.62 [-2.29; 5.52]	0.416
Week 100: Adjusted Mean Change (SE)	11.25 (1.42)	8.92 (1.43)	2.33 [-1.62; 6.28]	0.246
Pooled Analysis: General Vision				
Interaction test	p=0.580			
presence				
N'/ N	117 / 118	128 / 128		
Baseline Mean (SD)	58.12 (16.61)	56.25 (16.98)		
Week 52 Mean (SD)	71.11 (14.41)	70.73 (16.63)		
Week 100 Mean (SD)	74.16 (12.86)	71.37 (14.21)		
Week 28: Adjusted Mean Change (SE)	10.91 (1.24)	11.56 (1.19)		
Week 52: Adjusted Mean Change (SE)	11.22 (1.38)	11.53 (1.27)	-0.31 [-3.98; 3.37]	0.870
Week 100: Adjusted Mean Change (SE)	13.98 (1.37)	11.30 (1.29)	2.69 [-1.00; 6.37]	0.152
absence				
N'/ N	249 / 250	240 / 240		
Baseline Mean (SD)	63.13 (16.50)	62.08 (15.97)		
Week 52 Mean (SD)	73.69 (14.20)	70.91 (14.18)		
Week 100 Mean (SD)	73.44 (15.07)	71.47 (14.58)		
Week 28: Adjusted Mean Change (SE)	10.11 (0.87)	9.33 (0.89)		
Week 52: Adjusted Mean Change (SE)	11.93 (0.93)	9.84 (0.94)	2.10 [-0.50; 4.69]	0.113
Week 100: Adjusted Mean Change (SE)	12.02 (0.95)	10.36 (0.94)	1.66 [-0.96; 4.28]	0.214

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Ocular Pain				
Test of heterogeneity in main analysis: **p_H=0.664**				
KESTREL: Ocular Pain				
Interaction test	p=0.216			
presence				
N'/ N	61 / 62	61 / 61		
Baseline Mean (SD)	84.84 (19.65)	82.17 (22.76)		
Week 52 Mean (SD)	88.04 (16.45)	88.46 (14.61)		
Week 100 Mean (SD)	84.75 (18.09)	83.33 (22.97)		
Week 28: Adjusted Mean Change (SE)	3.33 (2.27)	7.64 (2.30)		
Week 52: Adjusted Mean Change (SE)	3.45 (2.18)	6.02 (2.08)	-2.57 [-8.47; 3.34]	0.393
Week 100: Adjusted Mean Change (SE)	0.73 (2.29)	1.25 (2.32)	-0.52 [-6.91; 5.87]	0.873
absence				
N'/ N	127 / 127	126 / 126		
Baseline Mean (SD)	82.68 (20.11)	82.14 (19.39)		
Week 52 Mean (SD)	88.83 (15.65)	85.85 (16.91)		
Week 100 Mean (SD)	86.70 (17.18)	84.31 (18.94)		
Week 28: Adjusted Mean Change (SE)	2.47 (1.61)	2.87 (1.64)		
Week 52: Adjusted Mean Change (SE)	5.69 (1.47)	3.70 (1.47)	1.99 [-2.09; 6.07]	0.339
Week 100: Adjusted Mean Change (SE)	4.18 (1.65)	2.16 (1.63)	2.02 [-2.53; 6.58]	0.383
KITE: Ocular Pain				
Interaction test	p=0.997			
presence				
N'/ N	56 / 56	67 / 67		
Baseline Mean (SD)	85.27 (18.48)	83.58 (17.97)		
Week 52 Mean (SD)	90.34 (16.59)	90.09 (16.01)		
Week 100 Mean (SD)	91.99 (13.90)	91.20 (15.67)		
Week 28: Adjusted Mean Change (SE)	5.67 (2.09)	2.25 (1.89)		
Week 52: Adjusted Mean Change (SE)	5.83 (2.22)	5.93 (1.95)	-0.10 [-5.90; 5.70]	0.973
Week 100: Adjusted Mean Change (SE)	6.59 (2.31)	7.43 (1.97)	-0.84 [-6.80; 5.12]	0.782

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
absence				
N'/ N	122 / 123	114 / 114		
Baseline Mean (SD)	83.81 (17.80)	81.80 (22.01)		
Week 52 Mean (SD)	88.13 (16.61)	85.60 (18.71)		
Week 100 Mean (SD)	89.67 (16.01)	88.04 (16.67)		
Week 28: Adjusted Mean Change (SE)	3.79 (1.43)	4.78 (1.50)		
Week 52: Adjusted Mean Change (SE)	4.28 (1.48)	2.39 (1.54)	1.88 [-2.31; 6.08]	0.378
Week 100: Adjusted Mean Change (SE)	5.74 (1.51)	4.20 (1.51)	1.55 [-2.65; 5.74]	0.469
Pooled Analysis: Ocular Pain				
Interaction test	p=0.334			
presence				
N'/ N	117 / 118	128 / 128		
Baseline Mean (SD)	85.04 (19.02)	82.91 (20.32)		
Week 52 Mean (SD)	89.17 (16.46)	89.32 (15.32)		
Week 100 Mean (SD)	87.92 (16.69)	87.50 (19.74)		
Week 28: Adjusted Mean Change (SE)	4.47 (1.55)	4.73 (1.49)		
Week 52: Adjusted Mean Change (SE)	4.64 (1.56)	5.91 (1.43)	-1.27 [-5.42; 2.88]	0.548
Week 100: Adjusted Mean Change (SE)	3.44 (1.62)	4.50 (1.52)	-1.06 [-5.40; 3.29]	0.632
absence				
N'/ N	249 / 250	240 / 240		
Baseline Mean (SD)	83.23 (18.98)	81.98 (20.63)		
Week 52 Mean (SD)	88.49 (16.09)	85.73 (17.72)		
Week 100 Mean (SD)	88.17 (16.63)	86.12 (17.93)		
Week 28: Adjusted Mean Change (SE)	3.12 (1.08)	3.77 (1.12)		
Week 52: Adjusted Mean Change (SE)	5.01 (1.05)	3.11 (1.07)	1.90 [-1.03; 4.83]	0.204
Week 100: Adjusted Mean Change (SE)	5.01 (1.12)	3.12 (1.11)	1.89 [-1.20; 4.98]	0.230

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.450**				
KESTREL: Near Activities				
Interaction test	p=0.951			
presence				
N'/ N	61 / 62	61 / 61		
Baseline Mean (SD)	59.02 (27.45)	60.31 (22.74)		
Week 52 Mean (SD)	74.73 (23.64)	76.84 (21.22)		
Week 100 Mean (SD)	77.33 (21.95)	72.40 (20.06)		
Week 28: Adjusted Mean Change (SE)	12.25 (2.36)	15.12 (2.39)		
Week 52: Adjusted Mean Change (SE)	10.26 (2.68)	12.61 (2.56)	-2.35 [-9.60; 4.90]	0.524
Week 100: Adjusted Mean Change (SE)	13.45 (2.50)	8.39 (2.53)	5.06 [-1.89; 12.01]	0.153
absence				
N'/ N	127 / 127	126 / 126		
Baseline Mean (SD)	65.65 (25.33)	68.22 (20.97)		
Week 52 Mean (SD)	81.23 (20.00)	79.60 (19.59)		
Week 100 Mean (SD)	80.67 (20.12)	79.25 (21.35)		
Week 28: Adjusted Mean Change (SE)	12.24 (1.67)	13.90 (1.70)		
Week 52: Adjusted Mean Change (SE)	14.62 (1.81)	14.05 (1.80)	0.58 [-4.43; 5.58]	0.821
Week 100: Adjusted Mean Change (SE)	14.88 (1.79)	13.34 (1.78)	1.55 [-3.41; 6.50]	0.540
KITE: Near Activities				
Interaction test	p=0.113			
presence				
N'/ N	56 / 56	67 / 67		
Baseline Mean (SD)	63.91 (25.48)	66.11 (24.42)		
Week 52 Mean (SD)	79.36 (20.37)	78.30 (23.67)		
Week 100 Mean (SD)	85.36 (17.78)	75.31 (26.84)		
Week 28: Adjusted Mean Change (SE)	7.82 (2.45)	4.50 (2.21)		
Week 52: Adjusted Mean Change (SE)	12.62 (2.52)	10.14 (2.22)	2.48 [-4.10; 9.05]	0.459
Week 100: Adjusted Mean Change (SE)	16.47 (2.74)	5.21 (2.37)	11.26 [4.16; 18.36]	0.002 *

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
absence				
N'/ N	121 / 123	114 / 114		
Baseline Mean (SD)	73.04 (20.28)	71.35 (23.45)		
Week 52 Mean (SD)	80.42 (20.87)	78.85 (21.15)		
Week 100 Mean (SD)	83.24 (19.11)	79.62 (20.54)		
Week 28: Adjusted Mean Change (SE)	5.64 (1.67)	6.79 (1.74)		
Week 52: Adjusted Mean Change (SE)	9.13 (1.68)	8.28 (1.75)	0.84 [-3.91; 5.60]	0.727
Week 100: Adjusted Mean Change (SE)	10.15 (1.80)	8.98 (1.82)	1.17 [-3.85; 6.19]	0.647
Pooled Analysis: Near Activities				
Interaction test	p=0.363			
presence				
N'/ N	117 / 118	128 / 128		
Baseline Mean (SD)	61.36 (26.53)	63.35 (23.72)		
Week 52 Mean (SD)	76.99 (22.10)	77.61 (22.45)		
Week 100 Mean (SD)	80.85 (20.52)	73.94 (23.82)		
Week 28: Adjusted Mean Change (SE)	10.13 (1.72)	9.71 (1.64)		
Week 52: Adjusted Mean Change (SE)	11.36 (1.86)	11.57 (1.71)	-0.20 [-5.14; 4.73]	0.936
Week 100: Adjusted Mean Change (SE)	14.72 (1.85)	6.96 (1.73)	7.76 [2.81; 12.71]	0.002 *
absence				
N'/ N	248 / 250	240 / 240		
Baseline Mean (SD)	69.25 (23.26)	69.70 (22.19)		
Week 52 Mean (SD)	80.83 (20.38)	79.25 (20.28)		
Week 100 Mean (SD)	81.94 (19.61)	79.43 (20.91)		
Week 28: Adjusted Mean Change (SE)	9.14 (1.20)	10.28 (1.23)		
Week 52: Adjusted Mean Change (SE)	12.00 (1.25)	11.12 (1.27)	0.87 [-2.62; 4.36]	0.624
Week 100: Adjusted Mean Change (SE)	12.67 (1.27)	11.08 (1.27)	1.59 [-1.94; 5.11]	0.377

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Distance Activities				
Test of heterogeneity in main analysis: **p_H=0.046 ***				
KESTREL: Distance Activities				
Interaction test	p=0.733			
presence				
N'/ N	61 / 62	61 / 61		
Baseline Mean (SD)	70.63 (25.38)	70.15 (22.04)		
Week 52 Mean (SD)	83.33 (19.18)	85.34 (16.05)		
Week 100 Mean (SD)	81.17 (21.13)	79.34 (22.18)		
Week 28: Adjusted Mean Change (SE)	7.23 (2.06)	12.36 (2.09)		
Week 52: Adjusted Mean Change (SE)	8.28 (2.05)	10.53 (1.97)	-2.25 [-7.80; 3.29]	0.425
Week 100: Adjusted Mean Change (SE)	7.10 (2.15)	4.78 (2.18)	2.31 [-3.67; 8.30]	0.448
absence				
N'/ N	127 / 127	126 / 126		
Baseline Mean (SD)	77.49 (22.83)	77.88 (20.31)		
Week 52 Mean (SD)	86.33 (16.27)	84.94 (17.61)		
Week 100 Mean (SD)	82.14 (19.37)	85.08 (16.48)		
Week 28: Adjusted Mean Change (SE)	7.43 (1.46)	7.20 (1.49)		
Week 52: Adjusted Mean Change (SE)	9.27 (1.39)	8.94 (1.38)	0.33 [-3.51; 4.17]	0.867
Week 100: Adjusted Mean Change (SE)	6.26 (1.54)	8.92 (1.53)	-2.67 [-6.93; 1.60]	0.220
KITE: Distance Activities				
Interaction test	p=0.956			
presence				
N'/ N	56 / 56	67 / 67		
Baseline Mean (SD)	74.33 (22.85)	73.32 (23.03)		
Week 52 Mean (SD)	88.83 (16.66)	84.77 (18.43)		
Week 100 Mean (SD)	91.99 (15.07)	83.95 (19.23)		
Week 28: Adjusted Mean Change (SE)	6.34 (2.13)	5.42 (1.93)		
Week 52: Adjusted Mean Change (SE)	12.54 (2.04)	9.80 (1.80)	2.74 [-2.60; 8.08]	0.313
Week 100: Adjusted Mean Change (SE)	13.15 (2.26)	7.59 (1.96)	5.56 [-0.31; 11.43]	0.063

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
absence				
N'/ N	122 / 123	114 / 114		
Baseline Mean (SD)	78.07 (20.79)	77.89 (22.01)		
Week 52 Mean (SD)	87.54 (17.91)	84.15 (18.99)		
Week 100 Mean (SD)	88.00 (16.19)	83.74 (18.67)		
Week 28: Adjusted Mean Change (SE)	6.03 (1.45)	5.22 (1.52)		
Week 52: Adjusted Mean Change (SE)	10.69 (1.36)	6.86 (1.42)	3.83 [-0.03; 7.69]	0.052
Week 100: Adjusted Mean Change (SE)	10.46 (1.49)	6.34 (1.50)	4.12 [-0.03; 8.27]	0.051
Pooled Analysis: Distance Activities				
Interaction test	p=0.835			
presence				
N'/ N	117 / 118	128 / 128		
Baseline Mean (SD)	72.40 (24.17)	71.81 (22.53)		
Week 52 Mean (SD)	86.02 (18.11)	85.04 (17.27)		
Week 100 Mean (SD)	85.91 (19.39)	81.78 (20.70)		
Week 28: Adjusted Mean Change (SE)	6.96 (1.49)	8.76 (1.43)		
Week 52: Adjusted Mean Change (SE)	10.48 (1.45)	10.25 (1.33)	0.23 [-3.62; 4.08]	0.907
Week 100: Adjusted Mean Change (SE)	9.97 (1.55)	6.37 (1.46)	3.60 [-0.57; 7.77]	0.090
absence				
N'/ N	249 / 250	240 / 240		
Baseline Mean (SD)	77.78 (21.81)	77.88 (21.09)		
Week 52 Mean (SD)	86.93 (17.06)	84.57 (18.22)		
Week 100 Mean (SD)	85.04 (18.06)	84.43 (17.54)		
Week 28: Adjusted Mean Change (SE)	6.71 (1.04)	6.19 (1.07)		
Week 52: Adjusted Mean Change (SE)	9.95 (0.97)	7.90 (0.99)	2.05 [-0.67; 4.77]	0.140
Week 100: Adjusted Mean Change (SE)	8.32 (1.07)	7.62 (1.07)	0.70 [-2.27; 3.67]	0.642

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.023 ***				
KESTREL: Social Functioning				
Interaction test	p=0.531			
presence				
N'/ N	61 / 62	61 / 61		
Baseline Mean (SD)	85.45 (21.55)	85.66 (16.43)		
Week 52 Mean (SD)	89.67 (19.42)	91.35 (15.57)		
Week 100 Mean (SD)	90.25 (16.23)	87.24 (17.77)		
Week 28: Adjusted Mean Change (SE)	1.05 (1.58)	4.34 (1.60)		
Week 52: Adjusted Mean Change (SE)	0.19 (1.85)	2.46 (1.76)	-2.27 [-7.26; 2.72]	0.372
Week 100: Adjusted Mean Change (SE)	1.98 (2.09)	-1.63 (2.12)	3.62 [-2.23; 9.46]	0.224
absence				
N'/ N	127 / 127	126 / 126		
Baseline Mean (SD)	90.45 (17.36)	91.87 (14.86)		
Week 52 Mean (SD)	93.81 (12.36)	94.88 (12.22)		
Week 100 Mean (SD)	90.82 (17.60)	94.13 (12.84)		
Week 28: Adjusted Mean Change (SE)	1.84 (1.12)	3.86 (1.14)		
Week 52: Adjusted Mean Change (SE)	3.34 (1.24)	4.68 (1.24)	-1.34 [-4.79; 2.11]	0.446
Week 100: Adjusted Mean Change (SE)	1.23 (1.51)	4.21 (1.49)	-2.98 [-7.15; 1.19]	0.161
KITE: Social Functioning				
Interaction test	p=0.442			
presence				
N'/ N	56 / 56	67 / 67		
Baseline Mean (SD)	87.05 (19.80)	86.19 (20.43)		
Week 52 Mean (SD)	96.31 (8.77)	93.32 (13.08)		
Week 100 Mean (SD)	97.76 (9.01)	90.05 (19.48)		
Week 28: Adjusted Mean Change (SE)	3.76 (1.88)	3.83 (1.70)		
Week 52: Adjusted Mean Change (SE)	9.03 (1.64)	6.34 (1.44)	2.69 [-1.59; 6.96]	0.217
Week 100: Adjusted Mean Change (SE)	9.30 (2.11)	2.22 (1.81)	7.08 [1.62; 12.55]	0.011 *

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
absence				
N'/ N	122 / 123	114 / 114		
Baseline Mean (SD)	89.04 (16.12)	86.51 (19.76)		
Week 52 Mean (SD)	94.63 (13.09)	90.49 (15.66)		
Week 100 Mean (SD)	93.89 (15.34)	91.85 (15.22)		
Week 28: Adjusted Mean Change (SE)	3.70 (1.28)	3.86 (1.34)		
Week 52: Adjusted Mean Change (SE)	6.63 (1.09)	3.07 (1.14)	3.56 [0.47; 6.65]	0.024 *
Week 100: Adjusted Mean Change (SE)	5.71 (1.38)	4.61 (1.39)	1.10 [-2.75; 4.95]	0.574
Pooled Analysis: Social Functioning				
Interaction test	p=0.358			
presence				
N'/ N	117 / 118	128 / 128		
Baseline Mean (SD)	86.22 (20.66)	85.94 (18.56)		
Week 52 Mean (SD)	92.92 (15.46)	92.39 (14.28)		
Week 100 Mean (SD)	93.54 (13.99)	88.73 (18.66)		
Week 28: Adjusted Mean Change (SE)	2.52 (1.22)	4.09 (1.17)		
Week 52: Adjusted Mean Change (SE)	4.64 (1.25)	4.51 (1.14)	0.13 [-3.18; 3.44]	0.939
Week 100: Adjusted Mean Change (SE)	5.58 (1.48)	0.38 (1.39)	5.21 [1.23; 9.19]	0.010 *
absence				
N'/ N	249 / 250	240 / 240		
Baseline Mean (SD)	89.76 (16.74)	89.32 (17.53)		
Week 52 Mean (SD)	94.21 (12.70)	92.83 (14.07)		
Week 100 Mean (SD)	92.34 (16.55)	93.03 (14.05)		
Week 28: Adjusted Mean Change (SE)	2.75 (0.85)	3.77 (0.88)		
Week 52: Adjusted Mean Change (SE)	4.99 (0.84)	3.87 (0.85)	1.12 [-1.21; 3.46]	0.345
Week 100: Adjusted Mean Change (SE)	3.45 (1.02)	4.29 (1.02)	-0.84 [-3.68; 1.99]	0.561

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Mental Health				
Test of heterogeneity in main analysis: **p_H=0.200**				
KESTREL: Mental Health				
Interaction test	p=0.594			
presence				
N'/ N	61 / 62	61 / 61		
Baseline Mean (SD)	59.53 (25.40)	62.60 (26.77)		
Week 52 Mean (SD)	76.22 (21.60)	78.37 (17.87)		
Week 100 Mean (SD)	71.00 (23.10)	72.92 (24.47)		
Week 28: Adjusted Mean Change (SE)	5.19 (2.22)	10.96 (2.24)		
Week 52: Adjusted Mean Change (SE)	11.30 (2.38)	12.00 (2.27)	-0.70 [-7.14; 5.73]	0.830
Week 100: Adjusted Mean Change (SE)	6.80 (2.59)	8.03 (2.62)	-1.23 [-8.43; 5.97]	0.737
absence				
N'/ N	127 / 127	126 / 126		
Baseline Mean (SD)	68.41 (24.27)	70.98 (20.55)		
Week 52 Mean (SD)	79.31 (19.23)	78.83 (17.96)		
Week 100 Mean (SD)	76.93 (20.37)	79.91 (19.46)		
Week 28: Adjusted Mean Change (SE)	8.58 (1.57)	8.46 (1.60)		
Week 52: Adjusted Mean Change (SE)	10.20 (1.61)	10.70 (1.60)	-0.50 [-4.95; 3.94]	0.823
Week 100: Adjusted Mean Change (SE)	9.74 (1.86)	11.98 (1.84)	-2.24 [-7.37; 2.89]	0.391
KITE: Mental Health				
Interaction test	p=0.089			
presence				
N'/ N	56 / 56	67 / 67		
Baseline Mean (SD)	63.28 (21.49)	64.27 (26.29)		
Week 52 Mean (SD)	83.10 (20.29)	74.89 (27.19)		
Week 100 Mean (SD)	86.86 (15.02)	80.32 (22.82)		
Week 28: Adjusted Mean Change (SE)	9.40 (2.30)	7.46 (2.08)		
Week 52: Adjusted Mean Change (SE)	16.99 (2.79)	7.89 (2.46)	9.09 [1.79; 16.40]	0.015 *
Week 100: Adjusted Mean Change (SE)	17.82 (2.85)	11.50 (2.46)	6.31 [-1.07; 13.70]	0.094

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
absence				
N'/ N	122 / 123	114 / 114		
Baseline Mean (SD)	71.52 (21.18)	66.67 (25.92)		
Week 52 Mean (SD)	80.63 (20.96)	77.85 (21.08)		
Week 100 Mean (SD)	83.08 (16.48)	79.21 (22.03)		
Week 28: Adjusted Mean Change (SE)	7.91 (1.57)	9.84 (1.64)		
Week 52: Adjusted Mean Change (SE)	10.71 (1.86)	9.93 (1.94)	0.79 [-4.50; 6.07]	0.770
Week 100: Adjusted Mean Change (SE)	11.88 (1.88)	11.29 (1.89)	0.59 [-4.65; 5.83]	0.825
Pooled Analysis: Mental Health				
Interaction test	p=0.424			
presence				
N'/ N	117 / 118	128 / 128		
Baseline Mean (SD)	61.32 (23.59)	63.48 (26.43)		
Week 52 Mean (SD)	79.58 (21.13)	76.53 (23.22)		
Week 100 Mean (SD)	77.95 (21.38)	76.84 (23.79)		
Week 28: Adjusted Mean Change (SE)	7.29 (1.60)	9.15 (1.53)		
Week 52: Adjusted Mean Change (SE)	14.12 (1.83)	9.86 (1.68)	4.26 [-0.60; 9.12]	0.086
Week 100: Adjusted Mean Change (SE)	11.94 (1.92)	9.91 (1.80)	2.03 [-3.12; 7.18]	0.439
absence				
N'/ N	249 / 250	240 / 240		
Baseline Mean (SD)	69.93 (22.82)	68.93 (23.30)		
Week 52 Mean (SD)	79.96 (20.06)	78.38 (19.43)		
Week 100 Mean (SD)	79.97 (18.76)	79.57 (20.69)		
Week 28: Adjusted Mean Change (SE)	8.28 (1.11)	9.04 (1.14)		
Week 52: Adjusted Mean Change (SE)	10.48 (1.23)	10.26 (1.25)	0.22 [-3.22; 3.66]	0.901
Week 100: Adjusted Mean Change (SE)	10.88 (1.33)	11.57 (1.32)	-0.69 [-4.36; 2.98]	0.714

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.132**				
KESTREL: Role Difficulties				
Interaction test	p=0.078			
presence				
N'/ N	61 / 62	61 / 61		
Baseline Mean (SD)	65.37 (30.57)	68.44 (27.73)		
Week 52 Mean (SD)	76.09 (29.32)	85.34 (21.11)		
Week 100 Mean (SD)	76.75 (30.20)	79.43 (26.36)		
Week 28: Adjusted Mean Change (SE)	2.59 (2.77)	10.26 (2.80)		
Week 52: Adjusted Mean Change (SE)	2.91 (3.16)	13.76 (3.02)	-10.85 [-19.41; -2.29]	0.013 *
Week 100: Adjusted Mean Change (SE)	6.12 (3.13)	8.39 (3.16)	-2.26 [-10.96; 6.43]	0.609
absence				
N'/ N	127 / 127	126 / 126		
Baseline Mean (SD)	75.20 (27.19)	73.41 (26.08)		
Week 52 Mean (SD)	82.77 (23.16)	82.08 (23.66)		
Week 100 Mean (SD)	84.04 (22.78)	79.85 (24.91)		
Week 28: Adjusted Mean Change (SE)	7.41 (1.96)	8.40 (1.99)		
Week 52: Adjusted Mean Change (SE)	8.24 (2.14)	9.44 (2.12)	-1.20 [-7.12; 4.71]	0.689
Week 100: Adjusted Mean Change (SE)	10.50 (2.24)	7.29 (2.22)	3.21 [-2.99; 9.41]	0.309
KITE: Role Difficulties				
Interaction test	p=0.237			
presence				
N'/ N	56 / 56	67 / 67		
Baseline Mean (SD)	62.05 (27.49)	64.55 (30.51)		
Week 52 Mean (SD)	84.94 (20.98)	78.66 (25.65)		
Week 100 Mean (SD)	88.78 (21.03)	79.17 (28.11)		
Week 28: Adjusted Mean Change (SE)	8.33 (2.82)	8.78 (2.55)		
Week 52: Adjusted Mean Change (SE)	17.18 (3.03)	10.03 (2.66)	7.15 [-0.76; 15.06]	0.076
Week 100: Adjusted Mean Change (SE)	17.19 (3.38)	8.74 (2.92)	8.45 [-0.30; 17.21]	0.058

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
absence				
N'/ N	122 / 123	114 / 114		
Baseline Mean (SD)	75.20 (26.26)	68.75 (28.62)		
Week 52 Mean (SD)	82.00 (22.43)	77.85 (25.14)		
Week 100 Mean (SD)	83.42 (23.52)	80.98 (23.62)		
Week 28: Adjusted Mean Change (SE)	6.94 (1.92)	7.76 (2.01)		
Week 52: Adjusted Mean Change (SE)	10.10 (2.02)	7.43 (2.10)	2.67 [-3.05; 8.40]	0.359
Week 100: Adjusted Mean Change (SE)	9.52 (2.23)	10.39 (2.24)	-0.87 [-7.08; 5.34]	0.784
Pooled Analysis: Role Difficulties				
Interaction test	p=0.596			
presence				
N'/ N	117 / 118	128 / 128		
Baseline Mean (SD)	63.78 (29.06)	66.41 (29.17)		
Week 52 Mean (SD)	80.42 (25.83)	81.82 (23.74)		
Week 100 Mean (SD)	82.02 (27.11)	79.29 (27.16)		
Week 28: Adjusted Mean Change (SE)	5.35 (1.98)	9.50 (1.90)		
Week 52: Adjusted Mean Change (SE)	9.80 (2.20)	11.79 (2.01)	-1.99 [-7.82; 3.83]	0.502
Week 100: Adjusted Mean Change (SE)	11.38 (2.29)	8.62 (2.15)	2.76 [-3.38; 8.90]	0.377
absence				
N'/ N	249 / 250	240 / 240		
Baseline Mean (SD)	75.20 (26.68)	71.20 (27.36)		
Week 52 Mean (SD)	82.39 (22.75)	80.11 (24.39)		
Week 100 Mean (SD)	83.74 (23.09)	80.39 (24.24)		
Week 28: Adjusted Mean Change (SE)	7.21 (1.38)	8.03 (1.42)		
Week 52: Adjusted Mean Change (SE)	9.19 (1.48)	8.51 (1.50)	0.68 [-3.44; 4.81]	0.744
Week 100: Adjusted Mean Change (SE)	10.07 (1.58)	8.75 (1.58)	1.32 [-3.06; 5.70]	0.555

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Dependency				
Test of heterogeneity in main analysis: **p_H=0.019 ***				
KESTREL: Dependency				
Interaction test	p=0.197			
presence				
N'/ N	61 / 62	61 / 61		
Baseline Mean (SD)	76.09 (28.48)	78.01 (27.13)		
Week 52 Mean (SD)	85.87 (25.21)	92.95 (16.29)		
Week 100 Mean (SD)	82.67 (23.98)	84.90 (25.65)		
Week 28: Adjusted Mean Change (SE)	2.66 (2.37)	9.27 (2.40)		
Week 52: Adjusted Mean Change (SE)	4.22 (2.58)	10.72 (2.46)	-6.50 [-13.46; 0.47]	0.068
Week 100: Adjusted Mean Change (SE)	1.72 (2.75)	3.75 (2.79)	-2.03 [-9.69; 5.63]	0.602
absence				
N'/ N	127 / 127	126 / 126		
Baseline Mean (SD)	84.12 (25.01)	85.05 (21.74)		
Week 52 Mean (SD)	90.37 (20.20)	91.59 (17.42)		
Week 100 Mean (SD)	88.03 (21.54)	90.14 (18.16)		
Week 28: Adjusted Mean Change (SE)	7.12 (1.68)	5.59 (1.71)		
Week 52: Adjusted Mean Change (SE)	6.12 (1.74)	7.80 (1.73)	-1.67 [-6.49; 3.14]	0.494
Week 100: Adjusted Mean Change (SE)	4.64 (1.98)	6.44 (1.96)	-1.79 [-7.25; 3.67]	0.519
KITE: Dependency				
Interaction test	p=0.334			
presence				
N'/ N	56 / 56	67 / 67		
Baseline Mean (SD)	81.10 (22.56)	80.72 (29.06)		
Week 52 Mean (SD)	92.61 (17.90)	86.21 (25.34)		
Week 100 Mean (SD)	95.73 (12.07)	86.42 (25.76)		
Week 28: Adjusted Mean Change (SE)	4.75 (2.30)	1.81 (2.08)		
Week 52: Adjusted Mean Change (SE)	9.37 (2.52)	3.21 (2.23)	6.16 [-0.44; 12.76]	0.067
Week 100: Adjusted Mean Change (SE)	8.71 (2.79)	1.22 (2.41)	7.50 [0.26; 14.73]	0.042 *

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
absence				
N'/ N	122 / 123	114 / 114		
Baseline Mean (SD)	84.49 (24.01)	82.60 (25.80)		
Week 52 Mean (SD)	90.42 (19.80)	87.05 (21.02)		
Week 100 Mean (SD)	91.94 (15.40)	87.95 (21.27)		
Week 28: Adjusted Mean Change (SE)	5.50 (1.57)	3.80 (1.64)		
Week 52: Adjusted Mean Change (SE)	6.29 (1.68)	2.88 (1.75)	3.41 [-1.36; 8.19]	0.161
Week 100: Adjusted Mean Change (SE)	5.71 (1.83)	3.89 (1.85)	1.81 [-3.31; 6.93]	0.487
Pooled Analysis: Dependency				
Interaction test	p=0.771			
presence				
N'/ N	117 / 118	128 / 128		
Baseline Mean (SD)	78.49 (25.83)	79.43 (28.08)		
Week 52 Mean (SD)	89.17 (22.08)	89.39 (21.71)		
Week 100 Mean (SD)	88.39 (20.63)	85.70 (25.59)		
Week 28: Adjusted Mean Change (SE)	3.86 (1.67)	5.60 (1.60)		
Week 52: Adjusted Mean Change (SE)	6.92 (1.81)	7.02 (1.67)	-0.10 [-4.92; 4.72]	0.967
Week 100: Adjusted Mean Change (SE)	5.21 (1.96)	2.71 (1.83)	2.50 [-2.75; 7.75]	0.350
absence				
N'/ N	249 / 250	240 / 240		
Baseline Mean (SD)	84.30 (24.48)	83.89 (23.74)		
Week 52 Mean (SD)	90.39 (19.95)	89.48 (19.26)		
Week 100 Mean (SD)	89.96 (18.81)	89.08 (19.70)		
Week 28: Adjusted Mean Change (SE)	6.29 (1.16)	4.55 (1.20)		
Week 52: Adjusted Mean Change (SE)	6.16 (1.22)	5.31 (1.24)	0.85 [-2.56; 4.26]	0.624
Week 100: Adjusted Mean Change (SE)	5.23 (1.35)	5.07 (1.35)	0.16 [-3.58; 3.90]	0.932

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Driving				
Test of heterogeneity in main analysis: **p_H=0.792**				
KESTREL: Driving				
Interaction test	p=0.230			
presence				
N'/ N	34 / 62	45 / 61		
Baseline Mean (SD)	79.66 (19.16)	72.69 (17.44)		
Week 52 Mean (SD)	86.22 (17.31)	83.82 (18.91)		
Week 100 Mean (SD)	86.00 (17.13)	78.42 (22.82)		
Week 28: Adjusted Mean Change (SE)	-1.37 (2.52)	8.56 (2.35)		
Week 52: Adjusted Mean Change (SE)	1.69 (3.05)	6.69 (2.74)	-5.00 [-13.05; 3.04]	0.221
Week 100: Adjusted Mean Change (SE)	0.92 (3.38)	1.08 (3.17)	-0.16 [-9.25; 8.92]	0.972
absence				
N'/ N	86 / 127	75 / 126		
Baseline Mean (SD)	80.04 (18.49)	79.83 (20.57)		
Week 52 Mean (SD)	83.56 (21.06)	84.63 (17.65)		
Week 100 Mean (SD)	81.77 (20.08)	80.76 (21.03)		
Week 28: Adjusted Mean Change (SE)	3.41 (1.65)	3.68 (1.81)		
Week 52: Adjusted Mean Change (SE)	4.25 (1.87)	5.36 (2.09)	-1.11 [-6.64; 4.41]	0.692
Week 100: Adjusted Mean Change (SE)	2.82 (2.11)	1.83 (2.30)	0.99 [-5.16; 7.14]	0.751
KITE: Driving				
Interaction test	p=0.452			
presence				
N'/ N	32 / 56	34 / 67		
Baseline Mean (SD)	75.78 (22.64)	77.21 (24.90)		
Week 52 Mean (SD)	88.19 (20.69)	86.73 (15.02)		
Week 100 Mean (SD)	89.29 (17.71)	83.67 (16.04)		
Week 28: Adjusted Mean Change (SE)	0.79 (2.66)	5.50 (2.50)		
Week 52: Adjusted Mean Change (SE)	8.11 (2.37)	4.99 (2.22)	3.13 [-3.27; 9.53]	0.336
Week 100: Adjusted Mean Change (SE)	6.98 (2.70)	1.97 (2.48)	5.01 [-2.20; 12.22]	0.172

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
absence				
N'/ N	71 / 123	62 / 114		
Baseline Mean (SD)	80.46 (19.23)	84.74 (19.53)		
Week 52 Mean (SD)	86.39 (15.79)	88.44 (16.28)		
Week 100 Mean (SD)	85.16 (13.93)	88.83 (13.53)		
Week 28: Adjusted Mean Change (SE)	0.72 (1.73)	5.23 (1.90)		
Week 52: Adjusted Mean Change (SE)	4.91 (1.51)	4.63 (1.66)	0.29 [-4.16; 4.73]	0.899
Week 100: Adjusted Mean Change (SE)	3.16 (1.67)	3.19 (1.79)	-0.03 [-4.86; 4.81]	0.992
Pooled Analysis: Driving				
Interaction test	p=0.634			
presence				
N'/ N	66 / 118	79 / 128		
Baseline Mean (SD)	77.78 (20.84)	74.63 (20.95)		
Week 52 Mean (SD)	87.17 (18.84)	85.11 (17.22)		
Week 100 Mean (SD)	87.50 (17.28)	80.90 (19.91)		
Week 28: Adjusted Mean Change (SE)	-0.15 (1.83)	7.25 (1.71)		
Week 52: Adjusted Mean Change (SE)	5.22 (1.96)	6.12 (1.79)	-0.90 [-6.09; 4.28]	0.732
Week 100: Adjusted Mean Change (SE)	4.03 (2.21)	1.72 (2.05)	2.31 [-3.59; 8.22]	0.442
absence				
N'/ N	157 / 250	137 / 240		
Baseline Mean (SD)	80.23 (18.77)	82.06 (20.18)		
Week 52 Mean (SD)	84.84 (18.85)	86.37 (17.06)		
Week 100 Mean (SD)	83.37 (17.47)	84.60 (18.23)		
Week 28: Adjusted Mean Change (SE)	2.07 (1.20)	4.30 (1.32)		
Week 52: Adjusted Mean Change (SE)	4.51 (1.22)	4.96 (1.35)	-0.45 [-4.03; 3.13]	0.806
Week 100: Adjusted Mean Change (SE)	2.90 (1.38)	2.37 (1.49)	0.53 [-3.45; 4.52]	0.793

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Color Vision				
Test of heterogeneity in main analysis: **p_H=0.477**				
KESTREL: Color Vision				
Interaction test	p=0.235			
presence				
N'/ N	60 / 62	58 / 61		
Baseline Mean (SD)	90.42 (17.28)	91.81 (15.80)		
Week 52 Mean (SD)	95.00 (14.69)	95.92 (12.86)		
Week 100 Mean (SD)	91.33 (17.34)	93.18 (14.63)		
Week 28: Adjusted Mean Change (SE)	0.10 (1.45)	1.82 (1.48)		
Week 52: Adjusted Mean Change (SE)	0.53 (1.56)	1.84 (1.52)	-1.31 [-5.57; 2.95]	0.545
Week 100: Adjusted Mean Change (SE)	-2.40 (1.74)	-1.09 (1.82)	-1.30 [-6.23; 3.62]	0.603
absence				
N'/ N	126 / 127	126 / 126		
Baseline Mean (SD)	94.25 (16.17)	95.04 (14.50)		
Week 52 Mean (SD)	97.33 (9.20)	95.91 (11.61)		
Week 100 Mean (SD)	96.47 (9.51)	95.92 (11.18)		
Week 28: Adjusted Mean Change (SE)	3.02 (1.02)	1.77 (1.04)		
Week 52: Adjusted Mean Change (SE)	2.95 (1.04)	1.80 (1.04)	1.16 [-1.74; 4.05]	0.432
Week 100: Adjusted Mean Change (SE)	2.24 (1.25)	1.73 (1.22)	0.51 [-2.92; 3.95]	0.770
KITE: Color Vision				
Interaction test	p=0.432			
presence				
N'/ N	56 / 56	66 / 67		
Baseline Mean (SD)	90.18 (18.26)	92.05 (15.29)		
Week 52 Mean (SD)	97.67 (7.35)	94.74 (12.26)		
Week 100 Mean (SD)	97.44 (7.68)	93.87 (16.19)		
Week 28: Adjusted Mean Change (SE)	4.89 (1.48)	4.96 (1.34)		
Week 52: Adjusted Mean Change (SE)	6.34 (1.37)	3.19 (1.19)	3.14 [-0.42; 6.70]	0.083
Week 100: Adjusted Mean Change (SE)	5.02 (1.66)	1.94 (1.43)	3.08 [-1.22; 7.37]	0.159

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
absence				
N'/ N	122 / 123	113 / 114		
Baseline Mean (SD)	93.03 (16.15)	91.59 (16.57)		
Week 52 Mean (SD)	97.50 (9.06)	95.00 (12.54)		
Week 100 Mean (SD)	97.25 (9.47)	95.79 (11.45)		
Week 28: Adjusted Mean Change (SE)	2.78 (1.00)	3.46 (1.05)		
Week 52: Adjusted Mean Change (SE)	5.28 (0.90)	3.31 (0.95)	1.97 [-0.59; 4.53]	0.132
Week 100: Adjusted Mean Change (SE)	4.91 (1.09)	4.08 (1.10)	0.83 [-2.20; 3.87]	0.590
Pooled Analysis: Color Vision				
Interaction test	p=0.653			
presence				
N'/ N	116 / 118	124 / 128		
Baseline Mean (SD)	90.30 (17.68)	91.94 (15.47)		
Week 52 Mean (SD)	96.31 (11.71)	95.28 (12.49)		
Week 100 Mean (SD)	94.03 (14.18)	93.56 (15.43)		
Week 28: Adjusted Mean Change (SE)	2.54 (1.05)	3.51 (1.01)		
Week 52: Adjusted Mean Change (SE)	3.48 (1.04)	2.51 (0.95)	0.96 [-1.79; 3.72]	0.493
Week 100: Adjusted Mean Change (SE)	1.25 (1.21)	0.30 (1.15)	0.95 [-2.31; 4.21]	0.568
absence				
N'/ N	248 / 250	239 / 240		
Baseline Mean (SD)	93.65 (16.14)	93.41 (15.58)		
Week 52 Mean (SD)	97.41 (9.11)	95.49 (12.03)		
Week 100 Mean (SD)	96.86 (9.47)	95.86 (11.28)		
Week 28: Adjusted Mean Change (SE)	2.90 (0.73)	2.52 (0.75)		
Week 52: Adjusted Mean Change (SE)	4.06 (0.69)	2.48 (0.70)	1.58 [-0.35; 3.50]	0.109
Week 100: Adjusted Mean Change (SE)	3.59 (0.83)	2.79 (0.83)	0.80 [-1.51; 3.10]	0.497

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.003 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.226			
presence				
N'/ N	61 / 62	61 / 61		
Baseline Mean (SD)	82.38 (25.14)	75.41 (23.49)		
Week 52 Mean (SD)	86.41 (22.80)	89.42 (17.40)		
Week 100 Mean (SD)	82.00 (24.76)	85.42 (21.16)		
Week 28: Adjusted Mean Change (SE)	3.69 (2.30)	11.52 (2.35)		
Week 52: Adjusted Mean Change (SE)	2.90 (2.48)	8.85 (2.36)	-5.96 [-12.67; 0.76]	0.082
Week 100: Adjusted Mean Change (SE)	-0.91 (2.79)	4.47 (2.84)	-5.38 [-13.19; 2.44]	0.177
absence				
N'/ N	126 / 127	125 / 126		
Baseline Mean (SD)	84.72 (19.99)	82.40 (22.90)		
Week 52 Mean (SD)	90.53 (17.89)	88.10 (18.05)		
Week 100 Mean (SD)	85.48 (20.63)	88.52 (20.67)		
Week 28: Adjusted Mean Change (SE)	2.05 (1.65)	5.67 (1.67)		
Week 52: Adjusted Mean Change (SE)	6.74 (1.67)	6.23 (1.66)	0.51 [-4.11; 5.14]	0.827
Week 100: Adjusted Mean Change (SE)	2.05 (2.03)	6.47 (1.99)	-4.42 [-10.01; 1.16]	0.120
KITE: Peripheral Vision				
Interaction test	p=0.125			
presence				
N'/ N	56 / 56	66 / 67		
Baseline Mean (SD)	80.80 (21.32)	86.36 (21.11)		
Week 52 Mean (SD)	90.91 (16.26)	89.47 (18.87)		
Week 100 Mean (SD)	96.15 (12.22)	87.74 (19.38)		
Week 28: Adjusted Mean Change (SE)	5.88 (2.13)	2.55 (1.94)		
Week 52: Adjusted Mean Change (SE)	8.53 (2.32)	4.51 (2.05)	4.02 [-2.07; 10.10]	0.195
Week 100: Adjusted Mean Change (SE)	11.05 (2.36)	2.03 (2.05)	9.02 [2.87; 15.16]	0.004 *

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
absence				
N'/ N	122 / 123	114 / 114		
Baseline Mean (SD)	84.22 (19.60)	83.77 (21.55)		
Week 52 Mean (SD)	89.25 (17.50)	86.68 (19.77)		
Week 100 Mean (SD)	90.76 (16.03)	87.77 (18.34)		
Week 28: Adjusted Mean Change (SE)	3.97 (1.45)	5.65 (1.52)		
Week 52: Adjusted Mean Change (SE)	5.33 (1.54)	2.83 (1.61)	2.50 [-1.88; 6.88]	0.262
Week 100: Adjusted Mean Change (SE)	6.10 (1.55)	3.41 (1.56)	2.69 [-1.63; 7.00]	0.221
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.912			
presence				
N'/ N	117 / 118	127 / 128		
Baseline Mean (SD)	81.62 (23.30)	81.10 (22.87)		
Week 52 Mean (SD)	88.61 (19.89)	89.45 (18.10)		
Week 100 Mean (SD)	88.20 (21.35)	86.63 (20.18)		
Week 28: Adjusted Mean Change (SE)	4.71 (1.58)	7.20 (1.52)		
Week 52: Adjusted Mean Change (SE)	5.54 (1.71)	6.98 (1.57)	-1.44 [-5.98; 3.11]	0.534
Week 100: Adjusted Mean Change (SE)	4.50 (1.86)	3.54 (1.75)	0.96 [-4.04; 5.95]	0.707
absence				
N'/ N	248 / 250	239 / 240		
Baseline Mean (SD)	84.48 (19.76)	83.05 (22.23)		
Week 52 Mean (SD)	89.90 (17.67)	87.44 (18.83)		
Week 100 Mean (SD)	88.11 (18.63)	88.16 (19.53)		
Week 28: Adjusted Mean Change (SE)	2.91 (1.11)	5.58 (1.14)		
Week 52: Adjusted Mean Change (SE)	5.97 (1.14)	4.59 (1.17)	1.38 [-1.83; 4.58]	0.399
Week 100: Adjusted Mean Change (SE)	3.92 (1.29)	4.88 (1.28)	-0.97 [-4.52; 2.59]	0.594

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
General Health				
Test of heterogeneity in main analysis: **p_H=0.834**				
KESTREL: General Health				
Interaction test	p=0.680			
presence				
N'/ N	61 / 62	61 / 61		
Baseline Mean (SD)	41.39 (21.35)	39.34 (22.57)		
Week 52 Mean (SD)	46.20 (24.13)	44.71 (23.40)		
Week 100 Mean (SD)	46.50 (22.02)	46.35 (21.26)		
Week 28: Adjusted Mean Change (SE)	4.01 (2.37)	4.46 (2.41)		
Week 52: Adjusted Mean Change (SE)	4.24 (3.00)	3.20 (2.86)	1.04 [-7.08; 9.16]	0.801
Week 100: Adjusted Mean Change (SE)	4.30 (2.84)	4.92 (2.89)	-0.63 [-8.58; 7.32]	0.877
absence				
N'/ N	127 / 127	126 / 126		
Baseline Mean (SD)	45.47 (20.99)	38.10 (18.90)		
Week 52 Mean (SD)	54.37 (23.85)	46.23 (20.64)		
Week 100 Mean (SD)	51.60 (23.71)	49.23 (21.37)		
Week 28: Adjusted Mean Change (SE)	4.66 (1.70)	4.99 (1.72)		
Week 52: Adjusted Mean Change (SE)	10.28 (2.03)	6.37 (2.01)	3.91 [-1.72; 9.53]	0.173
Week 100: Adjusted Mean Change (SE)	9.58 (2.06)	8.86 (2.03)	0.72 [-4.97; 6.42]	0.803
KITE: General Health				
Interaction test	p=0.935			
presence				
N'/ N	56 / 56	67 / 67		
Baseline Mean (SD)	44.64 (22.22)	43.66 (25.87)		
Week 52 Mean (SD)	48.86 (20.85)	46.98 (22.98)		
Week 100 Mean (SD)	52.56 (16.01)	51.39 (25.89)		
Week 28: Adjusted Mean Change (SE)	2.40 (2.46)	6.84 (2.23)		
Week 52: Adjusted Mean Change (SE)	4.84 (2.98)	2.03 (2.61)	2.81 [-4.96; 10.59]	0.477
Week 100: Adjusted Mean Change (SE)	7.50 (2.81)	5.14 (2.42)	2.36 [-4.92; 9.65]	0.524

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
absence				
N'/ N	122 / 123	114 / 114		
Baseline Mean (SD)	43.65 (19.43)	45.18 (21.00)		
Week 52 Mean (SD)	49.75 (22.33)	52.17 (23.63)		
Week 100 Mean (SD)	50.00 (21.29)	51.09 (20.27)		
Week 28: Adjusted Mean Change (SE)	4.02 (1.68)	2.76 (1.76)		
Week 52: Adjusted Mean Change (SE)	5.84 (1.98)	6.94 (2.06)	-1.10 [-6.72; 4.52]	0.701
Week 100: Adjusted Mean Change (SE)	5.61 (1.85)	5.87 (1.86)	-0.26 [-5.40; 4.89]	0.921
Pooled Analysis: General Health				
Interaction test	p=0.801			
presence				
N'/ N	117 / 118	128 / 128		
Baseline Mean (SD)	42.95 (21.74)	41.60 (24.36)		
Week 52 Mean (SD)	47.50 (22.50)	45.91 (23.10)		
Week 100 Mean (SD)	49.16 (19.75)	49.02 (23.84)		
Week 28: Adjusted Mean Change (SE)	3.23 (1.71)	5.85 (1.64)		
Week 52: Adjusted Mean Change (SE)	4.49 (2.11)	2.65 (1.93)	1.85 [-3.75; 7.45]	0.517
Week 100: Adjusted Mean Change (SE)	5.62 (2.00)	5.19 (1.88)	0.43 [-4.94; 5.81]	0.874
absence				
N'/ N	249 / 250	240 / 240		
Baseline Mean (SD)	44.58 (20.22)	41.46 (20.20)		
Week 52 Mean (SD)	52.09 (23.17)	48.99 (22.22)		
Week 100 Mean (SD)	50.81 (22.50)	50.13 (20.81)		
Week 28: Adjusted Mean Change (SE)	4.19 (1.19)	3.97 (1.23)		
Week 52: Adjusted Mean Change (SE)	7.95 (1.42)	6.69 (1.44)	1.26 [-2.70; 5.22]	0.532
Week 100: Adjusted Mean Change (SE)	7.50 (1.38)	7.48 (1.38)	0.02 [-3.81; 3.84]	0.994

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + status of SRF + treatment * status of SRF + visit * status of SRF + treatment * status of SRF * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + study + treatment * study + status of SRF + treatment * status of SRF + visit * status of SRF + treatment * status of SRF * visit.

Table 8.13 VFQ by exposure (week 100) (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Composite Score				
Test of heterogeneity in main analysis: **p_H=0.049 ***				
KESTREL: Composite Score				
Interaction test	p=0.471			
Non-exposed				
N'/ N	12 / 12	13 / 13		
Baseline Mean (SD)	73.37 (19.85)	80.23 (15.61)		
Week 52 Mean (SD)	94.15 (2.49)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	10.48 (3.97)	17.26 (5.24)		
Week 52: Adjusted Mean Change (SE)	9.32 (6.51)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	176 / 177	174 / 174		
Baseline Mean (SD)	76.86 (17.33)	76.56 (14.52)		
Week 52 Mean (SD)	84.91 (13.96)	85.15 (12.27)		
Week 100 Mean (SD)	83.05 (14.95)	83.33 (14.40)		
Week 28: Adjusted Mean Change (SE)	5.56 (0.81)	7.51 (0.81)		
Week 52: Adjusted Mean Change (SE)	6.91 (0.85)	8.07 (0.83)	-1.16 [-3.49; 1.16]	0.326
Week 100: Adjusted Mean Change (SE)	6.03 (0.94)	6.44 (0.93)	-0.41 [-3.01; 2.18]	0.755
KITE: Composite Score				
Interaction test	p=0.208			
Non-exposed				
N'/ N	17 / 17	12 / 12		
Baseline Mean (SD)	77.78 (14.83)	71.97 (17.76)		
Week 52 Mean (SD)	61.67 (17.03)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	-2.24 (3.25)	5.83 (5.68)		
Week 52: Adjusted Mean Change (SE)	-3.89 (6.50)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Exposed				
N'/ N	161 / 162	169 / 169		
Baseline Mean (SD)	77.83 (15.05)	76.78 (17.67)		
Week 52 Mean (SD)	86.83 (12.55)	83.54 (15.65)		
Week 100 Mean (SD)	88.08 (12.13)	84.05 (15.32)		
Week 28: Adjusted Mean Change (SE)	6.19 (0.78)	5.88 (0.76)		
Week 52: Adjusted Mean Change (SE)	9.20 (0.83)	6.33 (0.81)	2.87 [0.59; 5.15]	0.014 *
Week 100: Adjusted Mean Change (SE)	9.29 (0.97)	6.19 (0.92)	3.09 [0.46; 5.73]	0.021 *
Pooled Analysis: Composite Score				
Interaction test	p=0.079			
Non-exposed				
N'/ N	29 / 29	25 / 25		
Baseline Mean (SD)	75.96 (16.89)	76.27 (16.86)		
Week 52 Mean (SD)	77.91 (21.22)	N.E.		
Week 28: Adjusted Mean Change (SE)	3.12 (2.57)	12.27 (3.91)		
Week 52: Adjusted Mean Change (SE)	1.59 (4.58)	N.E.	N.E.	N.E.
Exposed				
N'/ N	337 / 339	343 / 343		
Baseline Mean (SD)	77.32 (16.26)	76.67 (16.13)		
Week 52 Mean (SD)	85.85 (13.30)	84.37 (14.02)		
Week 100 Mean (SD)	85.45 (13.89)	83.69 (14.85)		
Week 28: Adjusted Mean Change (SE)	5.90 (0.57)	6.67 (0.57)		
Week 52: Adjusted Mean Change (SE)	8.06 (0.60)	7.21 (0.58)	0.85 [-0.79; 2.49]	0.311
Week 100: Adjusted Mean Change (SE)	7.65 (0.67)	6.29 (0.65)	1.36 [-0.48; 3.20]	0.146
General Vision				
Test of heterogeneity in main analysis: **p_H=0.762**				
KESTREL: General Vision				
Interaction test	p=0.012 *			
Non-exposed				
N'/ N	12 / 12	13 / 13		
Baseline Mean (SD)	61.67 (18.01)	63.08 (11.09)		
Week 52 Mean (SD)	70.00 (14.14)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	6.10 (4.81)	25.45 (6.35)		
Week 52: Adjusted Mean Change (SE)	1.32 (8.42)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Exposed				
N'/ N	176 / 177	174 / 174		
Baseline Mean (SD)	61.25 (17.26)	60.00 (14.90)		
Week 52 Mean (SD)	73.06 (14.17)	71.14 (12.87)		
Week 100 Mean (SD)	73.61 (14.89)	72.33 (12.04)		
Week 28: Adjusted Mean Change (SE)	11.57 (0.98)	10.39 (0.98)		
Week 52: Adjusted Mean Change (SE)	11.96 (1.03)	10.51 (1.00)	1.44 [-1.38; 4.27]	0.316
Week 100: Adjusted Mean Change (SE)	13.10 (1.02)	11.73 (1.02)	1.37 [-1.47; 4.21]	0.343
KITE: General Vision				
Interaction test	p=0.453			
Non-exposed				
N'/ N	17 / 17	12 / 12		
Baseline Mean (SD)	67.06 (12.13)	60.00 (17.06)		
Week 52 Mean (SD)	50.00 (14.14)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	0.45 (4.40)	6.85 (7.64)		
Week 52: Adjusted Mean Change (SE)	-4.85 (9.29)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	161 / 162	169 / 169		
Baseline Mean (SD)	61.24 (16.38)	59.88 (18.45)		
Week 52 Mean (SD)	73.10 (14.30)	70.53 (17.14)		
Week 100 Mean (SD)	73.74 (13.83)	70.55 (16.47)		
Week 28: Adjusted Mean Change (SE)	9.90 (1.05)	9.59 (1.03)		
Week 52: Adjusted Mean Change (SE)	12.15 (1.15)	10.26 (1.12)	1.89 [-1.26; 5.05]	0.239
Week 100: Adjusted Mean Change (SE)	12.47 (1.19)	9.54 (1.13)	2.92 [-0.30; 6.15]	0.075
Pooled Analysis: General Vision				
Interaction test	p=0.013 *			
Non-exposed				
N'/ N	29 / 29	25 / 25		
Baseline Mean (SD)	64.83 (14.79)	61.60 (14.05)		
Week 52 Mean (SD)	60.00 (16.33)	N.E.		
Week 28: Adjusted Mean Change (SE)	3.09 (3.26)	17.37 (4.94)		
Week 52: Adjusted Mean Change (SE)	-2.42 (6.24)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Exposed				
N'/ N	337 / 339	343 / 343		
Baseline Mean (SD)	61.25 (16.82)	59.94 (16.72)		
Week 52 Mean (SD)	73.08 (14.21)	70.84 (15.08)		
Week 100 Mean (SD)	73.67 (14.37)	71.44 (14.43)		
Week 28: Adjusted Mean Change (SE)	10.75 (0.72)	9.99 (0.72)		
Week 52: Adjusted Mean Change (SE)	12.05 (0.77)	10.38 (0.75)	1.67 [-0.44; 3.79]	0.121
Week 100: Adjusted Mean Change (SE)	12.82 (0.78)	10.64 (0.76)	2.18 [0.05; 4.31]	0.045 *
Ocular Pain				
Test of heterogeneity in main analysis: **p_H=0.664**				
KESTREL: Ocular Pain				
Interaction test	p=0.327			
Non-exposed				
N'/ N	12 / 12	13 / 13		
Baseline Mean (SD)	78.13 (23.31)	85.58 (16.81)		
Week 52 Mean (SD)	93.75 (8.84)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	-2.22 (6.62)	10.10 (8.74)		
Week 52: Adjusted Mean Change (SE)	5.39 (9.85)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	176 / 177	174 / 174		
Baseline Mean (SD)	83.74 (19.71)	81.90 (20.76)		
Week 52 Mean (SD)	88.52 (15.93)	86.71 (16.19)		
Week 100 Mean (SD)	86.02 (17.46)	83.99 (20.28)		
Week 28: Adjusted Mean Change (SE)	2.98 (1.35)	4.34 (1.35)		
Week 52: Adjusted Mean Change (SE)	5.04 (1.23)	4.41 (1.20)	0.62 [-2.75; 4.00]	0.717
Week 100: Adjusted Mean Change (SE)	3.06 (1.34)	1.83 (1.33)	1.22 [-2.49; 4.94]	0.518

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Ocular Pain				
Interaction test	p=0.394			
Non-exposed				
N'/ N	17 / 17	12 / 12		
Baseline Mean (SD)	82.35 (14.02)	86.46 (13.55)		
Week 52 Mean (SD)	100.00 (0.00)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	2.34 (5.07)	-6.95 (8.80)		
Week 52: Adjusted Mean Change (SE)	13.20 (10.29)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	161 / 162	169 / 169		
Baseline Mean (SD)	84.47 (18.37)	82.17 (20.98)		
Week 52 Mean (SD)	88.64 (16.64)	87.33 (17.80)		
Week 100 Mean (SD)	90.36 (15.39)	89.21 (16.32)		
Week 28: Adjusted Mean Change (SE)	4.49 (1.21)	3.98 (1.18)		
Week 52: Adjusted Mean Change (SE)	4.68 (1.24)	3.82 (1.21)	0.85 [-2.56; 4.27]	0.623
Week 100: Adjusted Mean Change (SE)	6.00 (1.26)	5.45 (1.20)	0.56 [-2.87; 3.98]	0.749
Pooled Analysis: Ocular Pain				
Interaction test	p=0.819			
Non-exposed				
N'/ N	29 / 29	25 / 25		
Baseline Mean (SD)	80.60 (18.17)	86.00 (15.02)		
Week 52 Mean (SD)	96.88 (6.25)	N.E.		
Week 28: Adjusted Mean Change (SE)	0.58 (4.09)	2.74 (6.21)		
Week 52: Adjusted Mean Change (SE)	9.54 (7.14)	N.E.	N.E.	N.E.
Exposed				
N'/ N	337 / 339	343 / 343		
Baseline Mean (SD)	84.09 (19.06)	82.03 (20.84)		
Week 52 Mean (SD)	88.58 (16.25)	87.01 (16.97)		
Week 100 Mean (SD)	88.09 (16.62)	86.60 (18.56)		
Week 28: Adjusted Mean Change (SE)	3.71 (0.91)	4.14 (0.90)		
Week 52: Adjusted Mean Change (SE)	4.87 (0.88)	4.12 (0.85)	0.75 [-1.66; 3.16]	0.541
Week 100: Adjusted Mean Change (SE)	4.52 (0.92)	3.62 (0.89)	0.90 [-1.62; 3.42]	0.482

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.450**				
KESTREL: Near Activities				
Interaction test	p=0.379			
Non-exposed				
N'/ N	12 / 12	13 / 13		
Baseline Mean (SD)	55.56 (29.37)	70.51 (21.95)		
Week 52 Mean (SD)	75.00 (0.00)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	14.30 (6.82)	26.24 (8.99)		
Week 52: Adjusted Mean Change (SE)	6.51 (12.20)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	176 / 177	174 / 174		
Baseline Mean (SD)	64.04 (25.92)	65.28 (21.83)		
Week 52 Mean (SD)	79.28 (21.46)	78.69 (20.11)		
Week 100 Mean (SD)	79.51 (20.76)	77.00 (21.12)		
Week 28: Adjusted Mean Change (SE)	12.18 (1.38)	14.02 (1.39)		
Week 52: Adjusted Mean Change (SE)	13.34 (1.51)	13.42 (1.47)	-0.08 [-4.22; 4.06]	0.970
Week 100: Adjusted Mean Change (SE)	14.41 (1.46)	11.57 (1.45)	2.84 [-1.22; 6.90]	0.170
KITE: Near Activities				
Interaction test	p=0.330			
Non-exposed				
N'/ N	17 / 17	12 / 12		
Baseline Mean (SD)	73.53 (23.80)	68.75 (22.79)		
Week 52 Mean (SD)	45.83 (5.89)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	-1.83 (5.88)	8.84 (10.25)		
Week 52: Adjusted Mean Change (SE)	-14.69 (11.04)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Exposed				
N'/ N	160 / 162	169 / 169		
Baseline Mean (SD)	69.79 (22.28)	69.45 (24.02)		
Week 52 Mean (SD)	80.58 (20.38)	78.64 (22.08)		
Week 100 Mean (SD)	83.87 (18.68)	78.03 (23.07)		
Week 28: Adjusted Mean Change (SE)	6.88 (1.42)	5.86 (1.38)		
Week 52: Adjusted Mean Change (SE)	10.78 (1.40)	8.99 (1.36)	1.80 [-2.05; 5.64]	0.359
Week 100: Adjusted Mean Change (SE)	12.41 (1.51)	7.55 (1.44)	4.86 [0.74; 8.97]	0.021 *
Pooled Analysis: Near Activities				
Interaction test	p=0.142			
Non-exposed				
N'/ N	29 / 29	25 / 25		
Baseline Mean (SD)	66.09 (27.27)	69.67 (21.90)		
Week 52 Mean (SD)	60.42 (17.18)	N.E.		
Week 28: Adjusted Mean Change (SE)	5.97 (4.50)	18.46 (6.84)		
Week 52: Adjusted Mean Change (SE)	-4.28 (8.23)	N.E.	N.E.	N.E.
Exposed				
N'/ N	336 / 339	343 / 343		
Baseline Mean (SD)	66.78 (24.39)	67.33 (23.00)		
Week 52 Mean (SD)	79.92 (20.91)	78.67 (21.06)		
Week 100 Mean (SD)	81.59 (19.88)	77.51 (22.09)		
Week 28: Adjusted Mean Change (SE)	9.66 (1.00)	9.90 (0.99)		
Week 52: Adjusted Mean Change (SE)	12.11 (1.04)	11.19 (1.01)	0.91 [-1.94; 3.77]	0.530
Week 100: Adjusted Mean Change (SE)	13.48 (1.05)	9.56 (1.02)	3.92 [1.04; 6.81]	0.008 *
Distance Activities				
Test of heterogeneity in main analysis: **p_H=0.046 ***				
KESTREL: Distance Activities				
Interaction test	p=0.795			
Non-exposed				
N'/ N	12 / 12	13 / 13		
Baseline Mean (SD)	80.90 (22.92)	80.45 (23.04)		
Week 52 Mean (SD)	100.00 (0.00)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	12.27 (5.99)	16.50 (7.91)		
Week 52: Adjusted Mean Change (SE)	14.71 (8.97)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Exposed				
N'/ N	176 / 177	174 / 174		
Baseline Mean (SD)	74.88 (23.91)	74.98 (21.02)		
Week 52 Mean (SD)	85.20 (17.24)	85.07 (17.06)		
Week 100 Mean (SD)	81.80 (19.93)	83.19 (18.67)		
Week 28: Adjusted Mean Change (SE)	7.15 (1.22)	8.76 (1.22)		
Week 52: Adjusted Mean Change (SE)	8.82 (1.15)	9.37 (1.13)	-0.55 [-3.72; 2.61]	0.731
Week 100: Adjusted Mean Change (SE)	6.45 (1.26)	7.50 (1.25)	-1.05 [-4.54; 2.44]	0.555
KITE: Distance Activities				
Interaction test	p=0.229			
Non-exposed				
N'/ N	17 / 17	12 / 12		
Baseline Mean (SD)	77.94 (23.33)	73.96 (21.77)		
Week 52 Mean (SD)	62.50 (35.36)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	-0.73 (5.14)	10.50 (8.95)		
Week 52: Adjusted Mean Change (SE)	-6.84 (9.21)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	161 / 162	169 / 169		
Baseline Mean (SD)	76.79 (21.34)	76.36 (22.54)		
Week 52 Mean (SD)	88.29 (17.09)	84.39 (18.72)		
Week 100 Mean (SD)	89.19 (15.91)	83.82 (18.81)		
Week 28: Adjusted Mean Change (SE)	6.57 (1.23)	5.19 (1.20)		
Week 52: Adjusted Mean Change (SE)	11.66 (1.14)	7.95 (1.11)	3.71 [0.58; 6.83]	0.020 *
Week 100: Adjusted Mean Change (SE)	11.55 (1.25)	6.76 (1.19)	4.78 [1.40; 8.17]	0.006 *
Pooled Analysis: Distance Activities				
Interaction test	p=0.204			
Non-exposed				
N'/ N	29 / 29	25 / 25		
Baseline Mean (SD)	79.17 (22.79)	77.33 (22.21)		
Week 52 Mean (SD)	81.25 (29.76)	N.E.		
Week 28: Adjusted Mean Change (SE)	4.44 (3.93)	13.74 (5.97)		
Week 52: Adjusted Mean Change (SE)	3.23 (6.43)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Exposed				
N'/ N	337 / 339	343 / 343		
Baseline Mean (SD)	75.79 (22.71)	75.66 (21.76)		
Week 52 Mean (SD)	86.72 (17.21)	84.74 (17.86)		
Week 100 Mean (SD)	85.32 (18.47)	83.50 (18.71)		
Week 28: Adjusted Mean Change (SE)	6.91 (0.87)	6.98 (0.86)		
Week 52: Adjusted Mean Change (SE)	10.25 (0.82)	8.68 (0.79)	1.58 [-0.66; 3.81]	0.166
Week 100: Adjusted Mean Change (SE)	8.94 (0.89)	7.13 (0.86)	1.81 [-0.62; 4.23]	0.145
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.023 ***				
KESTREL: Social Functioning				
Interaction test	p=0.842			
Non-exposed				
N'/ N	12 / 12	13 / 13		
Baseline Mean (SD)	87.50 (15.99)	88.46 (16.51)		
Week 52 Mean (SD)	100.00 (0.00)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	8.05 (4.54)	12.08 (6.00)		
Week 52: Adjusted Mean Change (SE)	6.17 (8.68)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	176 / 177	174 / 174		
Baseline Mean (SD)	88.92 (19.13)	89.94 (15.60)		
Week 52 Mean (SD)	92.43 (15.03)	93.71 (13.47)		
Week 100 Mean (SD)	90.63 (17.08)	91.87 (14.94)		
Week 28: Adjusted Mean Change (SE)	1.32 (0.93)	3.82 (0.93)		
Week 52: Adjusted Mean Change (SE)	2.26 (1.04)	3.85 (1.01)	-1.60 [-4.45; 1.26]	0.272
Week 100: Adjusted Mean Change (SE)	1.43 (1.23)	2.21 (1.22)	-0.78 [-4.19; 2.64]	0.655

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Social Functioning				
Interaction test	p=0.744			
Non-exposed				
N'/ N	17 / 17	12 / 12		
Baseline Mean (SD)	86.76 (19.50)	82.29 (20.27)		
Week 52 Mean (SD)	75.00 (35.36)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	-0.23 (4.55)	2.70 (7.89)		
Week 52: Adjusted Mean Change (SE)	-2.40 (7.61)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	161 / 162	169 / 169		
Baseline Mean (SD)	88.59 (17.14)	86.69 (19.96)		
Week 52 Mean (SD)	95.42 (11.38)	91.58 (14.73)		
Week 100 Mean (SD)	95.04 (13.84)	91.18 (16.88)		
Week 28: Adjusted Mean Change (SE)	3.96 (1.09)	3.87 (1.06)		
Week 52: Adjusted Mean Change (SE)	7.57 (0.92)	4.34 (0.89)	3.22 [0.70; 5.74]	0.012 *
Week 100: Adjusted Mean Change (SE)	6.92 (1.16)	3.74 (1.10)	3.18 [0.03; 6.33]	0.048 *
Pooled Analysis: Social Functioning				
Interaction test	p=0.474			
Non-exposed				
N'/ N	29 / 29	25 / 25		
Baseline Mean (SD)	87.07 (17.83)	85.50 (18.29)		
Week 52 Mean (SD)	87.50 (25.00)	N.E.		
Week 28: Adjusted Mean Change (SE)	2.84 (3.23)	8.23 (4.88)		
Week 52: Adjusted Mean Change (SE)	1.77 (5.78)	N.E.	N.E.	N.E.
Exposed				
N'/ N	337 / 339	343 / 343		
Baseline Mean (SD)	88.76 (18.18)	88.34 (17.93)		
Week 52 Mean (SD)	93.90 (13.43)	92.67 (14.12)		
Week 100 Mean (SD)	92.73 (15.75)	91.52 (15.92)		
Week 28: Adjusted Mean Change (SE)	2.67 (0.72)	3.80 (0.71)		
Week 52: Adjusted Mean Change (SE)	4.94 (0.70)	4.07 (0.68)	0.86 [-1.05; 2.77]	0.376
Week 100: Adjusted Mean Change (SE)	4.15 (0.85)	2.90 (0.82)	1.25 [-1.07; 3.58]	0.289

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Mental Health				
Test of heterogeneity in main analysis: **p_H=0.200**				
KESTREL: Mental Health				
Interaction test	p=0.889			
Non-exposed				
N'/ N	12 / 12	13 / 13		
Baseline Mean (SD)	60.42 (25.61)	78.37 (16.06)		
Week 52 Mean (SD)	96.88 (4.42)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	16.23 (6.39)	19.71 (8.45)		
Week 52: Adjusted Mean Change (SE)	20.02 (10.95)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	176 / 177	174 / 174		
Baseline Mean (SD)	65.87 (24.92)	67.49 (23.33)		
Week 52 Mean (SD)	78.10 (19.98)	78.68 (17.88)		
Week 100 Mean (SD)	74.87 (21.47)	77.61 (21.41)		
Week 28: Adjusted Mean Change (SE)	7.08 (1.30)	9.05 (1.31)		
Week 52: Adjusted Mean Change (SE)	10.27 (1.34)	11.02 (1.30)	-0.74 [-4.41; 2.92]	0.690
Week 100: Adjusted Mean Change (SE)	8.55 (1.51)	10.59 (1.50)	-2.04 [-6.23; 2.15]	0.339
KITE: Mental Health				
Interaction test	p=0.057			
Non-exposed				
N'/ N	17 / 17	12 / 12		
Baseline Mean (SD)	68.01 (20.00)	53.65 (25.76)		
Week 52 Mean (SD)	50.00 (8.84)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	-0.90 (5.51)	20.37 (9.59)		
Week 52: Adjusted Mean Change (SE)	2.47 (12.58)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Exposed				
N'/ N	161 / 162	169 / 169		
Baseline Mean (SD)	69.02 (21.78)	66.64 (25.89)		
Week 52 Mean (SD)	81.82 (20.51)	76.71 (23.59)		
Week 100 Mean (SD)	84.21 (16.10)	79.62 (22.25)		
Week 28: Adjusted Mean Change (SE)	8.93 (1.32)	8.71 (1.29)		
Week 52: Adjusted Mean Change (SE)	13.07 (1.57)	9.02 (1.53)	4.06 [-0.26; 8.37]	0.065
Week 100: Adjusted Mean Change (SE)	14.05 (1.58)	11.23 (1.50)	2.81 [-1.47; 7.10]	0.198
Pooled Analysis: Mental Health				
Interaction test	p=0.104			
Non-exposed				
N'/ N	29 / 29	25 / 25		
Baseline Mean (SD)	64.87 (22.37)	66.50 (24.33)		
Week 52 Mean (SD)	73.44 (27.66)	N.E.		
Week 28: Adjusted Mean Change (SE)	6.30 (4.18)	19.70 (6.34)		
Week 52: Adjusted Mean Change (SE)	9.18 (8.28)	N.E.	N.E.	N.E.
Exposed				
N'/ N	337 / 339	343 / 343		
Baseline Mean (SD)	67.38 (23.49)	67.07 (24.59)		
Week 52 Mean (SD)	79.93 (20.29)	77.72 (20.84)		
Week 100 Mean (SD)	79.32 (19.63)	78.62 (21.82)		
Week 28: Adjusted Mean Change (SE)	8.02 (0.93)	8.86 (0.92)		
Week 52: Adjusted Mean Change (SE)	11.66 (1.03)	10.01 (1.00)	1.65 [-1.17; 4.48]	0.250
Week 100: Adjusted Mean Change (SE)	11.28 (1.09)	10.88 (1.06)	0.39 [-2.60; 3.38]	0.796
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.132**				
KESTREL: Role Difficulties				
Interaction test	p=0.384			
Non-exposed				
N'/ N	12 / 12	13 / 13		
Baseline Mean (SD)	75.00 (20.64)	78.85 (29.92)		
Week 52 Mean (SD)	100.00 (0.00)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	11.85 (8.00)	26.64 (10.56)		
Week 52: Adjusted Mean Change (SE)	13.17 (14.45)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Exposed				
N'/ N	176 / 177	174 / 174		
Baseline Mean (SD)	71.80 (29.12)	71.26 (26.41)		
Week 52 Mean (SD)	80.44 (25.39)	83.15 (22.83)		
Week 100 Mean (SD)	81.51 (25.73)	79.71 (25.31)		
Week 28: Adjusted Mean Change (SE)	5.55 (1.63)	8.60 (1.63)		
Week 52: Adjusted Mean Change (SE)	6.36 (1.78)	10.68 (1.74)	-4.32 [-9.22; 0.58]	0.084
Week 100: Adjusted Mean Change (SE)	8.90 (1.82)	7.47 (1.81)	1.44 [-3.61; 6.48]	0.576
KITE: Role Difficulties				
Interaction test	p=0.051			
Non-exposed				
N'/ N	17 / 17	12 / 12		
Baseline Mean (SD)	67.65 (27.26)	53.13 (30.21)		
Week 52 Mean (SD)	50.00 (35.36)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	-10.28 (6.74)	16.15 (11.69)		
Week 52: Adjusted Mean Change (SE)	-3.16 (13.91)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	161 / 162	169 / 169		
Baseline Mean (SD)	71.43 (27.33)	68.20 (29.09)		
Week 52 Mean (SD)	83.36 (21.56)	78.17 (25.26)		
Week 100 Mean (SD)	85.02 (22.86)	80.31 (25.29)		
Week 28: Adjusted Mean Change (SE)	8.41 (1.61)	7.98 (1.57)		
Week 52: Adjusted Mean Change (SE)	12.90 (1.70)	8.36 (1.65)	4.54 [-0.12; 9.21]	0.056
Week 100: Adjusted Mean Change (SE)	12.47 (1.87)	9.68 (1.78)	2.79 [-2.29; 7.87]	0.281
Pooled Analysis: Role Difficulties				
Interaction test	p=0.022 *			
Non-exposed				
N'/ N	29 / 29	25 / 25		
Baseline Mean (SD)	70.69 (24.61)	66.50 (32.22)		
Week 52 Mean (SD)	75.00 (35.36)	N.E.		
Week 28: Adjusted Mean Change (SE)	-1.28 (5.19)	22.08 (7.87)		
Week 52: Adjusted Mean Change (SE)	2.65 (9.98)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Exposed				
N'/ N	337 / 339	343 / 343		
Baseline Mean (SD)	71.62 (28.24)	69.75 (27.77)		
Week 52 Mean (SD)	81.88 (23.59)	80.72 (24.13)		
Week 100 Mean (SD)	83.18 (24.43)	80.01 (25.26)		
Week 28: Adjusted Mean Change (SE)	6.99 (1.15)	8.28 (1.14)		
Week 52: Adjusted Mean Change (SE)	9.60 (1.23)	9.56 (1.20)	0.05 [-3.33; 3.43]	0.977
Week 100: Adjusted Mean Change (SE)	10.71 (1.30)	8.57 (1.27)	2.14 [-1.43; 5.71]	0.240
Dependency				
Test of heterogeneity in main analysis: **p_H=0.019 ***				
KESTREL: Dependency				
Interaction test	p=0.729			
Non-exposed				
N'/ N	12 / 12	13 / 13		
Baseline Mean (SD)	69.44 (30.22)	87.82 (17.55)		
Week 52 Mean (SD)	100.00 (0.00)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	17.75 (6.87)	15.24 (9.05)		
Week 52: Adjusted Mean Change (SE)	13.26 (11.74)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	176 / 177	174 / 174		
Baseline Mean (SD)	82.34 (25.99)	82.38 (24.19)		
Week 52 Mean (SD)	88.83 (21.99)	92.04 (17.02)		
Week 100 Mean (SD)	86.17 (22.48)	88.41 (20.98)		
Week 28: Adjusted Mean Change (SE)	5.12 (1.39)	6.63 (1.40)		
Week 52: Adjusted Mean Change (SE)	5.24 (1.45)	8.66 (1.41)	-3.43 [-7.41; 0.55]	0.091
Week 100: Adjusted Mean Change (SE)	3.46 (1.60)	5.49 (1.59)	-2.03 [-6.48; 2.41]	0.369

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Dependency				
Interaction test	p=0.392			
Non-exposed				
N'/ N	17 / 17	12 / 12		
Baseline Mean (SD)	79.90 (22.45)	70.14 (35.08)		
Week 52 Mean (SD)	33.33 (0.00)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	-5.45 (5.52)	1.29 (9.61)		
Week 52: Adjusted Mean Change (SE)	-26.27 (11.12)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	161 / 162	169 / 169		
Baseline Mean (SD)	83.80 (23.70)	82.74 (26.25)		
Week 52 Mean (SD)	91.90 (18.06)	86.72 (22.71)		
Week 100 Mean (SD)	93.07 (14.55)	87.39 (22.96)		
Week 28: Adjusted Mean Change (SE)	5.96 (1.32)	3.06 (1.29)		
Week 52: Adjusted Mean Change (SE)	7.99 (1.38)	3.05 (1.35)	4.93 [1.14; 8.73]	0.011 *
Week 100: Adjusted Mean Change (SE)	7.12 (1.53)	2.92 (1.46)	4.20 [0.05; 8.36]	0.048 *
Pooled Analysis: Dependency				
Interaction test	p=0.489			
Non-exposed				
N'/ N	29 / 29	25 / 25		
Baseline Mean (SD)	75.57 (25.97)	79.33 (28.27)		
Week 52 Mean (SD)	66.67 (38.49)	N.E.		
Week 28: Adjusted Mean Change (SE)	4.15 (4.39)	9.02 (6.65)		
Week 52: Adjusted Mean Change (SE)	-8.30 (8.11)	N.E.	N.E.	N.E.
Exposed				
N'/ N	337 / 339	343 / 343		
Baseline Mean (SD)	83.04 (24.90)	82.56 (25.19)		
Week 52 Mean (SD)	90.34 (20.18)	89.45 (20.13)		
Week 100 Mean (SD)	89.45 (19.39)	87.90 (21.96)		
Week 28: Adjusted Mean Change (SE)	5.57 (0.97)	4.84 (0.96)		
Week 52: Adjusted Mean Change (SE)	6.60 (1.02)	5.88 (0.99)	0.72 [-2.06; 3.50]	0.611
Week 100: Adjusted Mean Change (SE)	5.34 (1.11)	4.22 (1.08)	1.12 [-1.92; 4.17]	0.470

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Driving				
Test of heterogeneity in main analysis: **p_H=0.792**				
KESTREL: Driving				
Interaction test	p=0.341			
Non-exposed				
N'/ N	7 / 12	10 / 13		
Baseline Mean (SD)	83.33 (20.97)	80.00 (18.92)		
Week 52 Mean (SD)	100.00 (0.00)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	3.02 (8.37)	16.89 (7.25)		
Week 52: Adjusted Mean Change (SE)	4.60 (10.76)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	113 / 177	110 / 174		
Baseline Mean (SD)	79.72 (18.53)	76.89 (19.82)		
Week 52 Mean (SD)	83.93 (20.17)	84.33 (18.02)		
Week 100 Mean (SD)	82.96 (19.30)	79.97 (21.54)		
Week 28: Adjusted Mean Change (SE)	1.94 (1.40)	5.03 (1.46)		
Week 52: Adjusted Mean Change (SE)	3.46 (1.61)	5.56 (1.66)	-2.10 [-6.65; 2.46]	0.365
Week 100: Adjusted Mean Change (SE)	2.26 (1.79)	1.38 (1.85)	0.88 [-4.19; 5.95]	0.731
KITE: Driving				
Interaction test	p=0.579			
Non-exposed				
N'/ N	8 / 17	5 / 12		
Baseline Mean (SD)	79.17 (18.90)	72.50 (35.55)		
Week 52 Mean (SD)	N.E.	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	-8.08 (7.08)	3.09 (9.97)		
Week 52: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Exposed				
N'/ N	95 / 162	91 / 169		
Baseline Mean (SD)	78.99 (20.56)	82.60 (20.93)		
Week 52 Mean (SD)	86.90 (17.22)	87.83 (15.76)		
Week 100 Mean (SD)	86.27 (15.03)	87.11 (14.52)		
Week 28: Adjusted Mean Change (SE)	1.13 (1.48)	5.39 (1.52)		
Week 52: Adjusted Mean Change (SE)	5.99 (1.28)	4.78 (1.33)	1.20 [-2.44; 4.85]	0.515
Week 100: Adjusted Mean Change (SE)	4.37 (1.43)	2.81 (1.45)	1.56 [-2.46; 5.59]	0.445
Pooled Analysis: Driving				
Interaction test	p=0.149			
Non-exposed				
N'/ N	15 / 29	15 / 25		
Baseline Mean (SD)	81.11 (19.28)	77.50 (24.59)		
Week 52 Mean (SD)	100.00 (0.00)	N.E.		
Week 28: Adjusted Mean Change (SE)	-3.48 (5.45)	11.94 (5.87)		
Week 52: Adjusted Mean Change (SE)	2.43 (8.98)	N.E.	N.E.	N.E.
Exposed				
N'/ N	208 / 339	201 / 343		
Baseline Mean (SD)	79.39 (19.44)	79.48 (20.48)		
Week 52 Mean (SD)	85.31 (18.87)	85.91 (17.08)		
Week 100 Mean (SD)	84.51 (17.46)	83.36 (18.83)		
Week 28: Adjusted Mean Change (SE)	1.57 (1.02)	5.19 (1.06)		
Week 52: Adjusted Mean Change (SE)	4.77 (1.04)	5.29 (1.08)	-0.52 [-3.47; 2.43]	0.729
Week 100: Adjusted Mean Change (SE)	3.28 (1.17)	2.09 (1.20)	1.18 [-2.11; 4.48]	0.481
Color Vision				
Test of heterogeneity in main analysis: **p_H=0.477**				
KESTREL: Color Vision				
Interaction test	p=0.998			
Non-exposed				
N'/ N	12 / 12	13 / 13		
Baseline Mean (SD)	89.58 (19.82)	88.46 (24.19)		
Week 52 Mean (SD)	100.00 (0.00)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	7.93 (4.16)	7.72 (5.48)		
Week 52: Adjusted Mean Change (SE)	5.56 (7.17)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Exposed				
N'/ N	174 / 177	171 / 174		
Baseline Mean (SD)	93.25 (16.38)	94.44 (14.03)		
Week 52 Mean (SD)	96.58 (11.23)	95.92 (11.98)		
Week 100 Mean (SD)	94.68 (12.96)	95.07 (12.36)		
Week 28: Adjusted Mean Change (SE)	1.82 (0.85)	1.63 (0.86)		
Week 52: Adjusted Mean Change (SE)	2.07 (0.87)	1.75 (0.86)	0.32 [-2.08; 2.72]	0.792
Week 100: Adjusted Mean Change (SE)	0.59 (1.02)	0.80 (1.02)	-0.21 [-3.04; 2.63]	0.886
KITE: Color Vision				
Interaction test	p=0.072			
Non-exposed				
N'/ N	17 / 17	12 / 12		
Baseline Mean (SD)	92.65 (21.22)	93.75 (11.31)		
Week 52 Mean (SD)	87.50 (17.68)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	-7.78 (3.50)	4.96 (6.07)		
Week 52: Adjusted Mean Change (SE)	-6.54 (6.16)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	161 / 162	167 / 169		
Baseline Mean (SD)	92.08 (16.40)	91.62 (16.38)		
Week 52 Mean (SD)	97.70 (8.40)	94.90 (12.39)		
Week 100 Mean (SD)	97.31 (8.94)	95.07 (13.40)		
Week 28: Adjusted Mean Change (SE)	4.12 (0.84)	4.02 (0.82)		
Week 52: Adjusted Mean Change (SE)	5.95 (0.75)	3.26 (0.73)	2.69 [0.63; 4.75]	0.011 *
Week 100: Adjusted Mean Change (SE)	5.12 (0.91)	3.27 (0.87)	1.84 [-0.63; 4.31]	0.143
Pooled Analysis: Color Vision				
Interaction test	p=0.097			
Non-exposed				
N'/ N	29 / 29	25 / 25		
Baseline Mean (SD)	91.38 (20.35)	91.00 (18.93)		
Week 52 Mean (SD)	93.75 (12.50)	N.E.		
Week 28: Adjusted Mean Change (SE)	-1.08 (2.73)	7.08 (4.14)		
Week 52: Adjusted Mean Change (SE)	-1.15 (4.70)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Exposed				
N'/ N	335 / 339	338 / 343		
Baseline Mean (SD)	92.69 (16.38)	93.05 (15.28)		
Week 52 Mean (SD)	97.13 (9.94)	95.42 (12.18)		
Week 100 Mean (SD)	95.94 (11.27)	95.07 (12.87)		
Week 28: Adjusted Mean Change (SE)	2.98 (0.61)	2.79 (0.61)		
Week 52: Adjusted Mean Change (SE)	3.99 (0.58)	2.47 (0.56)	1.53 [-0.05; 3.11]	0.058
Week 100: Adjusted Mean Change (SE)	2.90 (0.69)	1.91 (0.67)	0.98 [-0.90; 2.87]	0.307
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.003 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.794			
Non-exposed				
N'/ N	12 / 12	13 / 13		
Baseline Mean (SD)	72.92 (24.91)	82.69 (21.37)		
Week 52 Mean (SD)	100.00 (0.00)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	9.11 (6.70)	17.12 (8.84)		
Week 52: Adjusted Mean Change (SE)	8.95 (11.65)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	175 / 177	173 / 174		
Baseline Mean (SD)	84.71 (21.41)	79.91 (23.45)		
Week 52 Mean (SD)	89.12 (19.64)	88.54 (17.79)		
Week 100 Mean (SD)	84.27 (22.14)	87.50 (20.81)		
Week 28: Adjusted Mean Change (SE)	2.35 (1.37)	7.42 (1.37)		
Week 52: Adjusted Mean Change (SE)	5.45 (1.40)	7.02 (1.36)	-1.57 [-5.41; 2.27]	0.421
Week 100: Adjusted Mean Change (SE)	0.92 (1.64)	5.75 (1.63)	-4.83 [-9.38; -0.28]	0.038 *

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Peripheral Vision				
Interaction test	p=0.264			
Non-exposed				
N'/ N	17 / 17	12 / 12		
Baseline Mean (SD)	83.82 (19.65)	81.25 (21.65)		
Week 52 Mean (SD)	62.50 (17.68)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	-2.33 (5.15)	8.81 (8.95)		
Week 52: Adjusted Mean Change (SE)	-7.58 (10.57)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	161 / 162	168 / 169		
Baseline Mean (SD)	83.07 (20.27)	84.97 (21.39)		
Week 52 Mean (SD)	90.14 (16.83)	87.75 (19.41)		
Week 100 Mean (SD)	92.37 (15.16)	87.76 (18.66)		
Week 28: Adjusted Mean Change (SE)	4.99 (1.23)	4.39 (1.20)		
Week 52: Adjusted Mean Change (SE)	6.65 (1.29)	3.45 (1.26)	3.19 [-0.36; 6.75]	0.078
Week 100: Adjusted Mean Change (SE)	7.78 (1.30)	2.87 (1.24)	4.91 [1.37; 8.44]	0.007 *
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.254			
Non-exposed				
N'/ N	29 / 29	25 / 25		
Baseline Mean (SD)	79.31 (22.23)	82.00 (21.07)		
Week 52 Mean (SD)	81.25 (23.94)	N.E.		
Week 28: Adjusted Mean Change (SE)	2.32 (4.18)	13.56 (6.32)		
Week 52: Adjusted Mean Change (SE)	-0.33 (7.88)	N.E.	N.E.	N.E.
Exposed				
N'/ N	336 / 339	341 / 343		
Baseline Mean (SD)	83.93 (20.86)	82.40 (22.57)		
Week 52 Mean (SD)	89.62 (18.29)	88.15 (18.57)		
Week 100 Mean (SD)	88.14 (19.51)	87.63 (19.74)		
Week 28: Adjusted Mean Change (SE)	3.57 (0.93)	6.00 (0.92)		
Week 52: Adjusted Mean Change (SE)	5.95 (0.96)	5.39 (0.93)	0.56 [-2.06; 3.19]	0.674
Week 100: Adjusted Mean Change (SE)	4.14 (1.06)	4.36 (1.03)	-0.22 [-3.12; 2.68]	0.883

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
General Health				
Test of heterogeneity in main analysis: **p_H=0.834**				
KESTREL: General Health				
Interaction test	p=0.526			
Non-exposed				
N'/ N	12 / 12	13 / 13		
Baseline Mean (SD)	39.58 (29.11)	40.38 (24.02)		
Week 52 Mean (SD)	75.00 (35.36)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	0.38 (6.88)	7.83 (9.08)		
Week 52: Adjusted Mean Change (SE)	15.12 (13.99)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	176 / 177	174 / 174		
Baseline Mean (SD)	44.46 (20.56)	38.36 (19.87)		
Week 52 Mean (SD)	51.53 (23.99)	45.73 (21.52)		
Week 100 Mean (SD)	49.83 (23.19)	48.29 (21.31)		
Week 28: Adjusted Mean Change (SE)	4.63 (1.41)	4.74 (1.41)		
Week 52: Adjusted Mean Change (SE)	8.33 (1.70)	5.29 (1.65)	3.05 [-1.62; 7.71]	0.200
Week 100: Adjusted Mean Change (SE)	7.81 (1.67)	7.53 (1.66)	0.28 [-4.36; 4.92]	0.905
KITE: General Health				
Interaction test	p=0.688			
Non-exposed				
N'/ N	17 / 17	12 / 12		
Baseline Mean (SD)	44.12 (18.81)	41.67 (19.46)		
Week 52 Mean (SD)	12.50 (17.68)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 28: Adjusted Mean Change (SE)	-5.03 (5.95)	-9.35 (10.30)		
Week 52: Adjusted Mean Change (SE)	-35.43 (13.70)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.

	Treatment Groups		Comparison	
VFQ by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Exposed				
N'/ N	161 / 162	169 / 169		
Baseline Mean (SD)	43.94 (20.50)	44.82 (23.13)		
Week 52 Mean (SD)	50.00 (21.47)	50.17 (23.44)		
Week 100 Mean (SD)	50.76 (19.84)	51.20 (22.42)		
Week 28: Adjusted Mean Change (SE)	4.06 (1.42)	4.59 (1.39)		
Week 52: Adjusted Mean Change (SE)	6.25 (1.64)	5.13 (1.60)	1.12 [-3.39; 5.62]	0.626
Week 100: Adjusted Mean Change (SE)	6.52 (1.54)	5.70 (1.47)	0.82 [-3.36; 5.01]	0.699
Pooled Analysis: General Health				
Interaction test	p=0.719			
Non-exposed				
N'/ N	29 / 29	25 / 25		
Baseline Mean (SD)	42.24 (23.25)	41.00 (21.51)		
Week 52 Mean (SD)	43.75 (42.70)	N.E.		
Week 28: Adjusted Mean Change (SE)	-3.22 (4.51)	0.28 (6.82)		
Week 52: Adjusted Mean Change (SE)	-10.20 (9.82)	N.E.	N.E.	N.E.
Exposed				
N'/ N	337 / 339	343 / 343		
Baseline Mean (SD)	44.21 (20.50)	41.55 (21.75)		
Week 52 Mean (SD)	50.78 (22.76)	47.89 (22.55)		
Week 100 Mean (SD)	50.27 (21.62)	49.74 (21.88)		
Week 28: Adjusted Mean Change (SE)	4.24 (1.00)	4.75 (0.99)		
Week 52: Adjusted Mean Change (SE)	7.20 (1.19)	5.28 (1.15)	1.92 [-1.32; 5.16]	0.246
Week 100: Adjusted Mean Change (SE)	7.08 (1.14)	6.71 (1.11)	0.37 [-2.75; 3.48]	0.818

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + exposure (week 100) + treatment * exposure (week 100) + visit * exposure (week 100) + treatment * exposure (week 100) * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + study + treatment * study + exposure (week 100) + treatment * exposure (week 100) + visit * exposure (week 100) + treatment * exposure (week 100) * visit.

9 VFQ: Binary analysis (Gain)

Table 9.1 VFQ - Gain of 4 respectively 15 points (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
KESTREL, N''/N'/N	149 / 188 / 189	158 / 187 / 187			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	98 (52.1)	113 (60.4)	0.65 [0.41; 1.03] 0.064	0.86 [0.72; 1.03] 0.107	-0.08 [-0.18; 0.02] 0.104
KITE, N''/N'/N	144 / 178 / 179	150 / 181 / 181			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	98 (55.1)	100 (55.2)	1.03 [0.66; 1.60] 0.893	1.00 [0.83; 1.20] 0.971	-0.00 [-0.10; 0.10] 0.971
Pooled Analysis, N''/N'/N	293 / 366 / 368	308 / 368 / 368			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	196 (53.6)	213 (57.9)	0.83 [0.60; 1.13] 0.236	0.93 [0.81; 1.05] 0.238	-0.04 [-0.12; 0.03] 0.237
p_H=0.178					
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
KESTREL, N''/N'/N	144 / 188 / 189	146 / 187 / 187			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	99 (52.7)	105 (56.1)	0.83 [0.53; 1.29] 0.404	0.94 [0.78; 1.13] 0.498	-0.03 [-0.14; 0.07] 0.497
KITE, N''/N'/N	131 / 178 / 179	146 / 181 / 181			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	100 (56.2)	91 (50.3)	1.36 [0.88; 2.13] 0.169	1.12 [0.92; 1.36] 0.263	0.06 [-0.04; 0.16] 0.261
Pooled Analysis, N''/N'/N	275 / 366 / 368	292 / 368 / 368			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	199 (54.4)	196 (53.3)	1.07 [0.78; 1.46] 0.690	1.02 [0.89; 1.17] 0.764	0.01 [-0.06; 0.08] 0.764
p_H=0.121					
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
KESTREL, N''/N'/N	149 / 188 / 189	158 / 187 / 187			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	46 (24.5)	43 (23.0)	0.93 [0.50; 1.74] 0.829	1.06 [0.74; 1.53] 0.737	0.01 [-0.07; 0.10] 0.737
KITE, N''/N'/N	144 / 178 / 179	150 / 181 / 181			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	37 (20.8)	33 (18.2)	1.52 [0.83; 2.78] 0.179	1.14 [0.75; 1.74] 0.542	0.03 [-0.06; 0.11] 0.541

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N''/N'/N	293 / 366 / 368	308 / 368 / 368			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%) p_H=0.231	83 (22.7)	76 (20.7)	1.25 [0.81; 1.93] 0.303	1.10 [0.83; 1.44] 0.510	0.02 [-0.04; 0.08] 0.510
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
KESTREL, N''/N'/N	144 / 188 / 189	146 / 187 / 187			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	42 (22.3)	40 (21.4)	0.90 [0.49; 1.66] 0.741	1.04 [0.71; 1.53] 0.824	0.01 [-0.07; 0.09] 0.824
KITE, N''/N'/N	131 / 178 / 179	146 / 181 / 181			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	44 (24.7)	35 (19.3)	2.00 [1.07; 3.74] 0.030 *	1.28 [0.86; 1.89] 0.220	0.05 [-0.03; 0.14] 0.218
Pooled Analysis, N''/N'/N	275 / 366 / 368	292 / 368 / 368			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%) p_H=0.071	86 (23.5)	75 (20.4)	1.35 [0.87; 2.08] 0.179	1.15 [0.88; 1.52] 0.308	0.03 [-0.03; 0.09] 0.307

N: Number of patients
N': Number of patients in the analysis
N'': Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 9.2 VFQ - Gain of 4 respectively 15 points by age (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.178**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.957				
< 65 years					
N''/N'/N	82 / 103 / 104	83 / 93 / 93			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	60 (58.3)	65 (69.9)	0.64 [0.34; 1.22] 0.176	0.83 [0.67; 1.03] 0.091	-0.12 [-0.25; 0.02] 0.087
≥ 65 years					
N''/N'/N	67 / 85 / 85	75 / 94 / 94			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	38 (44.7)	48 (51.1)	0.66 [0.35; 1.26] 0.208	0.88 [0.64; 1.19] 0.398	-0.06 [-0.21; 0.08] 0.394
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.855				
< 65 years					
N''/N'/N	78 / 100 / 100	83 / 102 / 102			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	57 (57.0)	58 (56.9)	1.07 [0.59; 1.92] 0.825	1.00 [0.79; 1.27] 0.984	0.00 [-0.14; 0.14] 0.984
≥ 65 years					
N''/N'/N	66 / 78 / 79	67 / 79 / 79			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	41 (52.6)	42 (53.2)	0.98 [0.50; 1.92] 0.962	0.99 [0.74; 1.33] 0.940	-0.01 [-0.16; 0.15] 0.940
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.962				
< 65 years					
N''/N'/N	160 / 203 / 204	166 / 195 / 195			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	117 (57.6)	123 (63.1)	0.83 [0.54; 1.28] 0.404	0.91 [0.78; 1.07] 0.249	-0.06 [-0.15; 0.04] 0.248
≥ 65 years					
N''/N'/N	133 / 163 / 164	142 / 173 / 173			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	79 (48.5)	90 (52.0)	0.82 [0.52; 1.30] 0.400	0.93 [0.75; 1.15] 0.503	-0.04 [-0.14; 0.07] 0.501

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.121**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.869				
< 65 years					
N"/N'/N	78 / 103 / 104	76 / 93 / 93			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	60 (58.3)	61 (65.6)	0.80 [0.43; 1.49] 0.477	0.89 [0.71; 1.11] 0.290	-0.07 [-0.21; 0.06] 0.289
≥ 65 years					
N"/N'/N	66 / 85 / 85	70 / 94 / 94			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	39 (45.9)	44 (46.8)	0.86 [0.46; 1.62] 0.642	0.98 [0.71; 1.34] 0.901	-0.01 [-0.16; 0.14] 0.901
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.748				
< 65 years					
N"/N'/N	72 / 100 / 100	87 / 102 / 102			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	58 (58.0)	55 (53.9)	1.28 [0.71; 2.31] 0.410	1.08 [0.84; 1.37] 0.560	0.04 [-0.10; 0.18] 0.559
≥ 65 years					
N"/N'/N	59 / 78 / 79	59 / 79 / 79			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	42 (53.8)	36 (45.6)	1.48 [0.76; 2.91] 0.252	1.18 [0.86; 1.62] 0.302	0.08 [-0.07; 0.24] 0.298
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.712				
< 65 years					
N"/N'/N	150 / 203 / 204	163 / 195 / 195			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	118 (58.1)	116 (59.5)	1.01 [0.66; 1.55] 0.967	0.97 [0.83; 1.15] 0.756	-0.02 [-0.11; 0.08] 0.755
≥ 65 years					
N"/N'/N	125 / 163 / 164	129 / 173 / 173			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	81 (49.7)	80 (46.2)	1.14 [0.72; 1.80] 0.588	1.07 [0.86; 1.34] 0.537	0.03 [-0.07; 0.14] 0.536
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.231**					

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.804				
< 65 years					
N"/N'/N	82 / 103 / 104	83 / 93 / 93			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	28 (27.2)	27 (29.0)	1.00 [0.43; 2.31] 0.997	0.94 [0.60; 1.47] 0.774	-0.02 [-0.14; 0.11] 0.774
≥ 65 years					
N"/N'/N	67 / 85 / 85	75 / 94 / 94			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	18 (21.2)	16 (17.0)	0.85 [0.33; 2.18] 0.742	1.24 [0.68; 2.28] 0.480	0.04 [-0.07; 0.16] 0.480
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.938				
< 65 years					
N"/N'/N	78 / 100 / 100	83 / 102 / 102			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	21 (21.0)	20 (19.6)	1.49 [0.68; 3.27] 0.324	1.07 [0.62; 1.85] 0.806	0.01 [-0.10; 0.12] 0.806
≥ 65 years					
N"/N'/N	66 / 78 / 79	67 / 79 / 79			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	16 (20.5)	13 (16.5)	1.56 [0.61; 4.02] 0.356	1.25 [0.64; 2.42] 0.514	0.04 [-0.08; 0.16] 0.512
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.954				
< 65 years					
N"/N'/N	160 / 203 / 204	166 / 195 / 195			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	49 (24.1)	47 (24.1)	1.27 [0.72; 2.23] 0.412	0.99 [0.70; 1.40] 0.963	-0.00 [-0.09; 0.08] 0.962
≥ 65 years					
N"/N'/N	133 / 163 / 164	142 / 173 / 173			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	34 (20.9)	29 (16.8)	1.24 [0.64; 2.40] 0.531	1.25 [0.80; 1.95] 0.336	0.04 [-0.04; 0.12] 0.335
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.071**					

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.940				
< 65 years					
N"/N'/N	78 / 103 / 104	76 / 93 / 93			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	27 (26.2)	27 (29.0)	0.92 [0.42; 2.03] 0.836	0.90 [0.57; 1.42] 0.659	-0.03 [-0.15; 0.10] 0.660
≥ 65 years					
N"/N'/N	66 / 85 / 85	70 / 94 / 94			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	15 (17.6)	13 (13.8)	0.88 [0.34; 2.29] 0.788	1.28 [0.64; 2.52] 0.484	0.04 [-0.07; 0.15] 0.484
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.857				
< 65 years					
N"/N'/N	72 / 100 / 100	87 / 102 / 102			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	27 (27.0)	22 (21.6)	2.09 [0.95; 4.63] 0.069	1.25 [0.77; 2.04] 0.370	0.05 [-0.06; 0.17] 0.367
≥ 65 years					
N"/N'/N	59 / 78 / 79	59 / 79 / 79			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	17 (21.8)	13 (16.5)	1.86 [0.69; 5.05] 0.221	1.32 [0.69; 2.54] 0.397	0.05 [-0.07; 0.18] 0.394
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.879				
< 65 years					
N"/N'/N	150 / 203 / 204	163 / 195 / 195			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	54 (26.6)	49 (25.1)	1.38 [0.79; 2.42] 0.254	1.05 [0.76; 1.47] 0.755	0.01 [-0.07; 0.10] 0.755

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N"/N'/N	125 / 163 / 164	129 / 173 / 173			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	32 (19.6)	26 (15.0)	1.29 [0.65; 2.57] 0.465	1.30 [0.81; 2.08] 0.273	0.05 [-0.04; 0.13] 0.272

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + baseline value + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + baseline value + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 9.3 VFQ - Gain of 4 respectively 15 points by gender (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.178**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.421				
Male					
N''/N'/N	87 / 110 / 110	102 / 126 / 126			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	60 (54.5)	75 (59.5)	0.77 [0.44; 1.36] 0.373	0.92 [0.73; 1.15] 0.443	-0.05 [-0.18; 0.08] 0.441
Female					
N''/N'/N	62 / 78 / 79	56 / 61 / 61			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	38 (48.7)	38 (62.3)	0.52 [0.24; 1.13] 0.097	0.78 [0.58; 1.06] 0.108	-0.14 [-0.30; 0.03] 0.106
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.091				
Male					
N''/N'/N	98 / 119 / 120	94 / 115 / 115			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	62 (52.1)	66 (57.4)	0.78 [0.45; 1.34] 0.369	0.91 [0.72; 1.15] 0.417	-0.05 [-0.18; 0.07] 0.416
Female					
N''/N'/N	46 / 59 / 59	56 / 66 / 66			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	36 (61.0)	34 (51.5)	1.77 [0.82; 3.83] 0.148	1.18 [0.87; 1.62] 0.285	0.10 [-0.08; 0.27] 0.282
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.480				
Male					
N''/N'/N	185 / 229 / 230	196 / 241 / 241			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	122 (53.3)	141 (58.5)	0.77 [0.52; 1.14] 0.185	0.91 [0.78; 1.07] 0.264	-0.05 [-0.14; 0.04] 0.262

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N"/N'/N	108 / 137 / 138	112 / 127 / 127			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	74 (54.0)	72 (56.7)	0.98 [0.57; 1.67] 0.927	0.95 [0.77; 1.18] 0.676	-0.03 [-0.15; 0.10] 0.676
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.121**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.548				
Male					
N"/N'/N	83 / 110 / 110	94 / 126 / 126			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	55 (50.0)	70 (55.6)	0.75 [0.43; 1.31] 0.313	0.90 [0.71; 1.15] 0.396	-0.06 [-0.18; 0.07] 0.393
Female					
N"/N'/N	61 / 78 / 79	52 / 61 / 61			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	44 (56.4)	35 (57.4)	1.00 [0.47; 2.10] 0.996	0.98 [0.73; 1.32] 0.909	-0.01 [-0.18; 0.16] 0.909
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.287				
Male					
N"/N'/N	89 / 119 / 120	93 / 115 / 115			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	68 (57.1)	62 (53.9)	1.14 [0.66; 1.96] 0.651	1.06 [0.84; 1.33] 0.620	0.03 [-0.10; 0.16] 0.619
Female					
N"/N'/N	42 / 59 / 59	53 / 66 / 66			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	32 (54.2)	29 (43.9)	1.91 [0.87; 4.18] 0.105	1.23 [0.86; 1.77] 0.251	0.10 [-0.07; 0.28] 0.248
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.207				
Male					
N"/N'/N	172 / 229 / 230	187 / 241 / 241			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	123 (53.7)	132 (54.8)	0.93 [0.63; 1.37] 0.711	0.98 [0.83; 1.16] 0.799	-0.01 [-0.10; 0.08] 0.799

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N"/N'/N	103 / 137 / 138	105 / 127 / 127			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	76 (55.5)	64 (50.4)	1.42 [0.83; 2.43] 0.196	1.09 [0.87; 1.36] 0.476	0.04 [-0.08; 0.16] 0.475
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.231**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.005 *				
Male					
N"/N'/N	87 / 110 / 110	102 / 126 / 126			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	28 (25.5)	21 (16.7)	1.99 [0.87; 4.53] 0.102	1.53 [0.92; 2.53] 0.100	0.09 [-0.02; 0.19] 0.098
Female					
N"/N'/N	62 / 78 / 79	56 / 61 / 61			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	18 (23.1)	22 (36.1)	0.30 [0.11; 0.83] 0.021 *	0.64 [0.38; 1.08] 0.096	-0.13 [-0.28; 0.02] 0.095
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.877				
Male					
N"/N'/N	98 / 119 / 120	94 / 115 / 115			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	23 (19.3)	19 (16.5)	1.44 [0.67; 3.10] 0.347	1.17 [0.67; 2.03] 0.577	0.03 [-0.07; 0.13] 0.575
Female					
N"/N'/N	46 / 59 / 59	56 / 66 / 66			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	14 (23.7)	14 (21.2)	1.59 [0.58; 4.35] 0.362	1.12 [0.58; 2.15] 0.736	0.03 [-0.12; 0.17] 0.737
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.063				
Male					
N"/N'/N	185 / 229 / 230	196 / 241 / 241			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	51 (22.3)	40 (16.6)	1.75 [1.00; 3.06] 0.050 *	1.35 [0.93; 1.96] 0.112	0.06 [-0.01; 0.13] 0.112

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N"/N'/N	108 / 137 / 138	112 / 127 / 127			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	32 (23.4)	36 (28.3)	0.75 [0.37; 1.50] 0.414	0.81 [0.54; 1.21] 0.301	-0.06 [-0.16; 0.05] 0.303
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.071**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.736				
Male					
N"/N'/N	83 / 110 / 110	94 / 126 / 126			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	21 (19.1)	24 (19.0)	0.82 [0.37; 1.83] 0.632	1.00 [0.59; 1.70] 0.993	0.00 [-0.10; 0.10] 0.993
Female					
N"/N'/N	61 / 78 / 79	52 / 61 / 61			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	21 (26.9)	16 (26.2)	1.02 [0.39; 2.68] 0.967	1.03 [0.59; 1.79] 0.927	0.01 [-0.14; 0.15] 0.927
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.424				
Male					
N"/N'/N	89 / 119 / 120	93 / 115 / 115			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	30 (25.2)	19 (16.5)	2.35 [1.07; 5.18] 0.034 *	1.53 [0.91; 2.55] 0.107	0.09 [-0.02; 0.19] 0.100
Female					
N"/N'/N	42 / 59 / 59	53 / 66 / 66			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	14 (23.7)	16 (24.2)	1.37 [0.48; 3.93] 0.553	0.98 [0.52; 1.83] 0.946	-0.01 [-0.16; 0.14] 0.946
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.742				
Male					
N"/N'/N	172 / 229 / 230	187 / 241 / 241			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	51 (22.3)	43 (17.8)	1.43 [0.82; 2.48] 0.206	1.24 [0.86; 1.80] 0.239	0.04 [-0.03; 0.12] 0.238

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N"/N'/N	103 / 137 / 138	105 / 127 / 127			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	35 (25.5)	32 (25.2)	1.23 [0.61; 2.49] 0.568	1.00 [0.66; 1.52] 0.983	0.00 [-0.10; 0.11] 0.982

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 9.4 VFQ - Gain of 4 respectively 15 points by BCVA (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.178**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.612				
≤ 65 letters					
N"/N'/N	54 / 74 / 74	53 / 64 / 64			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	46 (62.2)	40 (62.5)	0.77 [0.35; 1.67] 0.508	0.99 [0.77; 1.29] 0.967	-0.00 [-0.17; 0.16] 0.967
> 65 letters					
N"/N'/N	95 / 114 / 115	105 / 123 / 123			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	52 (45.6)	73 (59.3)	0.60 [0.34; 1.05] 0.075	0.77 [0.60; 0.99] 0.038 *	-0.14 [-0.26; -0.01] 0.033 *
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.055				
≤ 65 letters					
N"/N'/N	52 / 65 / 65	75 / 91 / 91			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	44 (67.7)	53 (58.2)	1.79 [0.88; 3.63] 0.109	1.16 [0.91; 1.48] 0.223	0.09 [-0.06; 0.25] 0.224
> 65 letters					
N"/N'/N	92 / 113 / 114	75 / 90 / 90			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	54 (47.8)	47 (52.2)	0.72 [0.41; 1.30] 0.278	0.92 [0.69; 1.21] 0.529	-0.04 [-0.18; 0.09] 0.530
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.056				
≤ 65 letters					
N"/N'/N	106 / 139 / 139	128 / 155 / 155			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	90 (64.7)	93 (60.0)	1.23 [0.74; 2.06] 0.430	1.08 [0.90; 1.29] 0.402	0.05 [-0.06; 0.16] 0.399

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N"/N'/N	187 / 227 / 229	180 / 213 / 213			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	106 (46.7)	120 (56.3)	0.65 [0.43; 0.97] 0.035 *	0.83 [0.69; 1.00] 0.048 *	-0.09 [-0.19; -0.00] 0.047 *
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.121**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.046 *				
≤ 65 letters					
N"/N'/N	53 / 74 / 74	50 / 64 / 64			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	51 (68.9)	36 (56.3)	1.54 [0.72; 3.30] 0.269	1.23 [0.94; 1.60] 0.133	0.13 [-0.03; 0.29] 0.123
> 65 letters					
N"/N'/N	91 / 114 / 115	96 / 123 / 123			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	48 (42.1)	69 (56.1)	0.59 [0.34; 1.02] 0.061	0.75 [0.58; 0.98] 0.035 *	-0.14 [-0.27; -0.01] 0.030 *
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.029 *				
≤ 65 letters					
N"/N'/N	49 / 65 / 65	68 / 91 / 91			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	44 (67.7)	47 (51.6)	2.52 [1.23; 5.16] 0.011 *	1.31 [1.01; 1.70] 0.042 *	0.16 [0.01; 0.31] 0.040 *
> 65 letters					
N"/N'/N	82 / 113 / 114	78 / 90 / 90			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	56 (49.6)	44 (48.9)	0.89 [0.50; 1.60] 0.703	1.01 [0.76; 1.34] 0.925	0.01 [-0.13; 0.15] 0.925
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.002 *				
≤ 65 letters					
N"/N'/N	102 / 139 / 139	118 / 155 / 155			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	95 (68.3)	83 (53.5)	2.02 [1.20; 3.39] 0.008 *	1.27 [1.05; 1.53] 0.012 *	0.14 [0.03; 0.26] 0.011 *

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N"/N'/N	173 / 227 / 229	174 / 213 / 213			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	104 (45.8)	113 (53.1)	0.72 [0.48; 1.08] 0.112	0.86 [0.71; 1.05] 0.129	-0.07 [-0.17; 0.02] 0.129
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.231**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.828				
≤ 65 letters					
N"/N'/N	54 / 74 / 74	53 / 64 / 64			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	20 (27.0)	16 (25.0)	0.94 [0.33; 2.74] 0.915	1.08 [0.61; 1.90] 0.787	0.02 [-0.13; 0.17] 0.786
> 65 letters					
N"/N'/N	95 / 114 / 115	105 / 123 / 123			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	26 (22.8)	27 (22.0)	1.09 [0.49; 2.45] 0.825	1.04 [0.65; 1.67] 0.874	0.01 [-0.10; 0.11] 0.875
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.627				
≤ 65 letters					
N"/N'/N	52 / 65 / 65	75 / 91 / 91			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	15 (23.1)	21 (23.1)	1.68 [0.69; 4.10] 0.254	1.00 [0.56; 1.79] 1.000	-0.00 [-0.13; 0.13] 1.000
> 65 letters					
N"/N'/N	92 / 113 / 114	75 / 90 / 90			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	22 (19.5)	12 (13.3)	1.23 [0.52; 2.91] 0.631	1.46 [0.76; 2.79] 0.251	0.06 [-0.04; 0.16] 0.235
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.694				
≤ 65 letters					
N"/N'/N	106 / 139 / 139	128 / 155 / 155			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	35 (25.2)	37 (23.9)	1.36 [0.69; 2.68] 0.372	1.04 [0.69; 1.56] 0.849	0.01 [-0.09; 0.11] 0.849

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N"/N'/N	187 / 227 / 229	180 / 213 / 213			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	48 (21.1)	39 (18.3)	1.14 [0.64; 2.02] 0.662	1.18 [0.81; 1.73] 0.390	0.03 [-0.04; 0.11] 0.387
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.071**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.256				
≤ 65 letters					
N"/N'/N	53 / 74 / 74	50 / 64 / 64			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	22 (29.7)	14 (21.9)	1.50 [0.55; 4.11] 0.428	1.36 [0.76; 2.43] 0.300	0.08 [-0.07; 0.22] 0.289
> 65 letters					
N"/N'/N	91 / 114 / 115	96 / 123 / 123			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	20 (17.5)	26 (21.1)	0.71 [0.32; 1.58] 0.400	0.83 [0.49; 1.40] 0.486	-0.04 [-0.14; 0.06] 0.483
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.576				
≤ 65 letters					
N"/N'/N	49 / 65 / 65	68 / 91 / 91			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	18 (27.7)	26 (28.6)	1.67 [0.70; 3.98] 0.250	0.97 [0.58; 1.61] 0.904	-0.01 [-0.15; 0.13] 0.904
> 65 letters					
N"/N'/N	82 / 113 / 114	78 / 90 / 90			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	26 (23.0)	9 (10.0)	2.40 [0.94; 6.14] 0.068	2.30 [1.14; 4.66] 0.021 *	0.13 [0.03; 0.23] 0.010 *
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.605				
≤ 65 letters					
N"/N'/N	102 / 139 / 139	118 / 155 / 155			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	40 (28.8)	40 (25.8)	1.52 [0.79; 2.92] 0.213	1.13 [0.77; 1.65] 0.533	0.03 [-0.07; 0.14] 0.532

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N"/N'/N	173 / 227 / 229	174 / 213 / 213			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	46 (20.3)	35 (16.4)	1.20 [0.66; 2.16] 0.547	1.25 [0.83; 1.88] 0.279	0.04 [-0.03; 0.11] 0.276

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 9.5 VFQ - Gain of 4 respectively 15 points by region (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.178**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.177				
Region of the Americas					
N"/N'/N	70 / 90 / 90	72 / 83 / 83			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	49 (54.4)	61 (73.5)	0.41 [0.20; 0.84] 0.014 *	0.74 [0.59; 0.93] 0.010 *	-0.19 [-0.33; -0.05] 0.008 *
European Region					
N"/N'/N	55 / 68 / 69	61 / 75 / 75			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	32 (47.1)	35 (46.7)	1.07 [0.53; 2.18] 0.851	1.01 [0.71; 1.43] 0.963	0.00 [-0.16; 0.17] 0.963
Western Pacific Region					
N"/N'/N	24 / 30 / 30	25 / 29 / 29			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	17 (56.7)	17 (58.6)	0.60 [0.19; 1.83] 0.366	0.97 [0.62; 1.50] 0.879	-0.02 [-0.27; 0.23] 0.879
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.666				
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	17 / 26 / 26	14 / 21 / 21			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	16 (61.5)	15 (71.4)	0.62 [0.17; 2.23] 0.463	0.86 [0.57; 1.29] 0.473	-0.10 [-0.37; 0.17] 0.471
European Region					
N"/N'/N	112 / 134 / 135	112 / 132 / 132			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	72 (53.7)	71 (53.8)	1.04 [0.63; 1.74] 0.873	1.00 [0.80; 1.25] 0.993	-0.00 [-0.12; 0.12] 0.993
Western Pacific Region					
N"/N'/N	15 / 18 / 18	24 / 28 / 28			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	10 (55.6)	14 (50.0)	1.38 [0.39; 4.87] 0.615	1.11 [0.64; 1.94] 0.710	0.06 [-0.24; 0.35] 0.712

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.283				
Region of the Americas					
N"/N'/N	70 / 90 / 90	72 / 83 / 83			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	49 (54.4)	61 (73.5)	0.45 [0.20; 0.98] 0.045 *	0.74 [0.59; 0.93] 0.009 *	-0.19 [-0.33; -0.05] 0.008 *
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	17 / 26 / 26	14 / 21 / 21			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	16 (61.5)	15 (71.4)	0.56 [0.15; 2.19] 0.407	0.86 [0.57; 1.29] 0.482	-0.10 [-0.37; 0.17] 0.471
European Region					
N"/N'/N	167 / 202 / 204	173 / 207 / 207			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	104 (51.5)	106 (51.2)	1.04 [0.67; 1.60] 0.874	1.00 [0.83; 1.21] 0.984	0.00 [-0.10; 0.10] 0.984
Western Pacific Region					
N"/N'/N	39 / 48 / 48	49 / 57 / 57			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	27 (56.3)	31 (54.4)	0.94 [0.41; 2.14] 0.874	1.02 [0.73; 1.44] 0.900	0.01 [-0.18; 0.20] 0.899
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.121**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.744				
Region of the Americas					
N"/N'/N	67 / 90 / 90	66 / 83 / 83			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	53 (58.9)	55 (66.3)	0.78 [0.39; 1.54] 0.474	0.89 [0.71; 1.12] 0.317	-0.07 [-0.22; 0.07] 0.315
European Region					
N"/N'/N	51 / 68 / 69	56 / 75 / 75			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	32 (47.1)	36 (48.0)	1.00 [0.49; 2.02] 0.999	0.98 [0.69; 1.38] 0.910	-0.01 [-0.17; 0.15] 0.910
Western Pacific Region					
N"/N'/N	26 / 30 / 30	24 / 29 / 29			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	14 (46.7)	14 (48.3)	0.61 [0.20; 1.85] 0.387	0.97 [0.57; 1.65] 0.902	-0.02 [-0.27; 0.24] 0.902

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.870				
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	13 / 26 / 26	15 / 21 / 21			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	19 (73.1)	14 (66.7)	1.39 [0.38; 5.14] 0.621	1.10 [0.75; 1.61] 0.638	0.06 [-0.20; 0.33] 0.634
European Region					
N"/N'/N	106 / 134 / 135	108 / 132 / 132			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	71 (53.0)	61 (46.2)	1.42 [0.85; 2.38] 0.176	1.15 [0.90; 1.46] 0.271	0.07 [-0.05; 0.19] 0.268
Western Pacific Region					
N"/N'/N	12 / 18 / 18	23 / 28 / 28			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	10 (55.6)	16 (57.1)	0.99 [0.28; 3.49] 0.986	0.97 [0.58; 1.64] 0.916	-0.02 [-0.31; 0.28] 0.916
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.827				
Region of the Americas					
N"/N'/N	67 / 90 / 90	66 / 83 / 83			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	53 (58.9)	55 (66.3)	0.92 [0.43; 1.98] 0.826	0.89 [0.71; 1.12] 0.318	-0.07 [-0.22; 0.07] 0.315
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	13 / 26 / 26	15 / 21 / 21			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	19 (73.1)	14 (66.7)	1.16 [0.29; 4.60] 0.830	1.10 [0.75; 1.61] 0.636	0.06 [-0.20; 0.33] 0.634
European Region					
N"/N'/N	157 / 202 / 204	164 / 207 / 207			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	103 (51.0)	97 (46.9)	1.19 [0.77; 1.83] 0.433	1.09 [0.89; 1.33] 0.410	0.04 [-0.06; 0.14] 0.409
Western Pacific Region					
N"/N'/N	38 / 48 / 48	47 / 57 / 57			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	24 (50.0)	30 (52.6)	0.77 [0.34; 1.76] 0.543	0.97 [0.67; 1.41] 0.872	-0.02 [-0.21; 0.18] 0.871
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.231**					

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.045 *				
Region of the Americas					
N"/N'/N	70 / 90 / 90	72 / 83 / 83			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	27 (30.0)	28 (33.7)	0.76 [0.32; 1.80] 0.528	0.89 [0.57; 1.38] 0.598	-0.04 [-0.18; 0.10] 0.598
European Region					
N"/N'/N	55 / 68 / 69	61 / 75 / 75			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	8 (11.8)	13 (17.3)	0.50 [0.15; 1.70] 0.269	0.68 [0.30; 1.54] 0.353	-0.06 [-0.17; 0.06] 0.342
Western Pacific Region					
N"/N'/N	24 / 30 / 30	25 / 29 / 29			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	11 (36.7)	2 (6.9)	7.62 [1.20; 48.18] 0.031 *	5.32 [1.29; 21.94] 0.021 *	0.30 [0.10; 0.49] 0.003 *
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.670				
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	17 / 26 / 26	14 / 21 / 21			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	9 (34.6)	5 (23.8)	2.31 [0.52; 10.32] 0.273	1.45 [0.57; 3.68] 0.430	0.11 [-0.15; 0.37] 0.412
European Region					
N"/N'/N	112 / 134 / 135	112 / 132 / 132			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	24 (17.9)	23 (17.4)	1.24 [0.60; 2.55] 0.566	1.03 [0.61; 1.73] 0.917	0.00 [-0.09; 0.10] 0.917
Western Pacific Region					
N"/N'/N	15 / 18 / 18	24 / 28 / 28			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	4 (22.2)	5 (17.9)	2.22 [0.40; 12.26] 0.359	1.24 [0.38; 4.03] 0.715	0.04 [-0.20; 0.28] 0.720
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.104				
Region of the Americas					
N"/N'/N	70 / 90 / 90	72 / 83 / 83			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	27 (30.0)	28 (33.7)	1.01 [0.38; 2.71] 0.983	0.89 [0.57; 1.38] 0.599	-0.04 [-0.18; 0.10] 0.598

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	17 / 26 / 26	14 / 21 / 21			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	9 (34.6)	5 (23.8)	1.94 [0.36; 10.47] 0.441	1.45 [0.57; 3.68] 0.426	0.11 [-0.15; 0.37] 0.412
European Region					
N"/N'/N	167 / 202 / 204	173 / 207 / 207			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	32 (15.8)	36 (17.4)	0.89 [0.46; 1.72] 0.721	0.91 [0.59; 1.40] 0.659	-0.02 [-0.09; 0.06] 0.658
Western Pacific Region					
N"/N'/N	39 / 48 / 48	49 / 57 / 57			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	15 (31.3)	7 (12.3)	4.48 [1.37; 14.69] 0.013 *	2.64 [1.11; 6.29] 0.019 *	0.19 [0.03; 0.35] 0.018 *
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.071**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.530				
Region of the Americas					
N"/N'/N	67 / 90 / 90	66 / 83 / 83			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	27 (30.0)	25 (30.1)	1.07 [0.46; 2.46] 0.878	1.00 [0.63; 1.57] 0.986	-0.00 [-0.14; 0.14] 0.986
European Region					
N"/N'/N	51 / 68 / 69	56 / 75 / 75			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	8 (11.8)	12 (16.0)	0.55 [0.17; 1.79] 0.321	0.74 [0.32; 1.69] 0.469	-0.04 [-0.16; 0.07] 0.462
Western Pacific Region					
N"/N'/N	26 / 30 / 30	24 / 29 / 29			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	7 (23.3)	3 (10.3)	1.58 [0.30; 8.20] 0.587	2.26 [0.64; 7.89] 0.203	0.13 [-0.06; 0.32] 0.175
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.899				
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	13 / 26 / 26	15 / 21 / 21			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	10 (38.5)	6 (28.6)	2.07 [0.47; 9.22] 0.339	1.35 [0.59; 3.10] 0.484	0.10 [-0.17; 0.37] 0.471

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
European Region					
N''/N'/N	106 / 134 / 135	108 / 132 / 132			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	29 (21.6)	21 (15.9)	2.14 [0.99; 4.59] 0.052	1.36 [0.82; 2.26] 0.235	0.06 [-0.04; 0.15] 0.230
Western Pacific Region					
N''/N'/N	12 / 18 / 18	23 / 28 / 28			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	5 (27.8)	8 (28.6)	1.41 [0.28; 7.11] 0.678	0.97 [0.38; 2.51] 0.954	-0.01 [-0.27; 0.26] 0.953
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.929				
Region of the Americas					
N''/N'/N	67 / 90 / 90	66 / 83 / 83			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	27 (30.0)	25 (30.1)	1.76 [0.64; 4.84] 0.275	1.00 [0.63; 1.57] 0.986	-0.00 [-0.14; 0.14] 0.986
South-East Asia Region and Eastern Mediterranean Region					
N''/N'/N	13 / 26 / 26	15 / 21 / 21			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	10 (38.5)	6 (28.6)	1.24 [0.24; 6.25] 0.798	1.35 [0.59; 3.10] 0.482	0.10 [-0.17; 0.37] 0.471
European Region					
N''/N'/N	157 / 202 / 204	164 / 207 / 207			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	37 (18.3)	33 (15.9)	1.12 [0.56; 2.22] 0.747	1.14 [0.74; 1.75] 0.546	0.02 [-0.05; 0.10] 0.545

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Western Pacific Region					
N"/N'/N	38 / 48 / 48	47 / 57 / 57			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	12 (25.0)	11 (19.3)	1.44 [0.47; 4.36] 0.522	1.39 [0.66; 2.94] 0.382	0.07 [-0.09; 0.23] 0.379

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 9.6 VFQ - Gain of 4 respectively 15 points by diabetes type (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.178**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.181				
Type 1					
N"/N'/N	8 / 12 / 12	6 / 6 / 6			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	5 (41.7)	5 (83.3)	0.12 [0.01; 1.50] 0.101	0.50 [0.23; 1.07] 0.074	-0.42 [-0.82; -0.01] 0.046 *
Type 2					
N"/N'/N	141 / 176 / 177	152 / 181 / 181			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	93 (52.8)	108 (59.7)	0.70 [0.44; 1.11] 0.131	0.89 [0.74; 1.06] 0.195	-0.07 [-0.17; 0.03] 0.193
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.135				
Type 1					
N"/N'/N	18 / 19 / 19	7 / 7 / 7			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	8 (42.1)	5 (71.4)	0.25 [0.04; 1.72] 0.158	0.59 [0.29; 1.19] 0.142	-0.29 [-0.69; 0.11] 0.152
Type 2					
N"/N'/N	126 / 159 / 160	143 / 174 / 174			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	90 (56.6)	95 (54.6)	1.13 [0.71; 1.79] 0.600	1.04 [0.86; 1.26] 0.713	0.02 [-0.09; 0.13] 0.713
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.040 *				
Type 1					
N"/N'/N	26 / 31 / 31	13 / 13 / 13			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	13 (41.9)	10 (76.9)	0.17 [0.04; 0.80] 0.025 *	0.55 [0.33; 0.92] 0.040 *	-0.35 [-0.64; -0.06] 0.019 *

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N"/N'/N	267 / 335 / 337	295 / 355 / 355			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	183 (54.6)	203 (57.2)	0.90 [0.65; 1.24] 0.515	0.96 [0.84; 1.09] 0.498	-0.03 [-0.10; 0.05] 0.497
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.121**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.593				
Type 1					
N"/N'/N	9 / 12 / 12	4 / 6 / 6			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	6 (50.0)	4 (66.7)	0.47 [0.06; 3.83] 0.482	0.75 [0.34; 1.67] 0.481	-0.17 [-0.64; 0.30] 0.488
Type 2					
N"/N'/N	135 / 176 / 177	142 / 181 / 181			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	93 (52.8)	101 (55.8)	0.85 [0.54; 1.34] 0.475	0.95 [0.78; 1.15] 0.575	-0.03 [-0.13; 0.07] 0.574
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.349				
Type 1					
N"/N'/N	16 / 19 / 19	5 / 7 / 7			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	9 (47.4)	4 (57.1)	0.59 [0.10; 3.63] 0.569	0.83 [0.37; 1.84] 0.645	-0.10 [-0.53; 0.33] 0.656
Type 2					
N"/N'/N	115 / 159 / 160	141 / 174 / 174			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	91 (57.2)	87 (50.0)	1.45 [0.91; 2.29] 0.118	1.14 [0.94; 1.40] 0.186	0.07 [-0.03; 0.18] 0.185
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.275				
Type 1					
N"/N'/N	25 / 31 / 31	9 / 13 / 13			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	15 (48.4)	8 (61.5)	0.50 [0.13; 2.00] 0.330	0.79 [0.45; 1.39] 0.449	-0.13 [-0.45; 0.19] 0.431

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N"/N'/N	250 / 335 / 337	283 / 355 / 355			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	184 (54.9)	188 (53.0)	1.11 [0.80; 1.53] 0.527	1.04 [0.90; 1.19] 0.607	0.02 [-0.05; 0.09] 0.607
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.231**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.805				
Type 1					
N"/N'/N	8 / 12 / 12	6 / 6 / 6			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	3 (25.0)	2 (33.3)	0.67 [0.07; 6.75] 0.734	0.75 [0.17; 3.35] 0.706	-0.08 [-0.53; 0.37] 0.717
Type 2					
N"/N'/N	141 / 176 / 177	152 / 181 / 181			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	43 (24.4)	41 (22.7)	0.91 [0.47; 1.74] 0.770	1.08 [0.74; 1.57] 0.692	0.02 [-0.07; 0.11] 0.692
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.533				
Type 1					
N"/N'/N	18 / 19 / 19	7 / 7 / 7			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	2 (10.5)	1 (14.3)	0.65 [0.04; 10.25] 0.761	0.74 [0.08; 6.91] 0.789	-0.04 [-0.33; 0.26] 0.802
Type 2					
N"/N'/N	126 / 159 / 160	143 / 174 / 174			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	35 (22.0)	32 (18.4)	1.60 [0.86; 2.99] 0.139	1.20 [0.78; 1.84] 0.411	0.04 [-0.05; 0.12] 0.411
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.435				
Type 1					
N"/N'/N	26 / 31 / 31	13 / 13 / 13			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	5 (16.1)	3 (23.1)	0.62 [0.11; 3.62] 0.599	0.75 [0.21; 2.60] 0.656	-0.06 [-0.32; 0.20] 0.662

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N"/N'/N	267 / 335 / 337	295 / 355 / 355			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	78 (23.3)	73 (20.6)	1.29 [0.82; 2.01] 0.270	1.13 [0.85; 1.50] 0.397	0.03 [-0.04; 0.09] 0.397
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.071**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.462				
Type 1					
N"/N'/N	9 / 12 / 12	4 / 6 / 6			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	2 (16.7)	2 (33.3)	0.36 [0.03; 4.09] 0.413	0.50 [0.09; 2.73] 0.423	-0.17 [-0.60; 0.27] 0.450
Type 2					
N"/N'/N	135 / 176 / 177	142 / 181 / 181			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	40 (22.7)	38 (21.0)	0.93 [0.49; 1.75] 0.821	1.08 [0.73; 1.60] 0.692	0.02 [-0.07; 0.10] 0.692
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	16 / 19 / 19	5 / 7 / 7			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	5 (26.3)	0 (0.0)	N.E.	4.40 [0.27; 70.68] 0.296	0.26 [0.07; 0.46] 0.009 *
Type 2					
N"/N'/N	115 / 159 / 160	141 / 174 / 174			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	39 (24.5)	35 (20.1)	1.29 [0.77; 2.17] 0.334	1.22 [0.82; 1.82] 0.334	0.04 [-0.05; 0.13] 0.334
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.811				
Type 1					
N"/N'/N	25 / 31 / 31	9 / 13 / 13			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	7 (22.6)	2 (15.4)	1.65 [0.25; 11.06] 0.606	1.32 [0.34; 5.10] 0.677	0.07 [-0.17; 0.32] 0.557

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N"/N'/N	250 / 335 / 337	283 / 355 / 355			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	79 (23.6)	73 (20.6)	1.30 [0.83; 2.04] 0.252	1.15 [0.87; 1.52] 0.339	0.03 [-0.03; 0.09] 0.338

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Gain in VFQ-25 Composite Score of ≥ 15 points / KITE / Week 100: logit(proportion) = treatment [by diabetes type].

Table 9.7 VFQ - Gain of 4 respectively 15 points by HbA1c (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.178**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.251				
< 7.5 %					
N"/N'/N	63 / 76 / 76	93 / 107 / 107			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	41 (53.9)	64 (59.8)	0.86 [0.45; 1.67] 0.664	0.90 [0.70; 1.17] 0.435	-0.06 [-0.20; 0.09] 0.430
≥ 7.5 %					
N"/N'/N	86 / 111 / 112	65 / 80 / 80			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	56 (50.5)	49 (61.3)	0.50 [0.26; 0.96] 0.037 *	0.82 [0.64; 1.06] 0.134	-0.11 [-0.25; 0.03] 0.135
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.578				
< 7.5 %					
N"/N'/N	64 / 81 / 82	79 / 96 / 96			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	45 (55.6)	53 (55.2)	1.17 [0.62; 2.20] 0.632	1.01 [0.77; 1.31] 0.963	0.00 [-0.14; 0.15] 0.963
≥ 7.5 %					
N"/N'/N	80 / 97 / 97	71 / 85 / 85			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	53 (54.6)	47 (55.3)	0.91 [0.49; 1.68] 0.759	0.99 [0.76; 1.29] 0.929	-0.01 [-0.15; 0.14] 0.929
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.256				
< 7.5 %					
N"/N'/N	127 / 157 / 158	172 / 203 / 203			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	86 (54.8)	117 (57.6)	1.00 [0.63; 1.57] 0.984	0.95 [0.79; 1.15] 0.600	-0.03 [-0.13; 0.08] 0.599

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N"/N'/N	166 / 208 / 209	136 / 165 / 165			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	109 (52.4)	96 (58.2)	0.69 [0.44; 1.07] 0.099	0.90 [0.75; 1.08] 0.266	-0.06 [-0.16; 0.04] 0.264
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.121**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.877				
< 7.5 %					
N"/N'/N	57 / 76 / 76	90 / 107 / 107			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	38 (50.0)	60 (56.1)	0.84 [0.44; 1.60] 0.596	0.89 [0.67; 1.18] 0.423	-0.06 [-0.21; 0.09] 0.417
≥ 7.5 %					
N"/N'/N	86 / 111 / 112	56 / 80 / 80			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	60 (54.1)	45 (56.3)	0.78 [0.42; 1.47] 0.443	0.96 [0.74; 1.24] 0.763	-0.02 [-0.16; 0.12] 0.763
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.976				
< 7.5 %					
N"/N'/N	60 / 81 / 82	75 / 96 / 96			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	46 (56.8)	51 (53.1)	1.36 [0.72; 2.57] 0.342	1.07 [0.82; 1.40] 0.625	0.04 [-0.11; 0.18] 0.625
≥ 7.5 %					
N"/N'/N	71 / 97 / 97	71 / 85 / 85			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	54 (55.7)	40 (47.1)	1.38 [0.74; 2.57] 0.309	1.18 [0.89; 1.58] 0.251	0.09 [-0.06; 0.23] 0.245
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.952				
< 7.5 %					
N"/N'/N	117 / 157 / 158	165 / 203 / 203			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	84 (53.5)	111 (54.7)	1.07 [0.68; 1.69] 0.762	0.98 [0.81; 1.19] 0.817	-0.01 [-0.12; 0.09] 0.816

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N"/N'/N	157 / 208 / 209	127 / 165 / 165			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	114 (54.8)	85 (51.5)	1.05 [0.68; 1.63] 0.823	1.06 [0.88; 1.29] 0.548	0.03 [-0.07; 0.13] 0.547
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.231**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.678				
< 7.5 %					
N"/N'/N	63 / 76 / 76	93 / 107 / 107			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	20 (26.3)	26 (24.3)	1.12 [0.46; 2.74] 0.809	1.08 [0.65; 1.79] 0.756	0.02 [-0.11; 0.15] 0.758
≥ 7.5 %					
N"/N'/N	86 / 111 / 112	65 / 80 / 80			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	25 (22.5)	17 (21.3)	0.85 [0.34; 2.11] 0.730	1.06 [0.61; 1.83] 0.834	0.01 [-0.11; 0.13] 0.833
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.541				
< 7.5 %					
N"/N'/N	64 / 81 / 82	79 / 96 / 96			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	17 (21.0)	22 (22.9)	1.31 [0.57; 3.00] 0.528	0.92 [0.52; 1.60] 0.758	-0.02 [-0.14; 0.10] 0.757
≥ 7.5 %					
N"/N'/N	80 / 97 / 97	71 / 85 / 85			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	20 (20.6)	11 (12.9)	1.92 [0.77; 4.76] 0.161	1.59 [0.81; 3.13] 0.177	0.08 [-0.03; 0.18] 0.162
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.982				
< 7.5 %					
N"/N'/N	127 / 157 / 158	172 / 203 / 203			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	37 (23.6)	48 (23.6)	1.29 [0.71; 2.35] 0.407	1.00 [0.69; 1.46] 0.990	0.00 [-0.09; 0.09] 0.990

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N"/N'/N	166 / 208 / 209	136 / 165 / 165			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	45 (21.6)	28 (17.0)	1.30 [0.69; 2.46] 0.414	1.26 [0.82; 1.92] 0.284	0.04 [-0.04; 0.12] 0.279
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.071**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.853				
< 7.5 %					
N"/N'/N	57 / 76 / 76	90 / 107 / 107			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	17 (22.4)	25 (23.4)	0.87 [0.36; 2.11] 0.762	0.96 [0.56; 1.65] 0.875	-0.01 [-0.13; 0.11] 0.874
≥ 7.5 %					
N"/N'/N	86 / 111 / 112	56 / 80 / 80			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	24 (21.6)	15 (18.8)	0.98 [0.40; 2.39] 0.968	1.15 [0.65; 2.05] 0.629	0.03 [-0.09; 0.14] 0.624
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.659				
< 7.5 %					
N"/N'/N	60 / 81 / 82	75 / 96 / 96			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	19 (23.5)	22 (22.9)	1.75 [0.74; 4.17] 0.206	1.02 [0.60; 1.75] 0.932	0.01 [-0.12; 0.13] 0.932
≥ 7.5 %					
N"/N'/N	71 / 97 / 97	71 / 85 / 85			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	25 (25.8)	13 (15.3)	2.32 [0.94; 5.73] 0.069	1.69 [0.92; 3.08] 0.090	0.10 [-0.01; 0.22] 0.076
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.641				
< 7.5 %					
N"/N'/N	117 / 157 / 158	165 / 203 / 203			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	36 (22.9)	47 (23.2)	1.23 [0.67; 2.26] 0.513	0.99 [0.68; 1.45] 0.959	-0.00 [-0.09; 0.09] 0.959

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N"/N'/N	157 / 208 / 209	127 / 165 / 165			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	49 (23.6)	28 (17.0)	1.51 [0.80; 2.85] 0.201	1.39 [0.92; 2.10] 0.118	0.07 [-0.02; 0.15] 0.112

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 9.8 VFQ - Gain of 4 respectively 15 points by duration of DME (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.178**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.211				
≤ 3 months					
N"/N'/N	101 / 120 / 120	94 / 110 / 110			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	58 (48.3)	69 (62.7)	0.47 [0.26; 0.85] 0.012 *	0.77 [0.61; 0.97] 0.029 *	-0.14 [-0.27; -0.02] 0.026 *
> 3 - < 12 months					
N"/N'/N	21 / 30 / 30	31 / 39 / 39			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	18 (60.0)	24 (61.5)	1.14 [0.40; 3.24] 0.807	0.98 [0.66; 1.43] 0.897	-0.02 [-0.25; 0.22] 0.897
≥ 12 months					
N"/N'/N	27 / 38 / 39	33 / 38 / 38			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	22 (57.9)	20 (52.6)	1.04 [0.38; 2.85] 0.939	1.10 [0.73; 1.65] 0.645	0.05 [-0.17; 0.28] 0.644
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.642				
≤ 3 months					
N"/N'/N	67 / 84 / 85	74 / 92 / 92			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	44 (52.4)	47 (51.1)	1.05 [0.56; 1.96] 0.880	1.03 [0.77; 1.36] 0.864	0.01 [-0.13; 0.16] 0.864
> 3 - < 12 months					
N"/N'/N	43 / 51 / 51	42 / 49 / 49			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	30 (58.8)	28 (57.1)	1.32 [0.56; 3.10] 0.520	1.03 [0.74; 1.44] 0.865	0.02 [-0.18; 0.21] 0.865
≥ 12 months					
N"/N'/N	34 / 43 / 43	34 / 40 / 40			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	24 (55.8)	25 (62.5)	0.73 [0.29; 1.83] 0.497	0.89 [0.62; 1.28] 0.536	-0.07 [-0.28; 0.14] 0.535

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.449				
≤ 3 months					
N"/N'/N	168 / 204 / 205	168 / 202 / 202			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	102 (50.0)	116 (57.4)	0.71 [0.46; 1.08] 0.107	0.87 [0.72; 1.04] 0.126	-0.08 [-0.17; 0.02] 0.125
> 3 - < 12 months					
N"/N'/N	64 / 81 / 81	73 / 88 / 88			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	48 (59.3)	52 (59.1)	1.17 [0.60; 2.28] 0.636	1.01 [0.78; 1.29] 0.960	0.00 [-0.14; 0.15] 0.960
≥ 12 months					
N"/N'/N	61 / 81 / 82	67 / 78 / 78			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	46 (56.8)	45 (57.7)	0.86 [0.43; 1.69] 0.655	0.98 [0.75; 1.29] 0.902	-0.01 [-0.16; 0.14] 0.902
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.121**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.488				
≤ 3 months					
N"/N'/N	94 / 120 / 120	86 / 110 / 110			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	63 (52.5)	66 (60.0)	0.67 [0.38; 1.20] 0.180	0.88 [0.70; 1.10] 0.252	-0.07 [-0.20; 0.05] 0.251
> 3 - < 12 months					
N"/N'/N	22 / 30 / 30	27 / 39 / 39			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	17 (56.7)	21 (53.8)	1.37 [0.49; 3.80] 0.547	1.05 [0.69; 1.61] 0.815	0.03 [-0.21; 0.26] 0.815
≥ 12 months					
N"/N'/N	28 / 38 / 39	33 / 38 / 38			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	19 (50.0)	18 (47.4)	0.90 [0.33; 2.43] 0.831	1.06 [0.67; 1.68] 0.819	0.03 [-0.20; 0.25] 0.818

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.798				
≤ 3 months					
N"/N'/N	57 / 84 / 85	73 / 92 / 92			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	47 (56.0)	43 (46.7)	1.51 [0.80; 2.84] 0.199	1.20 [0.90; 1.60] 0.223	0.09 [-0.06; 0.24] 0.220
> 3 - < 12 months					
N"/N'/N	42 / 51 / 51	38 / 49 / 49			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	32 (62.7)	29 (59.2)	1.43 [0.60; 3.39] 0.416	1.06 [0.77; 1.45] 0.716	0.04 [-0.16; 0.23] 0.715
≥ 12 months					
N"/N'/N	32 / 43 / 43	35 / 40 / 40			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	21 (48.8)	19 (47.5)	1.04 [0.42; 2.59] 0.934	1.03 [0.66; 1.61] 0.903	0.01 [-0.20; 0.23] 0.903
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.706				
≤ 3 months					
N"/N'/N	151 / 204 / 205	159 / 202 / 202			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	110 (53.9)	109 (54.0)	1.01 [0.66; 1.53] 0.980	1.00 [0.83; 1.19] 0.959	-0.00 [-0.10; 0.09] 0.959
> 3 - < 12 months					
N"/N'/N	64 / 81 / 81	65 / 88 / 88			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	49 (60.5)	50 (56.8)	1.36 [0.70; 2.64] 0.356	1.06 [0.82; 1.36] 0.669	0.03 [-0.12; 0.18] 0.667
≥ 12 months					
N"/N'/N	60 / 81 / 82	68 / 78 / 78			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	40 (49.4)	37 (47.4)	0.96 [0.49; 1.89] 0.913	1.04 [0.76; 1.44] 0.806	0.02 [-0.14; 0.17] 0.805
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.231**					

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.245				
≤ 3 months					
N"/N'/N	101 / 120 / 120	94 / 110 / 110			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	30 (25.0)	28 (25.5)	0.83 [0.37; 1.86] 0.657	0.98 [0.63; 1.53] 0.937	-0.00 [-0.12; 0.11] 0.937
> 3 - < 12 months					
N"/N'/N	21 / 30 / 30	31 / 39 / 39			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	4 (13.3)	10 (25.6)	0.47 [0.11; 1.98] 0.302	0.52 [0.18; 1.50] 0.225	-0.12 [-0.31; 0.06] 0.188
≥ 12 months					
N"/N'/N	27 / 38 / 39	33 / 38 / 38			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	12 (31.6)	5 (13.2)	2.76 [0.58; 13.08] 0.201	2.40 [0.94; 6.15] 0.068	0.18 [0.00; 0.37] 0.048 *
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.811				
≤ 3 months					
N"/N'/N	67 / 84 / 85	74 / 92 / 92			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	19 (22.6)	15 (16.3)	1.83 [0.76; 4.40] 0.178	1.39 [0.75; 2.55] 0.292	0.06 [-0.05; 0.18] 0.290
> 3 - < 12 months					
N"/N'/N	43 / 51 / 51	42 / 49 / 49			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	9 (17.6)	10 (20.4)	1.36 [0.42; 4.35] 0.610	0.86 [0.38; 1.95] 0.725	-0.03 [-0.18; 0.13] 0.725
≥ 12 months					
N"/N'/N	34 / 43 / 43	34 / 40 / 40			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	9 (20.9)	8 (20.0)	1.13 [0.33; 3.92] 0.842	1.05 [0.45; 2.45] 0.916	0.01 [-0.16; 0.18] 0.916
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.575				
≤ 3 months					
N"/N'/N	168 / 204 / 205	168 / 202 / 202			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	49 (24.0)	43 (21.3)	1.25 [0.70; 2.23] 0.460	1.12 [0.78; 1.60] 0.551	0.02 [-0.06; 0.11] 0.551

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 3 - < 12 months					
N"/N'/N	64 / 81 / 81	73 / 88 / 88			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	13 (16.0)	20 (22.7)	0.86 [0.34; 2.14] 0.743	0.71 [0.37; 1.34] 0.282	-0.07 [-0.18; 0.05] 0.274
≥ 12 months					
N"/N'/N	61 / 81 / 82	67 / 78 / 78			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	21 (25.9)	13 (16.7)	1.74 [0.67; 4.55] 0.256	1.56 [0.84; 2.89] 0.156	0.09 [-0.03; 0.22] 0.152
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.071**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.570				
≤ 3 months					
N"/N'/N	94 / 120 / 120	86 / 110 / 110			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	27 (22.5)	26 (23.6)	0.78 [0.35; 1.71] 0.532	0.95 [0.59; 1.53] 0.838	-0.01 [-0.12; 0.10] 0.838
> 3 - < 12 months					
N"/N'/N	22 / 30 / 30	27 / 39 / 39			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	6 (20.0)	10 (25.6)	0.89 [0.24; 3.28] 0.862	0.78 [0.32; 1.91] 0.586	-0.06 [-0.25; 0.14] 0.577
≥ 12 months					
N"/N'/N	28 / 38 / 39	33 / 38 / 38			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	9 (23.7)	4 (10.5)	2.06 [0.41; 10.50] 0.383	2.25 [0.76; 6.68] 0.144	0.13 [-0.04; 0.30] 0.122
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.262				
≤ 3 months					
N"/N'/N	57 / 84 / 85	73 / 92 / 92			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	22 (26.2)	13 (14.1)	3.37 [1.31; 8.68] 0.012 *	1.85 [1.00; 3.44] 0.051	0.12 [0.00; 0.24] 0.045 *
> 3 - < 12 months					
N"/N'/N	42 / 51 / 51	38 / 49 / 49			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	14 (27.5)	14 (28.6)	1.69 [0.57; 5.02] 0.345	0.96 [0.51; 1.80] 0.901	-0.01 [-0.19; 0.16] 0.901

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months					
N"/N'/N	32 / 43 / 43	35 / 40 / 40			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	8 (18.6)	8 (20.0)	0.89 [0.24; 3.34] 0.862	0.93 [0.39; 2.24] 0.872	-0.01 [-0.18; 0.16] 0.872
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.880				
≤ 3 months					
N"/N'/N	151 / 204 / 205	159 / 202 / 202			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	49 (24.0)	39 (19.3)	1.52 [0.84; 2.76] 0.170	1.23 [0.85; 1.79] 0.264	0.05 [-0.03; 0.13] 0.264
> 3 - < 12 months					
N"/N'/N	64 / 81 / 81	65 / 88 / 88			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	20 (24.7)	24 (27.3)	1.20 [0.52; 2.76] 0.672	0.89 [0.53; 1.49] 0.665	-0.03 [-0.16; 0.10] 0.662
≥ 12 months					
N"/N'/N	60 / 81 / 82	68 / 78 / 78			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	17 (21.0)	12 (15.4)	1.23 [0.45; 3.38] 0.686	1.36 [0.70; 2.66] 0.367	0.06 [-0.06; 0.18] 0.364

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 9.9 VFQ - Gain of 4 respectively 15 points by DME type (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.178**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.199				
focal					
N''/N'/N	50 / 59 / 59	40 / 48 / 48			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	29 (49.2)	32 (66.7)	0.38 [0.16; 0.91] 0.029 *	0.74 [0.53; 1.02] 0.068	-0.18 [-0.36; 0.01] 0.063
diffuse					
N''/N'/N	97 / 127 / 127	114 / 134 / 134			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	67 (52.8)	79 (59.0)	0.75 [0.43; 1.29] 0.301	0.89 [0.72; 1.11] 0.315	-0.06 [-0.18; 0.06] 0.313
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.732				
focal					
N''/N'/N	48 / 63 / 63	51 / 66 / 66			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	35 (55.6)	34 (51.5)	1.07 [0.51; 2.22] 0.860	1.08 [0.78; 1.49] 0.646	0.04 [-0.13; 0.21] 0.645
diffuse					
N''/N'/N	95 / 114 / 115	95 / 109 / 109			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	62 (54.4)	64 (58.7)	0.91 [0.52; 1.60] 0.739	0.93 [0.74; 1.17] 0.514	-0.04 [-0.17; 0.09] 0.514
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.499				
focal					
N''/N'/N	98 / 122 / 122	91 / 114 / 114			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	64 (52.5)	66 (57.9)	0.67 [0.38; 1.16] 0.153	0.90 [0.72; 1.13] 0.384	-0.06 [-0.18; 0.07] 0.383

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N"/N'/N	192 / 241 / 242	209 / 243 / 243			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	129 (53.5)	143 (58.8)	0.84 [0.57; 1.25] 0.398	0.91 [0.78; 1.06] 0.238	-0.05 [-0.14; 0.03] 0.236
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.121**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.074				
focal					
N"/N'/N	50 / 59 / 59	35 / 48 / 48			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	26 (44.1)	29 (60.4)	0.42 [0.18; 0.97] 0.043 *	0.73 [0.51; 1.05] 0.092	-0.16 [-0.35; 0.02] 0.088
diffuse					
N"/N'/N	92 / 127 / 127	107 / 134 / 134			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	71 (55.9)	74 (55.2)	1.05 [0.61; 1.79] 0.867	1.01 [0.81; 1.26] 0.912	0.01 [-0.11; 0.13] 0.912
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.835				
focal					
N"/N'/N	46 / 63 / 63	54 / 66 / 66			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	35 (55.6)	32 (48.5)	1.22 [0.58; 2.54] 0.602	1.15 [0.82; 1.60] 0.422	0.07 [-0.10; 0.24] 0.420
diffuse					
N"/N'/N	84 / 114 / 115	88 / 109 / 109			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	64 (56.1)	57 (52.3)	1.34 [0.76; 2.37] 0.311	1.07 [0.84; 1.37] 0.565	0.04 [-0.09; 0.17] 0.564
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.147				
focal					
N"/N'/N	96 / 122 / 122	89 / 114 / 114			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	61 (50.0)	61 (53.5)	0.73 [0.42; 1.27] 0.262	0.94 [0.73; 1.19] 0.594	-0.03 [-0.16; 0.09] 0.595

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N"/N'/N	176 / 241 / 242	195 / 243 / 243			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	135 (56.0)	131 (53.9)	1.20 [0.82; 1.78] 0.351	1.04 [0.88; 1.22] 0.637	0.02 [-0.07; 0.11] 0.636
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.231**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.903				
focal					
N"/N'/N	50 / 59 / 59	40 / 48 / 48			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	13 (22.0)	8 (16.7)	0.93 [0.27; 3.20] 0.910	1.32 [0.60; 2.92] 0.491	0.05 [-0.10; 0.20] 0.481
diffuse					
N"/N'/N	97 / 127 / 127	114 / 134 / 134			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	32 (25.2)	33 (24.6)	1.02 [0.49; 2.14] 0.961	1.02 [0.67; 1.56] 0.915	0.01 [-0.10; 0.11] 0.915
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.477				
focal					
N"/N'/N	48 / 63 / 63	51 / 66 / 66			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	13 (20.6)	8 (12.1)	2.00 [0.68; 5.86] 0.206	1.70 [0.76; 3.83] 0.198	0.09 [-0.04; 0.21] 0.190
diffuse					
N"/N'/N	95 / 114 / 115	95 / 109 / 109			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	24 (21.1)	24 (22.0)	1.25 [0.59; 2.62] 0.562	0.96 [0.58; 1.58] 0.861	-0.01 [-0.12; 0.10] 0.861
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.608				
focal					
N"/N'/N	98 / 122 / 122	91 / 114 / 114			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	26 (21.3)	16 (14.0)	1.50 [0.67; 3.36] 0.330	1.50 [0.85; 2.64] 0.157	0.07 [-0.03; 0.17] 0.152

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N"/N'/N	192 / 241 / 242	209 / 243 / 243			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	56 (23.2)	57 (23.5)	1.16 [0.69; 1.96] 0.573	0.99 [0.72; 1.37] 0.971	-0.00 [-0.08; 0.07] 0.971
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.071**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.153				
focal					
N"/N'/N	50 / 59 / 59	35 / 48 / 48			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	11 (18.6)	11 (22.9)	0.43 [0.14; 1.37] 0.155	0.81 [0.39; 1.71] 0.587	-0.04 [-0.20; 0.11] 0.589
diffuse					
N"/N'/N	92 / 127 / 127	107 / 134 / 134			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	30 (23.6)	28 (20.9)	1.18 [0.56; 2.49] 0.655	1.13 [0.72; 1.78] 0.597	0.03 [-0.07; 0.13] 0.597
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.089				
focal					
N"/N'/N	46 / 63 / 63	54 / 66 / 66			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	15 (23.8)	6 (9.1)	4.49 [1.30; 15.53] 0.018 *	2.62 [1.08; 6.32] 0.032 *	0.15 [0.02; 0.27] 0.022 *
diffuse					
N"/N'/N	84 / 114 / 115	88 / 109 / 109			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	29 (25.4)	29 (26.6)	1.29 [0.61; 2.73] 0.512	0.96 [0.61; 1.49] 0.843	-0.01 [-0.13; 0.10] 0.843
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.886				
focal					
N"/N'/N	96 / 122 / 122	89 / 114 / 114			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	26 (21.3)	17 (14.9)	1.35 [0.60; 3.05] 0.470	1.40 [0.81; 2.42] 0.223	0.06 [-0.04; 0.16] 0.224

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N"/N'/N	176 / 241 / 242	195 / 243 / 243			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	59 (24.5)	57 (23.5)	1.26 [0.74; 2.13] 0.394	1.04 [0.76; 1.43] 0.810	0.01 [-0.07; 0.09] 0.810

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 9.10 VFQ - Gain of 4 respectively 15 points by CSFT (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.178**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.852				
< 450 µm					
N"/N'/N	85 / 107 / 107	81 / 96 / 96			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	54 (50.5)	54 (56.3)	0.69 [0.37; 1.27] 0.229	0.90 [0.69; 1.16] 0.409	-0.06 [-0.20; 0.08] 0.409
≥ 450 - < 650 µm					
N"/N'/N	55 / 69 / 70	61 / 71 / 71			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	39 (56.5)	46 (64.8)	0.62 [0.29; 1.31] 0.212	0.87 [0.67; 1.14] 0.319	-0.08 [-0.24; 0.08] 0.315
≥ 650 µm					
N"/N'/N	9 / 12 / 12	16 / 20 / 20			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	5 (41.7)	13 (65.0)	0.41 [0.08; 2.23] 0.304	0.64 [0.31; 1.35] 0.241	-0.23 [-0.58; 0.12] 0.190
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.220				
< 450 µm					
N"/N'/N	63 / 84 / 85	61 / 82 / 82			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	37 (44.0)	39 (47.6)	0.85 [0.45; 1.63] 0.629	0.93 [0.66; 1.29] 0.650	-0.04 [-0.19; 0.12] 0.649
≥ 450 - < 650 µm					
N"/N'/N	66 / 74 / 74	72 / 79 / 79			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	45 (60.8)	50 (63.3)	1.01 [0.51; 2.01] 0.976	0.96 [0.75; 1.23] 0.752	-0.02 [-0.18; 0.13] 0.752
≥ 650 µm					
N"/N'/N	15 / 20 / 20	16 / 19 / 19			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	16 (80.0)	10 (52.6)	3.59 [0.81; 15.93] 0.092	1.52 [0.94; 2.46] 0.087	0.27 [-0.01; 0.56] 0.060

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.573				
< 450 µm					
N"/N'/N	148 / 191 / 192	142 / 178 / 178			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	91 (47.6)	93 (52.2)	0.77 [0.50; 1.20] 0.255	0.91 [0.74; 1.11] 0.361	-0.05 [-0.15; 0.05] 0.359
≥ 450 - < 650 µm					
N"/N'/N	121 / 143 / 144	133 / 150 / 150			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	84 (58.7)	96 (64.0)	0.82 [0.49; 1.35] 0.433	0.92 [0.76; 1.10] 0.358	-0.05 [-0.16; 0.06] 0.356
≥ 650 µm					
N"/N'/N	24 / 32 / 32	32 / 39 / 39			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	21 (65.6)	23 (59.0)	1.43 [0.50; 4.09] 0.509	1.09 [0.73; 1.63] 0.652	0.05 [-0.18; 0.29] 0.659
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.121**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.760				
< 450 µm					
N"/N'/N	82 / 107 / 107	76 / 96 / 96			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	54 (50.5)	54 (56.3)	0.69 [0.38; 1.27] 0.234	0.90 [0.69; 1.16] 0.409	-0.06 [-0.20; 0.08] 0.409
≥ 450 - < 650 µm					
N"/N'/N	55 / 69 / 70	54 / 71 / 71			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	39 (56.5)	40 (56.3)	0.95 [0.46; 1.97] 0.892	1.00 [0.75; 1.34] 0.983	0.00 [-0.16; 0.17] 0.983
≥ 650 µm					
N"/N'/N	7 / 12 / 12	16 / 20 / 20			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	6 (50.0)	11 (55.0)	1.06 [0.21; 5.29] 0.942	0.91 [0.46; 1.81] 0.787	-0.05 [-0.41; 0.31] 0.784

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.068				
< 450 µm					
N"/N'/N	60 / 84 / 85	63 / 82 / 82			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	37 (44.0)	33 (40.2)	1.18 [0.61; 2.28] 0.620	1.09 [0.77; 1.56] 0.620	0.04 [-0.11; 0.19] 0.619
≥ 450 - < 650 µm					
N"/N'/N	56 / 74 / 74	67 / 79 / 79			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	47 (63.5)	50 (63.3)	1.17 [0.58; 2.34] 0.665	1.00 [0.79; 1.28] 0.977	0.00 [-0.15; 0.15] 0.977
≥ 650 µm					
N"/N'/N	15 / 20 / 20	15 / 19 / 19			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	16 (80.0)	7 (36.8)	7.77 [1.69; 35.72] 0.008 *	2.17 [1.16; 4.07] 0.016 *	0.43 [0.15; 0.71] 0.002 *
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.102				
< 450 µm					
N"/N'/N	142 / 191 / 192	139 / 178 / 178			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	91 (47.6)	87 (48.9)	0.90 [0.58; 1.40] 0.644	0.97 [0.79; 1.20] 0.778	-0.01 [-0.12; 0.09] 0.778
≥ 450 - < 650 µm					
N"/N'/N	111 / 143 / 144	121 / 150 / 150			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	86 (60.1)	90 (60.0)	1.06 [0.64; 1.75] 0.818	1.00 [0.83; 1.21] 0.972	0.00 [-0.11; 0.11] 0.972
≥ 650 µm					
N"/N'/N	22 / 32 / 32	31 / 39 / 39			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	22 (68.8)	18 (46.2)	3.16 [1.09; 9.14] 0.034 *	1.50 [0.95; 2.36] 0.066	0.22 [-0.01; 0.46] 0.064
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.231**					

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.225				
< 450 µm					
N"/N'/N	85 / 107 / 107	81 / 96 / 96			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	23 (21.5)	19 (19.8)	0.66 [0.27; 1.61] 0.358	1.09 [0.63; 1.87] 0.765	0.02 [-0.09; 0.13] 0.764
≥ 450 - < 650 µm					
N"/N'/N	55 / 69 / 70	61 / 71 / 71			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	21 (30.4)	16 (22.5)	1.56 [0.59; 4.15] 0.371	1.35 [0.77; 2.36] 0.293	0.08 [-0.07; 0.22] 0.288
≥ 650 µm					
N"/N'/N	9 / 12 / 12	16 / 20 / 20			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	2 (16.7)	8 (40.0)	0.16 [<0.01; 2.99] 0.222	0.42 [0.11; 1.65] 0.212	-0.23 [-0.53; 0.07] 0.129
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.736				
< 450 µm					
N"/N'/N	63 / 84 / 85	61 / 82 / 82			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	14 (16.7)	9 (11.0)	2.05 [0.74; 5.74] 0.169	1.52 [0.70; 3.31] 0.294	0.06 [-0.05; 0.16] 0.286
≥ 450 - < 650 µm					
N"/N'/N	66 / 74 / 74	72 / 79 / 79			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	18 (24.3)	19 (24.1)	1.41 [0.59; 3.36] 0.433	1.01 [0.58; 1.77] 0.968	0.00 [-0.13; 0.14] 0.968
≥ 650 µm					
N"/N'/N	15 / 20 / 20	16 / 19 / 19			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	5 (25.0)	5 (26.3)	1.00 [0.20; 5.08] 0.997	0.95 [0.33; 2.77] 0.925	-0.01 [-0.29; 0.26] 0.925
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.535				
< 450 µm					
N"/N'/N	148 / 191 / 192	142 / 178 / 178			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	37 (19.4)	28 (15.7)	1.19 [0.62; 2.28] 0.607	1.22 [0.78; 1.90] 0.377	0.04 [-0.04; 0.11] 0.375

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 450 - < 650 µm					
N''/N'/N	121 / 143 / 144	133 / 150 / 150			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	39 (27.3)	35 (23.3)	1.54 [0.81; 2.93] 0.192	1.17 [0.79; 1.73] 0.442	0.04 [-0.06; 0.14] 0.441
≥ 650 µm					
N''/N'/N	24 / 32 / 32	32 / 39 / 39			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	7 (21.9)	13 (33.3)	0.68 [0.18; 2.53] 0.562	0.66 [0.29; 1.52] 0.320	-0.11 [-0.32; 0.10] 0.304
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.071**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.578				
< 450 µm					
N''/N'/N	82 / 107 / 107	76 / 96 / 96			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	21 (19.6)	16 (16.7)	0.78 [0.32; 1.90] 0.583	1.18 [0.65; 2.12] 0.587	0.03 [-0.08; 0.14] 0.584
≥ 450 - < 650 µm					
N''/N'/N	55 / 69 / 70	54 / 71 / 71			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	19 (27.5)	17 (23.9)	1.10 [0.43; 2.80] 0.840	1.15 [0.65; 2.02] 0.627	0.04 [-0.11; 0.18] 0.627
≥ 650 µm					
N''/N'/N	7 / 12 / 12	16 / 20 / 20			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	2 (16.7)	7 (35.0)	0.26 [0.02; 3.64] 0.319	0.48 [0.12; 1.93] 0.299	-0.18 [-0.48; 0.11] 0.226
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.109				
< 450 µm					
N''/N'/N	60 / 84 / 85	63 / 82 / 82			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	15 (17.9)	9 (11.0)	2.57 [0.85; 7.71] 0.093	1.63 [0.75; 3.51] 0.214	0.07 [-0.04; 0.18] 0.204
≥ 450 - < 650 µm					
N''/N'/N	56 / 74 / 74	67 / 79 / 79			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	21 (28.4)	24 (30.4)	1.27 [0.53; 3.02] 0.593	0.93 [0.57; 1.53] 0.786	-0.02 [-0.16; 0.12] 0.786

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm					
N"/N'/N	15 / 20 / 20	15 / 19 / 19			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	8 (40.0)	2 (10.5)	12.39 [1.69; 90.97] 0.013 *	3.80 [0.92; 15.67] 0.065	0.29 [0.04; 0.55] 0.024 *
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.528				
< 450 µm					
N"/N'/N	142 / 191 / 192	139 / 178 / 178			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	36 (18.8)	25 (14.0)	1.32 [0.67; 2.61] 0.425	1.34 [0.84; 2.13] 0.223	0.05 [-0.03; 0.12] 0.219
≥ 450 - < 650 µm					
N"/N'/N	111 / 143 / 144	121 / 150 / 150			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	40 (28.0)	41 (27.3)	1.17 [0.62; 2.21] 0.623	1.02 [0.71; 1.48] 0.898	0.01 [-0.10; 0.11] 0.898
≥ 650 µm					
N"/N'/N	22 / 32 / 32	31 / 39 / 39			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	10 (31.3)	9 (23.1)	2.69 [0.73; 9.95] 0.137	1.41 [0.59; 3.39] 0.422	0.09 [-0.13; 0.30] 0.425

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 9.11 VFQ - Gain of 4 respectively 15 points by status of SRF (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.178**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.504				
presence					
N''/N'/N	46 / 61 / 62	52 / 61 / 61			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	34 (55.7)	43 (70.5)	0.51 [0.22; 1.18] 0.117	0.79 [0.60; 1.04] 0.096	-0.15 [-0.32; 0.02] 0.087
absence					
N''/N'/N	103 / 127 / 127	106 / 126 / 126			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	64 (50.4)	70 (55.6)	0.72 [0.42; 1.24] 0.239	0.91 [0.72; 1.14] 0.412	-0.05 [-0.17; 0.07] 0.410
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.180				
presence					
N''/N'/N	44 / 56 / 56	58 / 67 / 67			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	39 (69.6)	39 (58.2)	1.64 [0.75; 3.61] 0.217	1.20 [0.92; 1.56] 0.187	0.11 [-0.05; 0.28] 0.184
absence					
N''/N'/N	100 / 122 / 123	92 / 114 / 114			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	59 (48.4)	61 (53.5)	0.85 [0.50; 1.47] 0.567	0.90 [0.70; 1.16] 0.429	-0.05 [-0.18; 0.08] 0.429
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.681				
presence					
N''/N'/N	90 / 117 / 118	110 / 128 / 128			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	73 (62.4)	82 (64.1)	0.92 [0.52; 1.61] 0.768	0.97 [0.80; 1.18] 0.789	-0.02 [-0.14; 0.11] 0.790

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N"/N'/N	203 / 249 / 250	198 / 240 / 240			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	123 (49.4)	131 (54.6)	0.80 [0.54; 1.17] 0.242	0.91 [0.76; 1.07] 0.255	-0.05 [-0.14; 0.04] 0.253
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.121**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.714				
presence					
N"/N'/N	50 / 61 / 62	48 / 61 / 61			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	36 (59.0)	38 (62.3)	0.94 [0.42; 2.09] 0.876	0.95 [0.71; 1.26] 0.711	-0.03 [-0.21; 0.14] 0.711
absence					
N"/N'/N	94 / 127 / 127	98 / 126 / 126			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	63 (49.6)	67 (53.2)	0.78 [0.46; 1.34] 0.371	0.93 [0.73; 1.19] 0.570	-0.04 [-0.16; 0.09] 0.570
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.254				
presence					
N"/N'/N	39 / 56 / 56	54 / 67 / 67			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	39 (69.6)	36 (53.7)	2.03 [0.92; 4.47] 0.078	1.30 [0.98; 1.72] 0.071	0.16 [-0.01; 0.33] 0.066
absence					
N"/N'/N	92 / 122 / 123	92 / 114 / 114			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	61 (50.0)	55 (48.2)	1.16 [0.68; 2.00] 0.584	1.04 [0.80; 1.34] 0.788	0.02 [-0.11; 0.15] 0.788
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.313				
presence					
N"/N'/N	89 / 117 / 118	102 / 128 / 128			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	75 (64.1)	74 (57.8)	1.36 [0.78; 2.38] 0.280	1.11 [0.91; 1.35] 0.314	0.06 [-0.06; 0.19] 0.312

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N"/N'/N	186 / 249 / 250	190 / 240 / 240			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	124 (49.8)	122 (50.8)	0.96 [0.66; 1.41] 0.837	0.98 [0.82; 1.17] 0.825	-0.01 [-0.10; 0.08] 0.825
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.231**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.434				
presence					
N"/N'/N	46 / 61 / 62	52 / 61 / 61			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	19 (31.1)	22 (36.1)	0.69 [0.24; 1.93] 0.476	0.86 [0.52; 1.43] 0.566	-0.05 [-0.22; 0.12] 0.565
absence					
N"/N'/N	103 / 127 / 127	106 / 126 / 126			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	27 (21.3)	21 (16.7)	1.15 [0.52; 2.54] 0.723	1.28 [0.76; 2.13] 0.354	0.05 [-0.05; 0.14] 0.351
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.365				
presence					
N"/N'/N	44 / 56 / 56	58 / 67 / 67			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	20 (35.7)	16 (23.9)	2.12 [0.86; 5.25] 0.104	1.50 [0.86; 2.60] 0.154	0.12 [-0.04; 0.28] 0.152
absence					
N"/N'/N	100 / 122 / 123	92 / 114 / 114			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	17 (13.9)	17 (14.9)	1.20 [0.52; 2.76] 0.663	0.93 [0.50; 1.74] 0.831	-0.01 [-0.10; 0.08] 0.831
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.967				
presence					
N"/N'/N	90 / 117 / 118	110 / 128 / 128			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	39 (33.3)	38 (29.7)	1.30 [0.66; 2.54] 0.449	1.12 [0.77; 1.61] 0.562	0.03 [-0.08; 0.15] 0.563

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N"/N'/N	203 / 249 / 250	198 / 240 / 240			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	44 (17.7)	38 (15.8)	1.27 [0.72; 2.24] 0.406	1.12 [0.75; 1.66] 0.573	0.02 [-0.05; 0.09] 0.572
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.071**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.626				
presence					
N"/N'/N	50 / 61 / 62	48 / 61 / 61			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	18 (29.5)	20 (32.8)	0.76 [0.28; 2.05] 0.581	0.90 [0.53; 1.53] 0.696	-0.03 [-0.20; 0.13] 0.696
absence					
N"/N'/N	94 / 127 / 127	98 / 126 / 126			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	24 (18.9)	20 (15.9)	1.03 [0.47; 2.26] 0.932	1.19 [0.69; 2.04] 0.527	0.03 [-0.06; 0.12] 0.525
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.365				
presence					
N"/N'/N	39 / 56 / 56	54 / 67 / 67			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	22 (39.3)	16 (23.9)	2.83 [1.09; 7.34] 0.033 *	1.65 [0.96; 2.82] 0.069	0.15 [-0.01; 0.32] 0.065
absence					
N"/N'/N	92 / 122 / 123	92 / 114 / 114			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	22 (18.0)	19 (16.7)	1.59 [0.69; 3.63] 0.275	1.08 [0.62; 1.89] 0.782	0.01 [-0.08; 0.11] 0.782
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.723				
presence					
N"/N'/N	89 / 117 / 118	102 / 128 / 128			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	40 (34.2)	36 (28.1)	1.51 [0.76; 2.98] 0.236	1.21 [0.84; 1.76] 0.308	0.06 [-0.06; 0.18] 0.309

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N"/N'/N	186 / 249 / 250	190 / 240 / 240			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	46 (18.5)	39 (16.3)	1.29 [0.73; 2.26] 0.382	1.14 [0.77; 1.68] 0.517	0.02 [-0.04; 0.09] 0.516

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 9.12 VFQ - Gain of 4 respectively 15 points by exposure (week 52) (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by exposure (week 52) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.178**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.969				
Non-exposed					
N"/N'/N	56 / 71 / 71	61 / 75 / 75			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	35 (49.3)	40 (53.3)	0.64 [0.31; 1.33] 0.231	0.92 [0.67; 1.27] 0.626	-0.04 [-0.20; 0.12] 0.625
Exposed					
N"/N'/N	93 / 117 / 118	97 / 112 / 112			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	63 (53.8)	73 (65.2)	0.65 [0.37; 1.16] 0.146	0.83 [0.67; 1.02] 0.082	-0.11 [-0.24; 0.01] 0.079
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.699				
Non-exposed					
N"/N'/N	69 / 84 / 85	75 / 90 / 90			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	42 (50.0)	45 (50.0)	1.12 [0.59; 2.12] 0.728	1.00 [0.74; 1.35] 1.000	0.00 [-0.15; 0.15] 1.000
Exposed					
N"/N'/N	75 / 94 / 94	75 / 91 / 91			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	56 (59.6)	55 (60.4)	0.94 [0.50; 1.75] 0.842	0.99 [0.78; 1.25] 0.904	-0.01 [-0.15; 0.13] 0.904
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 52					
Interaction Test:	p = 0.780				
Non-exposed					
N"/N'/N	125 / 155 / 156	136 / 165 / 165			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	77 (49.7)	85 (51.5)	0.86 [0.53; 1.39] 0.544	0.96 [0.78; 1.20] 0.743	-0.02 [-0.13; 0.09] 0.742

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by exposure (week 52) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N"/N'/N	168 / 211 / 212	172 / 203 / 203			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	119 (56.4)	128 (63.1)	0.79 [0.52; 1.20] 0.266	0.89 [0.76; 1.05] 0.169	-0.07 [-0.16; 0.03] 0.167
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Test of heterogeneity in main analysis: **p_H=0.231**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.876				
Non-exposed					
N"/N'/N	56 / 71 / 71	61 / 75 / 75			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	17 (23.9)	14 (18.7)	0.87 [0.30; 2.53] 0.801	1.28 [0.68; 2.40] 0.438	0.05 [-0.08; 0.19] 0.436
Exposed					
N"/N'/N	93 / 117 / 118	97 / 112 / 112			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	29 (24.8)	29 (25.9)	0.97 [0.45; 2.10] 0.938	0.96 [0.61; 1.49] 0.847	-0.01 [-0.12; 0.10] 0.847
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.434				
Non-exposed					
N"/N'/N	69 / 84 / 85	75 / 90 / 90			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	15 (17.9)	18 (20.0)	1.18 [0.49; 2.82] 0.717	0.89 [0.48; 1.66] 0.719	-0.02 [-0.14; 0.09] 0.718
Exposed					
N"/N'/N	75 / 94 / 94	75 / 91 / 91			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	22 (23.4)	15 (16.5)	1.91 [0.82; 4.47] 0.136	1.42 [0.79; 2.56] 0.244	0.07 [-0.05; 0.18] 0.237
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 52					
Interaction Test:	p = 0.564				
Non-exposed					
N"/N'/N	125 / 155 / 156	136 / 165 / 165			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	32 (20.6)	32 (19.4)	1.08 [0.55; 2.11] 0.833	1.06 [0.69; 1.65] 0.782	0.01 [-0.08; 0.10] 0.781

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by exposure (week 52) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N"/N'/N	168 / 211 / 212	172 / 203 / 203			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	51 (24.2)	44 (21.7)	1.40 [0.79; 2.47] 0.250	1.11 [0.78; 1.59] 0.549	0.02 [-0.06; 0.11] 0.548

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 9.13 VFQ - Gain of 4 respectively 15 points by exposure (week 100) (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.121**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.568				
Non-exposed					
N"/N'/N	0 / 12 / 12	0 / 13 / 13			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	5 (41.7)	3 (23.1)	1.44 [0.20; 10.19] 0.712	1.81 [0.55; 5.98] 0.333	0.19 [-0.18; 0.55] 0.313
Exposed					
N"/N'/N	144 / 176 / 177	146 / 174 / 174			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	94 (53.4)	102 (58.6)	0.80 [0.51; 1.27] 0.354	0.91 [0.76; 1.10] 0.327	-0.05 [-0.16; 0.05] 0.325
KITE: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.465				
Non-exposed					
N"/N'/N	0 / 17 / 17	0 / 12 / 12			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	5 (29.4)	2 (16.7)	2.95 [0.42; 20.99] 0.279	1.76 [0.41; 7.63] 0.447	0.13 [-0.17; 0.43] 0.409
Exposed					
N"/N'/N	131 / 161 / 162	146 / 169 / 169			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	95 (59.0)	89 (52.7)	1.39 [0.87; 2.22] 0.165	1.12 [0.92; 1.36] 0.247	0.06 [-0.04; 0.17] 0.245
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 4 points, Week 100					
Interaction Test:	p = 0.386				
Non-exposed					
N"/N'/N	0 / 29 / 29	0 / 25 / 25			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	10 (34.5)	5 (20.0)	1.96 [0.51; 7.60] 0.331	1.79 [0.70; 4.53] 0.215	0.15 [-0.08; 0.39] 0.193

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N"/N'/N	275 / 337 / 339	292 / 343 / 343			
Gain in VFQ-25 Composite Score of ≥ 4 points, n (%)	189 (56.1)	191 (55.7)	1.06 [0.76; 1.47] 0.736	1.01 [0.88; 1.15] 0.918	0.00 [-0.07; 0.08] 0.918
Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Test of heterogeneity in main analysis: **p_H=0.071**					
KESTREL: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.204				
Non-exposed					
N"/N'/N	0 / 12 / 12	0 / 13 / 13			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	4 (33.3)	1 (7.7)	5.45 [0.32; 93.97] 0.243	4.33 [0.56; 33.53] 0.160	0.26 [-0.05; 0.56] 0.098
Exposed					
N"/N'/N	144 / 176 / 177	146 / 174 / 174			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	38 (21.6)	39 (22.4)	0.82 [0.44; 1.55] 0.545	0.96 [0.65; 1.43] 0.853	-0.01 [-0.10; 0.08] 0.853
KITE: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	N.E.				
Non-exposed					
N"/N'/N	0 / 17 / 17	0 / 12 / 12			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	1 (5.9)	0 (0.0)	N.E.	2.17 [0.10; 49.07] 0.627	0.06 [-0.05; 0.17] 0.303
Exposed					
N"/N'/N	131 / 161 / 162	146 / 169 / 169			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	43 (26.7)	35 (20.7)	1.40 [0.84; 2.32] 0.201	1.29 [0.87; 1.91] 0.202	0.06 [-0.03; 0.15] 0.200
Pooled Analysis: Gain in VFQ-25 Composite Score of ≥ 15 points, Week 100					
Interaction Test:	p = 0.178				
Non-exposed					
N"/N'/N	0 / 29 / 29	0 / 25 / 25			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	5 (17.2)	1 (4.0)	7.11 [0.62; 81.19] 0.114	3.52 [0.65; 19.05] 0.115	0.15 [-0.00; 0.31] 0.055

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N"/N'/N	275 / 337 / 339	292 / 343 / 343			
Gain in VFQ-25 Composite Score of ≥ 15 points, n (%)	81 (24.0)	74 (21.6)	1.30 [0.83; 2.03] 0.257	1.12 [0.85; 1.47] 0.440	0.02 [-0.04; 0.09] 0.440

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline value + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Gain in VFQ-25 Composite Score of ≥ 15 points / KITE / Week 100: logit(proportion) = treatment [by exposure (week 100)].

10 CSFT: Continuous analysis

Table 10.0 CSFT (FAS), return rates, Week 100

	Treatment Groups		
CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Total**
KESTREL: CSFT			
N	189	187	376
Baseline Returns, n (%)	189 (100.0)	187 (100.0)	376 (100.0)
Week 4 Returns, n (%)	186 (98.4)	184 (98.4)	370 (98.4)
Week 6 Returns, n (%)	186 (98.4)	180 (96.3)	366 (97.3)
Week 8 Returns, n (%)	185 (97.9)	182 (97.3)	367 (97.6)
Week 12 Returns, n (%)	187 (98.9)	181 (96.8)	368 (97.9)
Week 16 Returns, n (%)	182 (96.3)	180 (96.3)	362 (96.3)
Week 18 Returns, n (%)	181 (95.8)	173 (92.5)	354 (94.1)
Week 20 Returns, n (%)	179 (94.7)	178 (95.2)	357 (94.9)
Week 24 Returns, n (%)	177 (93.7)	177 (94.7)	354 (94.1)
Week 28 Returns, n (%)	176 (93.1)	171 (91.4)	347 (92.3)
Week 32 Returns, n (%)	162 (85.7)	162 (86.6)	324 (86.2)
Week 36 Returns, n (%)	167 (88.4)	165 (88.2)	332 (88.3)
Week 40 Returns, n (%)	164 (86.8)	163 (87.2)	327 (87.0)
Week 44 Returns, n (%)	158 (83.6)	162 (86.6)	320 (85.1)
Week 48 Returns, n (%)	155 (82.0)	160 (85.6)	315 (83.8)
Week 52 Returns, n (%)	154 (81.5)	160 (85.6)	314 (83.5)
Week 56 Returns, n (%)	147 (77.8)	152 (81.3)	299 (79.5)
Week 60 Returns, n (%)	148 (78.3)	150 (80.2)	298 (79.3)
Week 64 Returns, n (%)	150 (79.4)	153 (81.8)	303 (80.6)
Week 68 Returns, n (%)	145 (76.7)	147 (78.6)	292 (77.7)
Week 72 Returns, n (%)	150 (79.4)	147 (78.6)	297 (79.0)
Week 76 Returns, n (%)	142 (75.1)	149 (79.7)	291 (77.4)
Week 80 Returns, n (%)	150 (79.4)	141 (75.4)	291 (77.4)
Week 84 Returns, n (%)	148 (78.3)	138 (73.8)	286 (76.1)
Week 88 Returns, n (%)	141 (74.6)	144 (77.0)	285 (75.8)
Week 92 Returns, n (%)	144 (76.2)	140 (74.9)	284 (75.5)
Week 96 Returns, n (%)	140 (74.1)	140 (74.9)	280 (74.5)
Week 100 Returns, n (%)	148 (78.3)	145 (77.5)	293 (77.9)
KITE: CSFT			
N	179	181	360
Baseline Returns, n (%)	179 (100.0)	180 (99.4)	359 (99.7)
Week 4 Returns, n (%)	173 (96.6)	180 (99.4)	353 (98.1)

Treatment Groups			
CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Total**
Week 6 Returns, n (%)	174 (97.2)	177 (97.8)	351 (97.5)
Week 8 Returns, n (%)	173 (96.6)	175 (96.7)	348 (96.7)
Week 12 Returns, n (%)	176 (98.3)	175 (96.7)	351 (97.5)
Week 16 Returns, n (%)	172 (96.1)	171 (94.5)	343 (95.3)
Week 18 Returns, n (%)	172 (96.1)	170 (93.9)	342 (95.0)
Week 20 Returns, n (%)	170 (95.0)	167 (92.3)	337 (93.6)
Week 24 Returns, n (%)	171 (95.5)	170 (93.9)	341 (94.7)
Week 28 Returns, n (%)	170 (95.0)	171 (94.5)	341 (94.7)
Week 32 Returns, n (%)	167 (93.3)	168 (92.8)	335 (93.1)
Week 36 Returns, n (%)	162 (90.5)	163 (90.1)	325 (90.3)
Week 40 Returns, n (%)	149 (83.2)	156 (86.2)	305 (84.7)
Week 44 Returns, n (%)	143 (79.9)	156 (86.2)	299 (83.1)
Week 48 Returns, n (%)	148 (82.7)	151 (83.4)	299 (83.1)
Week 52 Returns, n (%)	147 (82.1)	152 (84.0)	299 (83.1)
Week 56 Returns, n (%)	139 (77.7)	145 (80.1)	284 (78.9)
Week 60 Returns, n (%)	141 (78.8)	149 (82.3)	290 (80.6)
Week 64 Returns, n (%)	144 (80.4)	148 (81.8)	292 (81.1)
Week 68 Returns, n (%)	143 (79.9)	148 (81.8)	291 (80.8)
Week 72 Returns, n (%)	138 (77.1)	145 (80.1)	283 (78.6)
Week 76 Returns, n (%)	138 (77.1)	148 (81.8)	286 (79.4)
Week 80 Returns, n (%)	135 (75.4)	150 (82.9)	285 (79.2)
Week 84 Returns, n (%)	134 (74.9)	146 (80.7)	280 (77.8)
Week 88 Returns, n (%)	134 (74.9)	145 (80.1)	279 (77.5)
Week 92 Returns, n (%)	132 (73.7)	141 (77.9)	273 (75.8)
Week 96 Returns, n (%)	135 (75.4)	139 (76.8)	274 (76.1)
Week 100 Returns, n (%)	133 (74.3)	145 (80.1)	278 (77.2)
Pooled Analysis: CSFT			
N	368	368	736
Baseline Returns, n (%)	368 (100.0)	367 (99.7)	735 (99.9)
Week 4 Returns, n (%)	359 (97.6)	364 (98.9)	723 (98.2)
Week 6 Returns, n (%)	360 (97.8)	357 (97.0)	717 (97.4)
Week 8 Returns, n (%)	358 (97.3)	357 (97.0)	715 (97.1)
Week 12 Returns, n (%)	363 (98.6)	356 (96.7)	719 (97.7)
Week 16 Returns, n (%)	354 (96.2)	351 (95.4)	705 (95.8)
Week 18 Returns, n (%)	353 (95.9)	343 (93.2)	696 (94.6)
Week 20 Returns, n (%)	349 (94.8)	345 (93.8)	694 (94.3)
Week 24 Returns, n (%)	348 (94.6)	347 (94.3)	695 (94.4)
Week 28 Returns, n (%)	346 (94.0)	342 (92.9)	688 (93.5)

Treatment Groups			
CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Total**
Week 32 Returns, n (%)	329 (89.4)	330 (89.7)	659 (89.5)
Week 36 Returns, n (%)	329 (89.4)	328 (89.1)	657 (89.3)
Week 40 Returns, n (%)	313 (85.1)	319 (86.7)	632 (85.9)
Week 44 Returns, n (%)	301 (81.8)	318 (86.4)	619 (84.1)
Week 48 Returns, n (%)	303 (82.3)	311 (84.5)	614 (83.4)
Week 52 Returns, n (%)	301 (81.8)	312 (84.8)	613 (83.3)
Week 56 Returns, n (%)	286 (77.7)	297 (80.7)	583 (79.2)
Week 60 Returns, n (%)	289 (78.5)	299 (81.3)	588 (79.9)
Week 64 Returns, n (%)	294 (79.9)	301 (81.8)	595 (80.8)
Week 68 Returns, n (%)	288 (78.3)	295 (80.2)	583 (79.2)
Week 72 Returns, n (%)	288 (78.3)	292 (79.3)	580 (78.8)
Week 76 Returns, n (%)	280 (76.1)	297 (80.7)	577 (78.4)
Week 80 Returns, n (%)	285 (77.4)	291 (79.1)	576 (78.3)
Week 84 Returns, n (%)	282 (76.6)	284 (77.2)	566 (76.9)
Week 88 Returns, n (%)	275 (74.7)	289 (78.5)	564 (76.6)
Week 92 Returns, n (%)	276 (75.0)	281 (76.4)	557 (75.7)
Week 96 Returns, n (%)	275 (74.7)	279 (75.8)	554 (75.3)
Week 100 Returns, n (%)	281 (76.4)	290 (78.8)	571 (77.6)

N: Number of patients
n (%): Number and percentage of patients with available data for the total score
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The return rate is the proportion of patients with available data for the total score at the given visit based on the whole study population.

Table 10.1 CSFT (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KESTREL: Central Subfield Thickness - Study Eye				
N'/ N	189 / 189	187 / 187		
Baseline Mean (SD)	453.06 (123.42)	475.60 (135.84)		
Week 52 Mean (SD)	292.54 (77.20)	309.03 (77.06)		
Week 100 Mean (SD)	279.53 (67.43)	296.57 (88.09)		
Week 52: Adjusted Mean Change (SE)	-167.18 (6.48)	-161.79 (6.48)	-5.39 [-23.38; 12.60]	0.557
Week 100: Adjusted Mean Change (SE)	-178.12 (6.70)	-175.66 (6.72)	-2.46 [-21.09; 16.17]	0.796
KITE: Central Subfield Thickness - Study Eye				
N'/ N	179 / 179	180 / 181		
Baseline Mean (SD)	481.13 (132.46)	484.35 (134.58)		
Week 52 Mean (SD)	279.35 (56.00)	309.87 (84.47)		
Week 100 Mean (SD)	273.35 (56.51)	296.44 (105.16)		
Week 52: Adjusted Mean Change (SE)	-200.99 (6.99)	-166.32 (6.95)	-34.67 [-54.06; -15.28]	<.001 *
Week 100: Adjusted Mean Change (SE)	-205.48 (8.37)	-180.46 (8.21)	-25.03 [-48.08; -1.97]	0.033 *
Pooled Analysis: Central Subfield Thickness - Study Eye p_H=0.131				
N'/ N	368 / 368	367 / 368		
Baseline Mean (SD)	466.72 (128.50)	479.89 (135.11)		
Week 52 Mean (SD)	286.10 (67.89)	309.43 (80.61)		
Week 100 Mean (SD)	276.60 (62.47)	296.51 (96.81)		
Week 52: Adjusted Mean Change (SE)	-183.51 (4.72)	-164.66 (4.71)	-18.85 [-31.95; -5.74]	0.005 *
Week 100: Adjusted Mean Change (SE)	-192.91 (5.32)	-177.88 (5.29)	-15.03 [-29.77; -0.30]	0.046 *

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study.

Exceptionally applied model (due to nonconvergence):
KESTREL: Adjusted mean change and mean difference obtained from MMRM with Toeplitz covariance matrix

Table 10.2 CSFT by age (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
CSFT by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Central Subfield Thickness - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.131**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.197			
< 65 years				
N'/ N	104 / 104	93 / 93		
Baseline Mean (SD)	464.56 (137.73)	498.43 (154.25)		
Week 52 Mean (SD)	292.19 (86.23)	314.23 (85.55)		
Week 100 Mean (SD)	277.75 (74.64)	293.33 (79.76)		
Week 52: Adjusted Mean Change (SE)	-172.00 (8.87)	-169.16 (9.17)	-2.84 [-27.86; 22.18]	0.824
Week 100: Adjusted Mean Change (SE)	-183.72 (9.44)	-189.76 (9.79)	6.04 [-20.63; 32.71]	0.657
≥ 65 years				
N'/ N	85 / 85	94 / 94		
Baseline Mean (SD)	439.00 (102.32)	453.01 (111.04)		
Week 52 Mean (SD)	292.99 (64.62)	303.42 (66.82)		
Week 100 Mean (SD)	281.69 (58.01)	300.03 (96.69)		
Week 52: Adjusted Mean Change (SE)	-162.99 (9.98)	-151.35 (9.43)	-11.64 [-38.55; 15.26]	0.396
Week 100: Adjusted Mean Change (SE)	-174.25 (10.46)	-158.95 (10.06)	-15.30 [-43.73; 13.13]	0.291
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.372			
< 65 years				
N'/ N	100 / 100	101 / 102		
Baseline Mean (SD)	481.69 (143.73)	490.44 (120.85)		
Week 52 Mean (SD)	272.82 (43.80)	314.88 (91.83)		
Week 100 Mean (SD)	270.30 (51.48)	294.05 (91.26)		
Week 52: Adjusted Mean Change (SE)	-212.58 (10.20)	-162.31 (10.06)	-50.27 [-78.40; -22.14]	<.001 *
Week 100: Adjusted Mean Change (SE)	-218.16 (10.33)	-181.84 (10.02)	-36.31 [-64.58; -8.05]	0.012 *

	Treatment Groups		Comparison	
CSFT by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 65 years				
N'/ N	79 / 79	79 / 79		
Baseline Mean (SD)	480.43 (117.57)	476.57 (150.76)		
Week 52 Mean (SD)	286.93 (67.02)	303.75 (74.72)		
Week 100 Mean (SD)	277.05 (62.32)	299.90 (123.22)		
Week 52: Adjusted Mean Change (SE)	-193.40 (11.27)	-171.74 (11.29)	-21.66 [-52.96; 9.63]	0.175
Week 100: Adjusted Mean Change (SE)	-205.70 (11.49)	-167.67 (11.53)	-38.02 [-69.96; -6.08]	0.020 *
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.778			
< 65 years				
N'/ N	204 / 204	194 / 195		
Baseline Mean (SD)	472.96 (140.62)	494.27 (137.57)		
Week 52 Mean (SD)	282.92 (69.72)	314.55 (88.48)		
Week 100 Mean (SD)	274.22 (64.61)	293.71 (85.80)		
Week 52: Adjusted Mean Change (SE)	-191.71 (6.83)	-166.57 (6.83)	-25.14 [-44.07; -6.20]	0.009 *
Week 100: Adjusted Mean Change (SE)	-199.76 (7.27)	-189.46 (7.11)	-10.29 [-30.22; 9.64]	0.311

	Treatment Groups		Comparison	
CSFT by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 65 years				
N'/ N	164 / 164	173 / 173		
Baseline Mean (SD)	458.96 (111.54)	463.77 (130.82)		
Week 52 Mean (SD)	289.96 (65.66)	303.57 (70.38)		
Week 100 Mean (SD)	279.50 (59.89)	299.97 (109.18)		
Week 52: Adjusted Mean Change (SE)	-175.96 (7.48)	-163.64 (7.33)	-12.32 [-32.85; 8.21]	0.239
Week 100: Adjusted Mean Change (SE)	-188.27 (8.00)	-168.41 (7.89)	-19.86 [-41.88; 2.16]	0.077

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + baseline category + age + treatment * age + visit * age + treatment * age * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + baseline category + study + treatment * study + age + treatment * age + visit * age + treatment * age * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
KITE: Adjusted mean change and mean difference obtained from MMRM with compound symmetry covariance matrix

Table 10.3 CSFT by gender (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
CSFT by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Central Subfield Thickness - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.131**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.617			
Male				
N'/ N	110 / 110	126 / 126		
Baseline Mean (SD)	459.21 (133.52)	480.73 (142.45)		
Week 52 Mean (SD)	297.17 (85.49)	310.66 (74.48)		
Week 100 Mean (SD)	279.76 (70.28)	307.67 (97.46)		
Week 52: Adjusted Mean Change (SE)	-161.84 (8.47)	-163.34 (7.89)	1.50 [-21.20; 24.20]	0.897
Week 100: Adjusted Mean Change (SE)	-173.55 (8.52)	-165.55 (8.01)	-8.00 [-30.94; 14.94]	0.494
Female				
N'/ N	79 / 79	61 / 61		
Baseline Mean (SD)	444.51 (108.05)	465.00 (121.46)		
Week 52 Mean (SD)	286.36 (64.64)	305.98 (82.25)		
Week 100 Mean (SD)	279.22 (63.95)	275.46 (62.37)		
Week 52: Adjusted Mean Change (SE)	-173.83 (9.92)	-156.94 (11.08)	-16.89 [-46.06; 12.28]	0.256
Week 100: Adjusted Mean Change (SE)	-185.12 (9.99)	-188.00 (11.29)	2.88 [-26.69; 32.45]	0.849
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.058			
Male				
N'/ N	120 / 120	114 / 115		
Baseline Mean (SD)	478.37 (132.56)	464.92 (116.99)		
Week 52 Mean (SD)	283.77 (56.70)	305.93 (72.08)		
Week 100 Mean (SD)	276.11 (51.17)	297.23 (107.07)		
Week 52: Adjusted Mean Change (SE)	-194.85 (9.32)	-172.68 (9.53)	-22.17 [-48.29; 3.96]	0.096
Week 100: Adjusted Mean Change (SE)	-204.68 (9.92)	-183.27 (9.94)	-21.41 [-48.94; 6.12]	0.127

	Treatment Groups		Comparison	
CSFT by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Female				
N'/ N	59 / 59	66 / 66		
Baseline Mean (SD)	486.76 (133.23)	517.91 (155.80)		
Week 52 Mean (SD)	270.23 (53.98)	316.55 (102.50)		
Week 100 Mean (SD)	267.36 (66.92)	295.06 (102.71)		
Week 52: Adjusted Mean Change (SE)	-217.78 (13.47)	-165.56 (12.46)	-52.22 [-88.18; -16.25]	0.004 *
Week 100: Adjusted Mean Change (SE)	-224.45 (14.82)	-187.58 (13.12)	-36.87 [-75.68; 1.94]	0.063
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.067			
Male				
N'/ N	230 / 230	240 / 241		
Baseline Mean (SD)	469.20 (133.08)	473.22 (130.95)		
Week 52 Mean (SD)	290.07 (71.81)	308.40 (73.19)		
Week 100 Mean (SD)	277.88 (61.00)	302.53 (102.16)		
Week 52: Adjusted Mean Change (SE)	-178.83 (6.38)	-167.57 (6.20)	-11.26 [-28.70; 6.17]	0.205
Week 100: Adjusted Mean Change (SE)	-190.20 (6.78)	-174.51 (6.57)	-15.70 [-34.20; 2.80]	0.096

	Treatment Groups		Comparison	
CSFT by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Female				
N'/ N	138 / 138	127 / 127		
Baseline Mean (SD)	462.57 (120.84)	492.50 (142.31)		
Week 52 Mean (SD)	279.57 (60.66)	311.27 (92.66)		
Week 100 Mean (SD)	274.48 (65.09)	285.45 (85.51)		
Week 52: Adjusted Mean Change (SE)	-194.02 (8.23)	-161.40 (8.37)	-32.62 [-55.64; -9.60]	0.005 *
Week 100: Adjusted Mean Change (SE)	-201.70 (8.82)	-189.57 (8.82)	-12.13 [-36.58; 12.33]	0.331

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + gender + treatment * gender + visit * gender + treatment * gender * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + gender + treatment * gender + visit * gender + treatment * gender * visit.

Exceptionally applied model (due to nonconvergence):
KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
KESTREL: Adjusted mean change and mean difference obtained from MMRM with compound symmetry covariance matrix

Table 10.4 CSFT by BCVA (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
CSFT by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Central Subfield Thickness - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.131**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.004 *			
≤ 65 letters				
N'/ N	74 / 74	64 / 64		
Baseline Mean (SD)	499.58 (158.35)	539.72 (168.78)		
Week 52 Mean (SD)	297.63 (107.98)	301.25 (85.18)		
Week 100 Mean (SD)	273.85 (80.51)	279.92 (101.20)		
Week 52: Adjusted Mean Change (SE)	-175.19 (10.64)	-193.05 (11.09)	17.86 [-12.18; 47.90]	0.244
Week 100: Adjusted Mean Change (SE)	-197.49 (11.25)	-215.36 (11.74)	17.87 [-13.95; 49.69]	0.271
> 65 letters				
N'/ N	115 / 115	123 / 123		
Baseline Mean (SD)	423.13 (82.19)	442.24 (100.71)		
Week 52 Mean (SD)	289.63 (52.59)	313.10 (72.55)		
Week 100 Mean (SD)	282.89 (58.56)	305.33 (79.52)		
Week 52: Adjusted Mean Change (SE)	-162.07 (8.29)	-144.34 (7.98)	-17.73 [-40.25; 4.78]	0.123
Week 100: Adjusted Mean Change (SE)	-166.73 (8.75)	-153.78 (8.55)	-12.95 [-36.88; 10.98]	0.289
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.043 *			
≤ 65 letters				
N'/ N	65 / 65	91 / 91		
Baseline Mean (SD)	545.26 (151.52)	530.74 (149.20)		
Week 52 Mean (SD)	280.67 (73.97)	315.31 (101.21)		
Week 100 Mean (SD)	261.80 (55.41)	301.32 (136.17)		
Week 52: Adjusted Mean Change (SE)	-233.65 (12.66)	-178.43 (10.56)	-55.23 [-87.38; -23.08]	<.001 *
Week 100: Adjusted Mean Change (SE)	-249.27 (13.61)	-195.51 (11.39)	-53.76 [-88.40; -19.12]	0.002 *

	Treatment Groups		Comparison	
CSFT by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 65 letters				
N'/ N	114 / 114	89 / 90		
Baseline Mean (SD)	444.57 (104.52)	436.92 (97.85)		
Week 52 Mean (SD)	278.62 (43.60)	304.50 (64.05)		
Week 100 Mean (SD)	280.08 (56.37)	292.08 (66.95)		
Week 52: Adjusted Mean Change (SE)	-184.64 (9.52)	-162.04 (10.67)	-22.59 [-50.54; 5.36]	0.113
Week 100: Adjusted Mean Change (SE)	-189.05 (10.22)	-175.00 (10.86)	-14.05 [-43.21; 15.10]	0.345
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.789			
≤ 65 letters				
N'/ N	139 / 139	155 / 155		
Baseline Mean (SD)	520.94 (156.32)	534.45 (157.10)		
Week 52 Mean (SD)	289.46 (93.13)	309.36 (94.67)		
Week 100 Mean (SD)	268.17 (69.76)	292.25 (122.56)		
Week 52: Adjusted Mean Change (SE)	-205.56 (8.06)	-180.99 (7.64)	-24.57 [-46.09; -3.04]	0.025 *
Week 100: Adjusted Mean Change (SE)	-224.58 (8.11)	-190.23 (7.76)	-34.35 [-56.11; -12.59]	0.002 *

	Treatment Groups		Comparison	
CSFT by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 65 letters				
N'/ N	229 / 229	212 / 213		
Baseline Mean (SD)	433.80 (94.38)	440.00 (99.32)		
Week 52 Mean (SD)	284.21 (48.56)	309.49 (69.05)		
Week 100 Mean (SD)	281.56 (57.39)	299.44 (74.28)		
Week 52: Adjusted Mean Change (SE)	-172.24 (6.22)	-151.49 (6.45)	-20.75 [-38.18; -3.32]	0.020 *
Week 100: Adjusted Mean Change (SE)	-176.89 (6.30)	-163.47 (6.51)	-13.42 [-31.06; 4.21]	0.136

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + BCVA + treatment * BCVA + visit * BCVA + treatment * BCVA * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + BCVA + treatment * BCVA + visit * BCVA + treatment * BCVA * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL and KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with compound symmetry covariance matrix: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + BCVA + treatment * BCVA + treatment * BCVA * visit

Table 10.5 CSFT by region (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
CSFT by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Central Subfield Thickness - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.131**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.156			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	462.47 (127.67)	501.63 (157.36)		
Week 52 Mean (SD)	301.85 (96.54)	324.35 (93.89)		
Week 100 Mean (SD)	285.26 (82.99)	307.17 (110.34)		
Week 52: Adjusted Mean Change (SE)	-163.14 (9.35)	-148.99 (9.73)	-14.15 [-40.61; 12.31]	0.295
Week 100: Adjusted Mean Change (SE)	-176.92 (9.50)	-165.27 (9.90)	-11.65 [-38.54; 15.24]	0.396
European Region				
N'/ N	69 / 69	75 / 75		
Baseline Mean (SD)	445.86 (130.28)	448.01 (111.11)		
Week 52 Mean (SD)	288.21 (56.07)	290.92 (51.65)		
Week 100 Mean (SD)	273.21 (46.72)	282.13 (50.05)		
Week 52: Adjusted Mean Change (SE)	-160.13 (10.65)	-172.23 (10.29)	12.09 [-16.97; 41.15]	0.415
Week 100: Adjusted Mean Change (SE)	-174.98 (10.66)	-180.28 (10.44)	5.30 [-23.96; 34.57]	0.722
Western Pacific Region				
N'/ N	30 / 30	29 / 29		
Baseline Mean (SD)	441.43 (91.58)	472.45 (115.65)		
Week 52 Mean (SD)	276.08 (50.13)	309.07 (68.32)		
Week 100 Mean (SD)	278.62 (62.06)	301.54 (88.71)		
Week 52: Adjusted Mean Change (SE)	-193.06 (16.18)	-164.66 (16.35)	-28.40 [-73.44; 16.64]	0.217
Week 100: Adjusted Mean Change (SE)	-190.52 (16.18)	-175.71 (16.65)	-14.81 [-60.27; 30.64]	0.523

	Treatment Groups		Comparison	
CSFT by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.583			
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	480.73 (99.01)	454.76 (104.13)		
Week 52 Mean (SD)	264.12 (49.40)	277.43 (80.02)		
Week 100 Mean (SD)	263.00 (32.53)	264.93 (70.63)		
Week 52: Adjusted Mean Change (SE)	-226.76 (20.63)	-171.08 (22.85)	-55.67 [-115.84; 4.49]	0.070
Week 100: Adjusted Mean Change (SE)	-233.03 (21.70)	-180.03 (22.60)	-52.99 [-114.23; 8.24]	0.090
European Region				
N'/ N	135 / 135	131 / 132		
Baseline Mean (SD)	479.79 (133.13)	485.82 (132.37)		
Week 52 Mean (SD)	281.76 (57.03)	318.68 (89.07)		
Week 100 Mean (SD)	276.18 (60.45)	302.69 (111.20)		
Week 52: Adjusted Mean Change (SE)	-198.74 (8.70)	-167.50 (8.79)	-31.24 [-55.40; -7.09]	0.011 *
Week 100: Adjusted Mean Change (SE)	-206.67 (8.77)	-177.40 (8.86)	-29.27 [-53.62; -4.91]	0.019 *
Western Pacific Region				
N'/ N	18 / 18	28 / 28		
Baseline Mean (SD)	491.78 (171.66)	499.64 (163.53)		
Week 52 Mean (SD)	278.31 (55.80)	287.29 (52.16)		
Week 100 Mean (SD)	259.08 (34.43)	287.55 (92.59)		
Week 52: Adjusted Mean Change (SE)	-211.07 (23.59)	-155.17 (19.16)	-55.91 [-115.18; 3.36]	0.064
Week 100: Adjusted Mean Change (SE)	-228.20 (24.69)	-163.54 (19.40)	-64.66 [-125.91; -3.41]	0.039 *

	Treatment Groups		Comparison	
CSFT by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.030 *			
Region of the Americas				
N'/ N	90 / 90	83 / 83		
Baseline Mean (SD)	462.47 (127.67)	501.63 (157.36)		
Week 52 Mean (SD)	301.85 (96.54)	324.35 (93.89)		
Week 100 Mean (SD)	285.26 (82.99)	307.17 (110.34)		
Week 52: Adjusted Mean Change (SE)	-178.01 (10.74)	-152.14 (10.95)	-25.87 [-55.92; 4.19]	0.092
Week 100: Adjusted Mean Change (SE)	-193.71 (11.60)	-173.44 (11.73)	-20.27 [-52.59; 12.06]	0.219
South-East Asia Region and Eastern Mediterranean Region				
N'/ N	26 / 26	21 / 21		
Baseline Mean (SD)	480.73 (99.01)	454.76 (104.13)		
Week 52 Mean (SD)	264.12 (49.40)	277.43 (80.02)		
Week 100 Mean (SD)	263.00 (32.53)	264.93 (70.63)		
Week 52: Adjusted Mean Change (SE)	-203.83 (20.74)	-182.50 (22.39)	-21.33 [-81.11; 38.45]	0.484
Week 100: Adjusted Mean Change (SE)	-211.75 (23.52)	-211.88 (23.60)	0.13 [-65.14; 65.40]	0.997
European Region				
N'/ N	204 / 204	206 / 207		
Baseline Mean (SD)	468.31 (132.83)	472.06 (126.10)		
Week 52 Mean (SD)	283.89 (56.63)	308.95 (78.98)		
Week 100 Mean (SD)	275.16 (56.01)	295.63 (95.07)		
Week 52: Adjusted Mean Change (SE)	-180.23 (6.83)	-169.07 (6.73)	-11.16 [-29.94; 7.61]	0.244
Week 100: Adjusted Mean Change (SE)	-188.60 (7.15)	-180.39 (7.08)	-8.21 [-27.93; 11.50]	0.414

	Treatment Groups		Comparison	
CSFT by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Western Pacific Region				
N'/ N	48 / 48	57 / 57		
Baseline Mean (SD)	460.31 (128.22)	485.81 (140.60)		
Week 52 Mean (SD)	276.93 (51.70)	298.82 (61.64)		
Week 100 Mean (SD)	272.45 (55.13)	294.85 (89.85)		
Week 52: Adjusted Mean Change (SE)	-204.51 (13.80)	-163.65 (12.58)	-40.86 [-77.47; -4.25]	0.029 *
Week 100: Adjusted Mean Change (SE)	-214.54 (14.78)	-177.24 (13.06)	-37.30 [-75.95; 1.35]	0.059

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + region + treatment * region + visit * region + treatment * region * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + region + treatment * region + visit * region + treatment * region * visit.

Exceptionally applied model (due to nonconvergence):
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
KESTREL and KITE: Adjusted mean change and mean difference obtained from MMRM with compound symmetry covariance matrix

Table 10.6 CSFT by diabetes type (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
CSFT by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Central Subfield Thickness - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.131**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.232			
Type 1				
N'/ N	12 / 12	6 / 6		
Baseline Mean (SD)	466.42 (103.48)	499.33 (158.35)		
Week 52 Mean (SD)	283.11 (55.71)	294.33 (29.15)		
Week 100 Mean (SD)	259.70 (47.00)	279.75 (54.09)		
Week 52: Adjusted Mean Change (SE)	-192.50 (26.94)	-184.48 (34.96)	-8.03 [-94.55; 78.50]	0.856
Week 100: Adjusted Mean Change (SE)	-213.20 (27.10)	-226.44 (42.47)	13.24 [-85.53; 112.00]	0.793
Type 2				
N'/ N	177 / 177	181 / 181		
Baseline Mean (SD)	452.16 (124.86)	474.81 (135.47)		
Week 52 Mean (SD)	293.12 (78.45)	309.60 (78.32)		
Week 100 Mean (SD)	280.97 (68.58)	297.04 (88.94)		
Week 52: Adjusted Mean Change (SE)	-165.87 (6.83)	-159.82 (6.68)	-6.06 [-24.80; 12.69]	0.526
Week 100: Adjusted Mean Change (SE)	-176.51 (7.24)	-173.53 (7.10)	-2.98 [-22.87; 16.91]	0.769
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.026 *			
Type 1				
N'/ N	19 / 19	7 / 7		
Baseline Mean (SD)	466.74 (117.11)	445.29 (148.29)		
Week 52 Mean (SD)	268.44 (32.01)	328.71 (94.08)		
Week 100 Mean (SD)	261.18 (37.14)	310.00 (101.56)		
Week 52: Adjusted Mean Change (SE)	-206.62 (22.47)	-123.17 (36.63)	-83.45 [-167.69; 0.79]	0.052
Week 100: Adjusted Mean Change (SE)	-219.71 (23.50)	-140.89 (39.94)	-78.82 [-169.64; 12.00]	0.089

	Treatment Groups		Comparison	
CSFT by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Type 2				
N'/ N	160 / 160	173 / 174		
Baseline Mean (SD)	482.84 (134.40)	485.93 (134.22)		
Week 52 Mean (SD)	280.87 (58.50)	308.95 (84.23)		
Week 100 Mean (SD)	275.13 (58.72)	295.96 (105.61)		
Week 52: Adjusted Mean Change (SE)	-201.50 (8.16)	-172.10 (7.73)	-29.40 [-51.43; -7.37]	0.009 *
Week 100: Adjusted Mean Change (SE)	-209.56 (8.81)	-186.88 (8.08)	-22.67 [-46.10; 0.76]	0.058
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.014 *			
Type 1				
N'/ N	31 / 31	13 / 13		
Baseline Mean (SD)	466.61 (110.25)	470.23 (149.10)		
Week 52 Mean (SD)	273.33 (40.92)	312.85 (71.40)		
Week 100 Mean (SD)	260.63 (40.17)	296.56 (80.67)		
Week 52: Adjusted Mean Change (SE)	-197.96 (17.01)	-150.83 (25.30)	-47.14 [-106.89; 12.62]	0.122
Week 100: Adjusted Mean Change (SE)	-213.27 (17.57)	-176.45 (28.89)	-36.82 [-103.10; 29.46]	0.276
Type 2				
N'/ N	337 / 337	354 / 355		
Baseline Mean (SD)	466.73 (130.19)	480.25 (134.78)		
Week 52 Mean (SD)	287.35 (69.92)	309.29 (81.09)		
Week 100 Mean (SD)	278.30 (64.21)	296.50 (97.40)		
Week 52: Adjusted Mean Change (SE)	-183.24 (5.28)	-165.89 (5.09)	-17.36 [-31.72; -2.99]	0.018 *
Week 100: Adjusted Mean Change (SE)	-192.59 (5.64)	-180.15 (5.36)	-12.44 [-27.70; 2.81]	0.110

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + diabetes type + treatment * diabetes type + visit * diabetes type + treatment * diabetes type * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + diabetes type + treatment * diabetes type + visit * diabetes type + treatment * diabetes type * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL and KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix

Table 10.7 CSFT by HbA1c (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
CSFT by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Central Subfield Thickness - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.131**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.249			
< 7.5 %				
N'/ N	76 / 76	107 / 107		
Baseline Mean (SD)	450.93 (125.61)	468.36 (119.82)		
Week 52 Mean (SD)	295.11 (75.53)	304.77 (75.21)		
Week 100 Mean (SD)	280.17 (59.25)	294.70 (81.96)		
Week 52: Adjusted Mean Change (SE)	-163.67 (10.29)	-162.72 (8.59)	-0.96 [-27.24; 25.32]	0.943
Week 100: Adjusted Mean Change (SE)	-174.41 (11.08)	-173.04 (8.94)	-1.38 [-29.30; 26.55]	0.923
≥ 7.5 %				
N'/ N	112 / 112	80 / 80		
Baseline Mean (SD)	455.76 (122.28)	485.29 (154.96)		
Week 52 Mean (SD)	290.76 (78.70)	315.25 (79.88)		
Week 100 Mean (SD)	279.48 (73.01)	299.62 (98.02)		
Week 52: Adjusted Mean Change (SE)	-170.81 (8.72)	-158.15 (10.27)	-12.66 [-39.09; 13.77]	0.348
Week 100: Adjusted Mean Change (SE)	-182.81 (9.13)	-178.93 (11.37)	-3.88 [-32.49; 24.74]	0.790
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.224			
< 7.5 %				
N'/ N	82 / 82	96 / 96		
Baseline Mean (SD)	501.54 (137.30)	502.91 (147.02)		
Week 52 Mean (SD)	281.45 (50.17)	316.40 (93.68)		
Week 100 Mean (SD)	280.87 (69.19)	297.97 (128.31)		
Week 52: Adjusted Mean Change (SE)	-210.66 (11.40)	-170.23 (10.31)	-40.43 [-70.54; -10.32]	0.009 *
Week 100: Adjusted Mean Change (SE)	-217.69 (12.16)	-188.30 (10.92)	-29.39 [-61.42; 2.63]	0.072

	Treatment Groups		Comparison	
CSFT by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 7.5 %				
N'/ N	97 / 97	84 / 85		
Baseline Mean (SD)	463.89 (126.39)	463.14 (116.04)		
Week 52 Mean (SD)	277.63 (60.60)	302.51 (72.67)		
Week 100 Mean (SD)	266.97 (42.44)	294.83 (74.15)		
Week 52: Adjusted Mean Change (SE)	-195.04 (10.36)	-169.81 (11.15)	-25.23 [-55.07; 4.61]	0.097
Week 100: Adjusted Mean Change (SE)	-204.89 (11.22)	-180.86 (11.53)	-24.03 [-55.56; 7.50]	0.135
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.915			
< 7.5 %				
N'/ N	158 / 158	203 / 203		
Baseline Mean (SD)	477.20 (133.81)	484.69 (134.16)		
Week 52 Mean (SD)	288.12 (63.94)	310.09 (84.10)		
Week 100 Mean (SD)	280.53 (64.22)	296.18 (105.09)		
Week 52: Adjusted Mean Change (SE)	-187.13 (7.66)	-166.54 (6.65)	-20.59 [-40.48; -0.70]	0.042 *
Week 100: Adjusted Mean Change (SE)	-195.91 (8.21)	-180.39 (6.98)	-15.51 [-36.65; 5.62]	0.150
≥ 7.5 %				
N'/ N	209 / 209	164 / 165		
Baseline Mean (SD)	459.53 (123.97)	473.95 (136.45)		
Week 52 Mean (SD)	284.58 (70.86)	308.60 (76.18)		
Week 100 Mean (SD)	273.85 (61.32)	296.94 (85.14)		
Week 52: Adjusted Mean Change (SE)	-182.83 (6.72)	-163.96 (7.56)	-18.87 [-38.70; 0.97]	0.062
Week 100: Adjusted Mean Change (SE)	-193.80 (7.15)	-179.52 (8.07)	-14.28 [-35.43; 6.86]	0.185

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + HbA1c + treatment * HbA1c + visit * HbA1c + treatment * HbA1c * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + HbA1c + treatment * HbA1c + visit * HbA1c + treatment * HbA1c * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL and KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix

Table 10.8 CSFT by duration of DME (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
CSFT by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Central Subfield Thickness - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.131**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.439			
≤ 3 months				
N'/ N	120 / 120	110 / 110		
Baseline Mean (SD)	447.94 (119.13)	493.07 (128.48)		
Week 52 Mean (SD)	297.16 (89.27)	316.40 (82.21)		
Week 100 Mean (SD)	285.95 (75.81)	296.19 (74.97)		
Week 52: Adjusted Mean Change (SE)	-160.73 (8.19)	-157.61 (8.56)	-3.12 [-26.36; 20.12]	0.793
Week 100: Adjusted Mean Change (SE)	-170.22 (8.63)	-178.66 (9.16)	8.44 [-16.25; 33.13]	0.503
> 3 - < 12 months				
N'/ N	30 / 30	39 / 39		
Baseline Mean (SD)	451.57 (127.38)	461.15 (172.90)		
Week 52 Mean (SD)	286.33 (37.22)	301.68 (76.45)		
Week 100 Mean (SD)	268.36 (28.56)	316.30 (140.02)		
Week 52: Adjusted Mean Change (SE)	-178.19 (16.86)	-167.08 (14.78)	-11.11 [-55.06; 32.84]	0.620
Week 100: Adjusted Mean Change (SE)	-200.07 (18.09)	-156.66 (16.37)	-43.41 [-91.23; 4.42]	0.075
≥ 12 months				
N'/ N	39 / 39	38 / 38		
Baseline Mean (SD)	469.97 (134.75)	439.84 (104.83)		
Week 52 Mean (SD)	280.44 (48.08)	295.12 (60.34)		
Week 100 Mean (SD)	265.86 (55.04)	281.39 (60.58)		
Week 52: Adjusted Mean Change (SE)	-181.61 (15.41)	-163.12 (14.40)	-18.49 [-59.79; 22.81]	0.380
Week 100: Adjusted Mean Change (SE)	-192.43 (16.23)	-180.63 (14.72)	-11.80 [-54.71; 31.11]	0.590

	Treatment Groups		Comparison	
CSFT by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.275			
≤ 3 months				
N'/ N	85 / 85	91 / 92		
Baseline Mean (SD)	472.81 (130.19)	478.84 (122.27)		
Week 52 Mean (SD)	282.16 (51.15)	315.39 (90.76)		
Week 100 Mean (SD)	279.48 (62.32)	292.66 (93.99)		
Week 52: Adjusted Mean Change (SE)	-197.53 (11.22)	-159.27 (10.67)	-38.26 [-68.62; -7.90]	0.014 *
Week 100: Adjusted Mean Change (SE)	-205.98 (12.38)	-183.51 (11.20)	-22.47 [-55.21; 10.27]	0.179
> 3 - < 12 months				
N'/ N	51 / 51	49 / 49		
Baseline Mean (SD)	516.24 (138.13)	503.51 (132.81)		
Week 52 Mean (SD)	282.41 (65.61)	299.95 (78.38)		
Week 100 Mean (SD)	269.42 (54.84)	291.08 (89.66)		
Week 52: Adjusted Mean Change (SE)	-211.06 (14.06)	-184.57 (14.48)	-26.49 [-66.00; 13.03]	0.189
Week 100: Adjusted Mean Change (SE)	-224.11 (14.56)	-190.86 (15.46)	-33.24 [-74.82; 8.34]	0.117
≥ 12 months				
N'/ N	43 / 43	40 / 40		
Baseline Mean (SD)	455.95 (124.37)	473.43 (162.06)		
Week 52 Mean (SD)	270.03 (52.45)	309.94 (78.31)		
Week 100 Mean (SD)	267.50 (47.47)	309.94 (139.03)		
Week 52: Adjusted Mean Change (SE)	-200.29 (15.79)	-176.53 (16.11)	-23.77 [-67.96; 20.43]	0.292
Week 100: Adjusted Mean Change (SE)	-201.88 (16.99)	-181.76 (16.38)	-20.13 [-66.34; 26.09]	0.393

	Treatment Groups		Comparison	
CSFT by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.885			
≤ 3 months				
N'/ N	205 / 205	201 / 202		
Baseline Mean (SD)	458.25 (124.13)	486.63 (125.59)		
Week 52 Mean (SD)	291.19 (76.59)	315.95 (85.83)		
Week 100 Mean (SD)	283.54 (70.95)	294.58 (83.90)		
Week 52: Adjusted Mean Change (SE)	-178.05 (6.73)	-158.47 (6.74)	-19.59 [-38.25; -0.93]	0.040 *
Week 100: Adjusted Mean Change (SE)	-186.92 (7.22)	-181.01 (7.15)	-5.91 [-25.83; 14.01]	0.561
> 3 - < 12 months				
N'/ N	81 / 81	88 / 88		
Baseline Mean (SD)	492.28 (137.09)	484.74 (152.44)		
Week 52 Mean (SD)	283.79 (56.93)	300.68 (77.03)		
Week 100 Mean (SD)	269.06 (47.34)	301.55 (113.00)		
Week 52: Adjusted Mean Change (SE)	-195.11 (10.67)	-176.88 (10.29)	-18.23 [-47.28; 10.81]	0.219
Week 100: Adjusted Mean Change (SE)	-211.34 (11.20)	-176.47 (11.16)	-34.87 [-65.85; -3.90]	0.027 *

	Treatment Groups		Comparison	
CSFT by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 12 months				
N'/ N	82 / 82	78 / 78		
Baseline Mean (SD)	462.62 (128.80)	457.06 (137.36)		
Week 52 Mean (SD)	274.56 (50.46)	302.53 (69.78)		
Week 100 Mean (SD)	266.73 (50.71)	296.09 (108.48)		
Week 52: Adjusted Mean Change (SE)	-190.50 (10.99)	-169.82 (10.76)	-20.67 [-50.82; 9.47]	0.179
Week 100: Adjusted Mean Change (SE)	-196.01 (11.73)	-180.99 (10.97)	-15.02 [-46.48; 16.44]	0.349

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + duration of DME + treatment * duration of DME + visit * duration of DME + treatment * duration of DME * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + duration of DME + treatment * duration of DME + visit * duration of DME + treatment * duration of DME * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL and KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix

Table 10.9 CSFT by DME type (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
CSFT by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Central Subfield Thickness - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.131**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.045 *			
focal				
N'/ N	59 / 59	48 / 48		
Baseline Mean (SD)	408.02 (80.19)	429.79 (118.53)		
Week 52 Mean (SD)	283.10 (40.53)	319.65 (90.65)		
Week 100 Mean (SD)	278.84 (45.57)	305.40 (91.26)		
Week 52: Adjusted Mean Change (SE)	-160.44 (11.54)	-130.11 (12.94)	-30.33 [-64.28; 3.62]	0.080
Week 100: Adjusted Mean Change (SE)	-165.88 (12.02)	-145.02 (13.91)	-20.86 [-56.85; 15.13]	0.256
diffuse				
N'/ N	127 / 127	134 / 134		
Baseline Mean (SD)	474.48 (134.92)	493.37 (140.05)		
Week 52 Mean (SD)	296.77 (90.60)	304.50 (72.41)		
Week 100 Mean (SD)	276.56 (69.82)	291.71 (86.76)		
Week 52: Adjusted Mean Change (SE)	-172.59 (8.07)	-173.00 (7.66)	0.41 [-21.40; 22.22]	0.971
Week 100: Adjusted Mean Change (SE)	-190.17 (8.60)	-187.77 (8.17)	-2.40 [-25.65; 20.85]	0.840
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.354			
focal				
N'/ N	63 / 63	66 / 66		
Baseline Mean (SD)	444.05 (104.24)	429.76 (88.66)		
Week 52 Mean (SD)	280.67 (53.38)	307.98 (76.83)		
Week 100 Mean (SD)	277.37 (62.26)	287.66 (73.92)		
Week 52: Adjusted Mean Change (SE)	-173.39 (13.21)	-157.17 (12.55)	-16.22 [-51.82; 19.38]	0.372
Week 100: Adjusted Mean Change (SE)	-187.09 (13.90)	-180.98 (12.99)	-6.10 [-43.25; 31.04]	0.747

	Treatment Groups		Comparison	
CSFT by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
diffuse				
N'/ N	115 / 115	108 / 109		
Baseline Mean (SD)	502.43 (141.99)	519.34 (147.00)		
Week 52 Mean (SD)	278.68 (57.78)	311.52 (89.50)		
Week 100 Mean (SD)	271.48 (53.73)	299.67 (115.86)		
Week 52: Adjusted Mean Change (SE)	-217.64 (9.46)	-178.29 (9.74)	-39.36 [-65.92; -12.79]	0.004 *
Week 100: Adjusted Mean Change (SE)	-224.42 (10.32)	-190.83 (10.28)	-33.60 [-62.08; -5.12]	0.021 *
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.622			
focal				
N'/ N	122 / 122	114 / 114		
Baseline Mean (SD)	426.62 (94.75)	429.77 (101.81)		
Week 52 Mean (SD)	281.92 (46.97)	313.05 (82.85)		
Week 100 Mean (SD)	278.14 (53.93)	294.72 (81.22)		
Week 52: Adjusted Mean Change (SE)	-166.77 (8.75)	-145.00 (8.98)	-21.77 [-46.27; 2.73]	0.082
Week 100: Adjusted Mean Change (SE)	-176.34 (9.16)	-165.44 (9.43)	-10.90 [-36.59; 14.80]	0.406
diffuse				
N'/ N	242 / 242	242 / 243		
Baseline Mean (SD)	487.76 (138.74)	504.96 (143.48)		
Week 52 Mean (SD)	287.86 (76.57)	307.65 (80.40)		
Week 100 Mean (SD)	274.16 (62.61)	295.30 (100.72)		
Week 52: Adjusted Mean Change (SE)	-194.82 (6.18)	-175.93 (6.10)	-18.90 [-35.90; -1.89]	0.029 *
Week 100: Adjusted Mean Change (SE)	-206.99 (6.66)	-189.62 (6.47)	-17.36 [-35.54; 0.82]	0.061

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + DME type + treatment * DME type + visit * DME type + treatment * DME type * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + DME type + treatment * DME type + visit * DME type + treatment * DME type * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL and KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix

Table 10.10 CSFT by CSFT (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
CSFT by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Central Subfield Thickness - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.131**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.038 *			
< 450 µm				
N'/ N	107 / 107	96 / 96		
Baseline Mean (SD)	370.59 (40.70)	378.51 (42.69)		
Week 52 Mean (SD)	275.36 (38.76)	291.45 (42.93)		
Week 100 Mean (SD)	271.15 (43.90)	290.83 (63.00)		
Week 52: Adjusted Mean Change (SE)	-94.18 (8.43)	-90.17 (8.87)	-4.01 [-28.00; 19.99]	0.743
Week 100: Adjusted Mean Change (SE)	-100.18 (8.47)	-93.88 (9.02)	-6.30 [-30.55; 17.95]	0.611
≥ 450 - < 650 µm				
N'/ N	70 / 70	71 / 71		
Baseline Mean (SD)	523.04 (53.27)	524.11 (54.66)		
Week 52 Mean (SD)	300.53 (71.12)	325.46 (92.41)		
Week 100 Mean (SD)	285.24 (72.98)	294.85 (77.55)		
Week 52: Adjusted Mean Change (SE)	-224.69 (10.44)	-199.75 (10.25)	-24.94 [-53.62; 3.74]	0.088
Week 100: Adjusted Mean Change (SE)	-237.85 (10.53)	-225.89 (10.47)	-11.96 [-41.06; 17.15]	0.421
≥ 650 µm				
N'/ N	12 / 12	20 / 20		
Baseline Mean (SD)	780.25 (111.66)	769.40 (115.04)		
Week 52 Mean (SD)	407.11 (208.23)	337.56 (122.63)		
Week 100 Mean (SD)	329.38 (165.28)	329.25 (179.86)		
Week 52: Adjusted Mean Change (SE)	-358.08 (25.59)	-432.98 (19.57)	74.90 [11.86; 137.95]	0.020 *
Week 100: Adjusted Mean Change (SE)	-419.71 (26.15)	-438.30 (19.58)	18.59 [-45.35; 82.53]	0.569

	Treatment Groups		Comparison	
CSFT by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=<.001 *			
< 450 µm				
N'/ N	85 / 85	82 / 82		
Baseline Mean (SD)	376.29 (38.23)	375.21 (45.69)		
Week 52 Mean (SD)	272.54 (36.76)	291.81 (46.67)		
Week 100 Mean (SD)	264.03 (36.15)	297.21 (114.00)		
Week 52: Adjusted Mean Change (SE)	-102.35 (10.90)	-83.56 (11.07)	-18.79 [-49.27; 11.70]	0.227
Week 100: Adjusted Mean Change (SE)	-110.45 (10.98)	-80.73 (11.07)	-29.72 [-60.32; 0.88]	0.057
≥ 450 - < 650 µm				
N'/ N	74 / 74	79 / 79		
Baseline Mean (SD)	527.28 (58.31)	533.10 (59.84)		
Week 52 Mean (SD)	292.29 (69.89)	320.85 (96.76)		
Week 100 Mean (SD)	291.50 (72.22)	283.09 (68.66)		
Week 52: Adjusted Mean Change (SE)	-235.14 (11.38)	-207.84 (10.97)	-27.30 [-58.34; 3.74]	0.085
Week 100: Adjusted Mean Change (SE)	-246.54 (11.67)	-236.27 (11.11)	-10.27 [-41.91; 21.37]	0.525
≥ 650 µm				
N'/ N	20 / 20	19 / 19		
Baseline Mean (SD)	755.95 (88.86)	752.68 (120.38)		
Week 52 Mean (SD)	253.63 (44.17)	331.56 (124.82)		
Week 100 Mean (SD)	244.07 (36.06)	352.00 (171.40)		
Week 52: Adjusted Mean Change (SE)	-512.79 (22.21)	-356.51 (22.63)	-156.27 [-218.43; -94.12]	<.001 *
Week 100: Adjusted Mean Change (SE)	-513.99 (22.44)	-333.55 (22.86)	-180.44 [-243.22; -117.66]	<.001 *

	Treatment Groups		Comparison	
CSFT by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.248			
< 450 µm				
N'/ N	192 / 192	178 / 178		
Baseline Mean (SD)	373.11 (39.63)	376.99 (44.00)		
Week 52 Mean (SD)	274.15 (37.82)	291.60 (44.42)		
Week 100 Mean (SD)	268.15 (40.83)	293.74 (89.64)		
Week 52: Adjusted Mean Change (SE)	-104.23 (6.35)	-87.72 (6.54)	-16.51 [-34.40; 1.37]	0.070
Week 100: Adjusted Mean Change (SE)	-114.24 (6.39)	-98.57 (6.59)	-15.67 [-33.68; 2.33]	0.088
≥ 450 - < 650 µm				
N'/ N	144 / 144	150 / 150		
Baseline Mean (SD)	525.22 (55.76)	528.85 (57.43)		
Week 52 Mean (SD)	296.15 (70.30)	322.96 (94.46)		
Week 100 Mean (SD)	288.40 (72.34)	288.38 (72.72)		
Week 52: Adjusted Mean Change (SE)	-226.47 (7.16)	-206.33 (6.99)	-20.14 [-39.76; -0.53]	0.044 *
Week 100: Adjusted Mean Change (SE)	-236.48 (7.20)	-217.18 (7.03)	-19.30 [-39.03; 0.43]	0.055
≥ 650 µm				
N'/ N	32 / 32	39 / 39		
Baseline Mean (SD)	765.06 (96.99)	761.26 (116.41)		
Week 52 Mean (SD)	308.88 (146.04)	334.56 (121.75)		
Week 100 Mean (SD)	273.74 (106.04)	340.26 (173.26)		
Week 52: Adjusted Mean Change (SE)	-436.34 (14.35)	-385.37 (12.99)	-50.97 [-88.86; -13.08]	0.008 *
Week 100: Adjusted Mean Change (SE)	-446.35 (14.36)	-396.22 (13.01)	-50.13 [-88.08; -12.18]	0.010 *

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + CSFT + treatment * CSFT + visit * CSFT + treatment * CSFT * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + study + treatment * study + CSFT + treatment * CSFT + visit * CSFT + treatment * CSFT * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL and KITE: Adjusted mean change and mean difference obtained from MMRM with compound symmetry covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with compound symmetry covariance matrix:
Change from baseline = treatment + visit + treatment * visit + age category + study + treatment * study + CSFT + treatment * CSFT

Table 10.11 CSFT by status of SRF (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
CSFT by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Central Subfield Thickness - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.131**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.494			
presence				
N'/ N	62 / 62	61 / 61		
Baseline Mean (SD)	515.03 (145.81)	570.00 (164.84)		
Week 52 Mean (SD)	309.35 (110.24)	316.92 (92.89)		
Week 100 Mean (SD)	282.88 (90.37)	306.68 (122.58)		
Week 52: Adjusted Mean Change (SE)	-177.97 (11.39)	-179.36 (11.53)	1.38 [-30.08; 32.84]	0.931
Week 100: Adjusted Mean Change (SE)	-197.52 (11.73)	-196.00 (12.44)	-1.51 [-34.75; 31.72]	0.929
absence				
N'/ N	127 / 127	126 / 126		
Baseline Mean (SD)	422.81 (98.10)	429.90 (89.21)		
Week 52 Mean (SD)	284.70 (54.44)	305.22 (68.31)		
Week 100 Mean (SD)	277.72 (51.40)	291.71 (65.74)		
Week 52: Adjusted Mean Change (SE)	-161.30 (8.06)	-152.06 (7.99)	-9.24 [-31.37; 12.89]	0.413
Week 100: Adjusted Mean Change (SE)	-168.13 (8.62)	-165.44 (8.48)	-2.69 [-26.26; 20.88]	0.823
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.010 *			
presence				
N'/ N	56 / 56	66 / 67		
Baseline Mean (SD)	533.30 (136.32)	566.45 (146.65)		
Week 52 Mean (SD)	281.67 (61.17)	301.46 (92.33)		
Week 100 Mean (SD)	275.13 (61.22)	286.47 (105.05)		
Week 52: Adjusted Mean Change (SE)	-219.80 (13.59)	-208.49 (12.39)	-11.30 [-47.07; 24.47]	0.536
Week 100: Adjusted Mean Change (SE)	-228.58 (14.89)	-218.00 (12.92)	-10.58 [-48.95; 27.79]	0.589

	Treatment Groups		Comparison	
CSFT by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
absence				
N'/ N	123 / 123	114 / 114		
Baseline Mean (SD)	457.38 (124.12)	436.82 (100.51)		
Week 52 Mean (SD)	278.32 (53.85)	314.97 (79.40)		
Week 100 Mean (SD)	272.61 (54.76)	302.25 (105.37)		
Week 52: Adjusted Mean Change (SE)	-194.41 (9.08)	-147.93 (9.40)	-46.48 [-72.02; -20.93]	<.001 *
Week 100: Adjusted Mean Change (SE)	-203.01 (9.68)	-166.16 (9.86)	-36.85 [-63.87; -9.83]	0.008 *
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.014 *			
presence				
N'/ N	118 / 118	127 / 128		
Baseline Mean (SD)	523.70 (141.08)	568.16 (155.04)		
Week 52 Mean (SD)	296.10 (90.75)	308.83 (92.49)		
Week 100 Mean (SD)	279.56 (78.90)	295.97 (113.49)		
Week 52: Adjusted Mean Change (SE)	-198.70 (8.79)	-194.88 (8.44)	-3.82 [-27.51; 19.87]	0.752
Week 100: Adjusted Mean Change (SE)	-212.59 (9.32)	-207.75 (8.95)	-4.84 [-29.97; 20.29]	0.706
absence				
N'/ N	250 / 250	240 / 240		
Baseline Mean (SD)	439.82 (112.77)	433.18 (94.61)		
Week 52 Mean (SD)	281.56 (54.11)	309.76 (73.66)		
Week 100 Mean (SD)	275.19 (53.01)	296.79 (87.02)		
Week 52: Adjusted Mean Change (SE)	-177.53 (6.05)	-150.00 (6.13)	-27.53 [-44.35; -10.72]	0.001 *
Week 100: Adjusted Mean Change (SE)	-185.32 (6.46)	-165.69 (6.47)	-19.62 [-37.47; -1.78]	0.031 *

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + status of SRF + treatment * status of SRF + visit * status of SRF + treatment * status of SRF * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + status of SRF + treatment * status of SRF + visit * status of SRF + treatment * status of SRF * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL and KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix

Table 10.13 CSFT by exposure (week 100) (FAS), continuous analysis, week 100

	Treatment Groups		Comparison	
CSFT by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Central Subfield Thickness - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.131**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.096			
Non-exposed				
N'/ N	12 / 12	13 / 13		
Baseline Mean (SD)	497.42 (168.16)	449.69 (139.63)		
Week 52 Mean (SD)	440.50 (231.22)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 52: Adjusted Mean Change (SE)	-68.24 (51.49)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.
Exposed				
N'/ N	177 / 177	174 / 174		
Baseline Mean (SD)	450.06 (119.84)	477.53 (135.76)		
Week 52 Mean (SD)	290.59 (73.42)	309.03 (77.06)		
Week 100 Mean (SD)	279.53 (67.43)	296.57 (88.09)		
Week 52: Adjusted Mean Change (SE)	-169.00 (6.68)	-159.50 (6.59)	-9.50 [-27.91; 8.91]	0.312
Week 100: Adjusted Mean Change (SE)	-179.34 (6.99)	-174.72 (6.99)	-4.61 [-24.01; 14.78]	0.641
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.133			
Non-exposed				
N'/ N	17 / 17	12 / 12		
Baseline Mean (SD)	465.82 (160.86)	479.92 (244.32)		
Week 52 Mean (SD)	272.00 (47.62)	N.E.		
Week 100 Mean (SD)	N.E.	N.E.		
Week 52: Adjusted Mean Change (SE)	-270.95 (50.81)	N.E.	N.E.	N.E.
Week 100: Adjusted Mean Change (SE)	N.E.	N.E.	N.E.	N.E.

	Treatment Groups		Comparison	
CSFT by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Exposed				
N'/ N	162 / 162	168 / 169		
Baseline Mean (SD)	482.74 (129.62)	484.67 (124.41)		
Week 52 Mean (SD)	279.50 (56.30)	309.87 (84.47)		
Week 100 Mean (SD)	273.35 (56.51)	296.44 (105.16)		
Week 52: Adjusted Mean Change (SE)	-202.31 (7.75)	-171.70 (7.59)	-30.60 [-51.87; -9.33]	0.005 *
Week 100: Adjusted Mean Change (SE)	-211.99 (8.22)	-185.60 (7.90)	-26.39 [-48.74; -4.04]	0.021 *
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.920			
Non-exposed				
N'/ N	29 / 29	25 / 25		
Baseline Mean (SD)	478.90 (161.70)	464.20 (193.25)		
Week 52 Mean (SD)	339.40 (151.72)	N.E.		
Week 52: Adjusted Mean Change (SE)	-180.66 (35.91)	N.E.	N.E.	N.E.
Exposed				
N'/ N	339 / 339	342 / 343		
Baseline Mean (SD)	465.68 (125.49)	481.04 (130.17)		
Week 52 Mean (SD)	285.20 (65.78)	309.43 (80.61)		
Week 100 Mean (SD)	276.60 (62.47)	296.51 (96.81)		
Week 52: Adjusted Mean Change (SE)	-185.28 (5.09)	-165.44 (5.00)	-19.84 [-33.83; -5.84]	0.005 *
Week 100: Adjusted Mean Change (SE)	-195.22 (5.36)	-180.06 (5.26)	-15.15 [-29.88; -0.43]	0.044 *

N: Number of patients
N': Number of patients in the analysis
CI: Confidence interval
SD: Standard deviation
SE: Standard error
N.E.: Not estimable
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: None

Adjusted mean change and mean difference obtained from MMRM with unstructured covariance matrix:
KESTREL and KITE: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + exposure (week 100) + treatment * exposure (week 100) + visit * exposure (week 100) + treatment * exposure (week 100) * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + exposure (week 100) + treatment * exposure (week 100) + visit * exposure (week 100) + treatment * exposure (week 100) * visit.

Exceptionally applied model (due to nonconvergence):
KESTREL and KITE: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix
Pooled Analysis: Adjusted mean change and mean difference obtained from MMRM with first-order autoregressive covariance matrix

11 Presence of SRF and/or IRF in the study eye: Binary analysis

Table 11.1 Presence of SRF and/or IRF in the study eye (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Presence of SRF in the study eye, Week 52					
KESTREL, N''/N'/N	154 / 189 / 189	161 / 187 / 187			
Presence of SRF in the study eye, n (%)	4 (2.1)	4 (2.1)	0.98 [0.24; 4.08] 0.982	0.99 [0.25; 3.90] 0.988	-0.00 [-0.03; 0.03] 0.988
KITE, N''/N'/N	147 / 179 / 179	152 / 181 / 181			
Presence of SRF in the study eye, n (%)	3 (1.7)	6 (3.3)	0.58 [0.14; 2.44] 0.460	0.51 [0.13; 1.99] 0.329	-0.02 [-0.05; 0.02] 0.318
Pooled Analysis, N''/N'/N	301 / 368 / 368	313 / 368 / 368			
Presence of SRF in the study eye, n (%)	7 (1.9)	10 (2.7)	0.75 [0.28; 2.07] 0.584	0.70 [0.27; 1.82] 0.463	-0.01 [-0.03; 0.01] 0.462
p_H=0.600					
Presence of SRF in the study eye, Week 100					
KESTREL, N''/N'/N	148 / 189 / 189	145 / 187 / 187			
Presence of SRF in the study eye, n (%)	3 (1.6)	2 (1.1)	1.49 [0.25; 9.03] 0.663	1.48 [0.25; 8.78] 0.663	0.01 [-0.02; 0.03] 0.661
KITE, N''/N'/N	133 / 179 / 179	145 / 181 / 181			
Presence of SRF in the study eye, n (%)	4 (2.2)	5 (2.8)	0.93 [0.24; 3.62] 0.918	0.81 [0.22; 2.96] 0.749	-0.01 [-0.04; 0.03] 0.748
Pooled Analysis, N''/N'/N	281 / 368 / 368	290 / 368 / 368			
Presence of SRF in the study eye, n (%)	7 (1.9)	7 (1.9)	1.18 [0.38; 3.70] 0.776	1.00 [0.36; 2.83] 0.995	0.00 [-0.02; 0.02] 0.995
p_H=0.677					
Presence of IRF in the study eye, Week 52					
KESTREL, N''/N'/N	154 / 189 / 189	161 / 187 / 187			
Presence of IRF in the study eye, n (%)	114 (60.3)	137 (73.3)	0.54 [0.35; 0.84] 0.006 *	0.82 [0.71; 0.95] 0.008 *	-0.13 [-0.22; -0.04] 0.007 *
KITE, N''/N'/N	147 / 179 / 179	152 / 181 / 181			
Presence of IRF in the study eye, n (%)	96 (53.6)	132 (72.9)	0.43 [0.27; 0.67] <.001 *	0.74 [0.63; 0.87] <.001 *	-0.19 [-0.29; -0.10] <.001 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N''/N'/N	301 / 368 / 368	313 / 368 / 368			
Presence of IRF in the study eye, n (%) p_H=0.503	210 (57.1)	269 (73.1)	0.48 [0.35; 0.65] <.001 *	0.78 [0.70; 0.87] <.001 *	-0.16 [-0.23; -0.09] <.001 *
Presence of IRF in the study eye, Week 100					
KESTREL, N''/N'/N	148 / 189 / 189	145 / 187 / 187			
Presence of IRF in the study eye, n (%)	78 (41.3)	102 (54.5)	0.58 [0.38; 0.87] 0.009 *	0.76 [0.61; 0.94] 0.011 *	-0.13 [-0.23; -0.03] 0.009 *
KITE, N''/N'/N	133 / 179 / 179	145 / 181 / 181			
Presence of IRF in the study eye, n (%)	73 (40.8)	103 (56.9)	0.52 [0.34; 0.79] 0.002 *	0.72 [0.58; 0.89] 0.003 *	-0.16 [-0.26; -0.06] 0.002 *
Pooled Analysis, N''/N'/N	281 / 368 / 368	290 / 368 / 368			
Presence of IRF in the study eye, n (%) p_H=0.733	151 (41.0)	205 (55.7)	0.55 [0.41; 0.74] <.001 *	0.74 [0.63; 0.86] <.001 *	-0.15 [-0.22; -0.08] <.001 *
Presence of SRF and/or IRF in the study eye, Week 52					
KESTREL, N''/N'/N	189 / 189 / 189	187 / 187 / 187			
Presence of SRF and/or IRF in the study eye, n (%)	114 (60.3)	137 (73.3)	0.54 [0.35; 0.84] 0.006 *	0.82 [0.71; 0.95] 0.008 *	-0.13 [-0.22; -0.04] 0.007 *
KITE, N''/N'/N	179 / 179 / 179	181 / 181 / 181			
Presence of SRF and/or IRF in the study eye, n (%)	97 (54.2)	132 (72.9)	0.45 [0.29; 0.70] <.001 *	0.74 [0.63; 0.87] <.001 *	-0.19 [-0.28; -0.09] <.001 *
Pooled Analysis, N''/N'/N	368 / 368 / 368	368 / 368 / 368			
Presence of SRF and/or IRF in the study eye, n (%) p_H=0.574	211 (57.3)	269 (73.1)	0.49 [0.36; 0.67] <.001 *	0.78 [0.70; 0.87] <.001 *	-0.16 [-0.23; -0.09] <.001 *
Presence of SRF and/or IRF in the study eye, Week 100					
KESTREL, N''/N'/N	189 / 189 / 189	187 / 187 / 187			
Presence of SRF and/or IRF in the study eye, n (%)	79 (41.8)	101 (54.0)	0.60 [0.40; 0.91] 0.016 *	0.77 [0.62; 0.96] 0.019 *	-0.12 [-0.22; -0.02] 0.017 *
KITE, N''/N'/N	179 / 179 / 179	181 / 181 / 181			
Presence of SRF and/or IRF in the study eye, n (%)	73 (40.8)	103 (56.9)	0.52 [0.34; 0.79] 0.002 *	0.72 [0.58; 0.89] 0.003 *	-0.16 [-0.26; -0.06] 0.002 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N''/N'/N	368 / 368 / 368	368 / 368 / 368			
Presence of SRF and/or IRF in the study eye, n (%) p_H=0.603	152 (41.3)	204 (55.4)	0.57 [0.42; 0.76] <.001 *	0.75 [0.64; 0.87] <.001 *	-0.14 [-0.21; -0.07] <.001 *

N: Number of patients
N': Number of patients in the analysis
N'': Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Presence of SRF in the study eye / KESTREL / Week 100: logit(proportion) = treatment.

Table 11.2 Presence of SRF and/or IRF in the study eye by age (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Presence of SRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.600**					
KESTREL: Presence of SRF in the study eye, Week 52					
Interaction Test:	p = 0.458				
< 65 years					
N"/N'/N	86 / 104 / 104	84 / 93 / 93			
Presence of SRF in the study eye, n (%)	2 (1.9)	3 (3.2)	0.64 [0.10; 4.01] 0.635	0.60 [0.10; 3.49] 0.566	-0.01 [-0.06; 0.03] 0.567
≥ 65 years					
N"/N'/N	68 / 85 / 85	77 / 94 / 94			
Presence of SRF in the study eye, n (%)	2 (2.4)	1 (1.1)	2.04 [0.18; 23.80] 0.568	2.21 [0.20; 23.96] 0.514	0.01 [-0.03; 0.05] 0.510
KITE: Presence of SRF in the study eye, Week 52					
Interaction Test:	N.E.				
< 65 years					
N"/N'/N	79 / 100 / 100	84 / 102 / 102			
Presence of SRF in the study eye, n (%)	3 (3.0)	5 (4.9)	0.60 [0.14; 2.58] 0.493	0.61 [0.15; 2.49] 0.493	-0.02 [-0.07; 0.03] 0.487
≥ 65 years					
N"/N'/N	68 / 79 / 79	68 / 79 / 79			
Presence of SRF in the study eye, n (%)	0 (0.0)	1 (1.3)	N.E.	0.33 [0.01; 8.06] 0.499	-0.01 [-0.04; 0.01] 0.314
Pooled Analysis: Presence of SRF in the study eye, Week 52					
Interaction Test:	p = 0.724				
< 65 years					
N"/N'/N	165 / 204 / 204	168 / 195 / 195			
Presence of SRF in the study eye, n (%)	5 (2.5)	8 (4.1)	0.68 [0.21; 2.19] 0.518	0.61 [0.20; 1.82] 0.367	-0.02 [-0.05; 0.02] 0.368

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N"/N'/N	136 / 164 / 164	145 / 173 / 173			
Presence of SRF in the study eye, n (%)	2 (1.2)	2 (1.2)	1.03 [0.14; 7.60] 0.976	1.06 [0.19; 5.95] 0.946	0.00 [-0.02; 0.02] 0.940
Presence of IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.503**					
KESTREL: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.595				
< 65 years					
N"/N'/N	86 / 104 / 104	84 / 93 / 93			
Presence of IRF in the study eye, n (%)	63 (60.6)	66 (71.0)	0.60 [0.33; 1.10] 0.099	0.85 [0.70; 1.04] 0.125	-0.10 [-0.24; 0.03] 0.122
≥ 65 years					
N"/N'/N	68 / 85 / 85	77 / 94 / 94			
Presence of IRF in the study eye, n (%)	51 (60.0)	71 (75.5)	0.47 [0.25; 0.90] 0.023 *	0.79 [0.65; 0.98] 0.030 *	-0.16 [-0.29; -0.02] 0.025 *
KITE: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.718				
< 65 years					
N"/N'/N	79 / 100 / 100	84 / 102 / 102			
Presence of IRF in the study eye, n (%)	52 (52.0)	74 (72.5)	0.40 [0.22; 0.72] 0.002 *	0.72 [0.57; 0.90] 0.003 *	-0.21 [-0.34; -0.07] 0.002 *
≥ 65 years					
N"/N'/N	68 / 79 / 79	68 / 79 / 79			
Presence of IRF in the study eye, n (%)	44 (55.7)	58 (73.4)	0.47 [0.24; 0.92] 0.027 *	0.76 [0.60; 0.96] 0.022 *	-0.18 [-0.32; -0.03] 0.018 *
Pooled Analysis: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.893				
< 65 years					
N"/N'/N	165 / 204 / 204	168 / 195 / 195			
Presence of IRF in the study eye, n (%)	115 (56.4)	140 (71.8)	0.49 [0.32; 0.74] <.001 *	0.78 [0.67; 0.91] 0.001 *	-0.16 [-0.25; -0.06] 0.001 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N"/N'/N	136 / 164 / 164	145 / 173 / 173			
Presence of IRF in the study eye, n (%)	95 (57.9)	129 (74.6)	0.47 [0.29; 0.74] 0.001 *	0.78 [0.67; 0.91] 0.001 *	-0.17 [-0.27; -0.07] 0.001 *
Presence of IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.733**					
KESTREL: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.885				
< 65 years					
N"/N'/N	81 / 104 / 104	75 / 93 / 93			
Presence of IRF in the study eye, n (%)	43 (41.3)	50 (53.8)	0.60 [0.34; 1.05] 0.073	0.77 [0.57; 1.03] 0.083	-0.12 [-0.26; 0.01] 0.079
≥ 65 years					
N"/N'/N	67 / 85 / 85	70 / 94 / 94			
Presence of IRF in the study eye, n (%)	35 (41.2)	52 (55.3)	0.56 [0.31; 1.01] 0.056	0.74 [0.54; 1.02] 0.064	-0.14 [-0.29; 0.00] 0.056
KITE: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.835				
< 65 years					
N"/N'/N	73 / 100 / 100	86 / 102 / 102			
Presence of IRF in the study eye, n (%)	38 (38.0)	56 (54.9)	0.50 [0.29; 0.88] 0.016 *	0.69 [0.51; 0.94] 0.018 *	-0.17 [-0.30; -0.03] 0.015 *
≥ 65 years					
N"/N'/N	60 / 79 / 79	59 / 79 / 79			
Presence of IRF in the study eye, n (%)	35 (44.3)	47 (59.5)	0.55 [0.29; 1.03] 0.063	0.74 [0.55; 1.01] 0.060	-0.15 [-0.31; 0.00] 0.053
Pooled Analysis: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.967				
< 65 years					
N"/N'/N	154 / 204 / 204	161 / 195 / 195			
Presence of IRF in the study eye, n (%)	81 (39.7)	106 (54.4)	0.55 [0.37; 0.82] 0.003 *	0.73 [0.59; 0.90] 0.003 *	-0.15 [-0.24; -0.05] 0.003 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N"/N'/N	127 / 164 / 164	129 / 173 / 173			
Presence of IRF in the study eye, n (%)	70 (42.7)	99 (57.2)	0.55 [0.36; 0.85] 0.008 *	0.74 [0.60; 0.93] 0.007 *	-0.15 [-0.25; -0.04] 0.007 *
Presence of SRF and/or IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.574**					
KESTREL: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.595				
< 65 years					
N"/N'/N	104 / 104 / 104	93 / 93 / 93			
Presence of SRF and/or IRF in the study eye, n (%)	63 (60.6)	66 (71.0)	0.60 [0.33; 1.10] 0.099	0.85 [0.70; 1.04] 0.125	-0.10 [-0.24; 0.03] 0.122
≥ 65 years					
N"/N'/N	85 / 85 / 85	94 / 94 / 94			
Presence of SRF and/or IRF in the study eye, n (%)	51 (60.0)	71 (75.5)	0.47 [0.25; 0.90] 0.023 *	0.79 [0.65; 0.98] 0.030 *	-0.16 [-0.29; -0.02] 0.025 *
KITE: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.963				
< 65 years					
N"/N'/N	100 / 100 / 100	102 / 102 / 102			
Presence of SRF and/or IRF in the study eye, n (%)	53 (53.0)	74 (72.5)	0.45 [0.25; 0.80] 0.007 *	0.73 [0.59; 0.91] 0.005 *	-0.20 [-0.33; -0.06] 0.003 *
≥ 65 years					
N"/N'/N	79 / 79 / 79	79 / 79 / 79			
Presence of SRF and/or IRF in the study eye, n (%)	44 (55.7)	58 (73.4)	0.46 [0.23; 0.89] 0.021 *	0.76 [0.60; 0.96] 0.022 *	-0.18 [-0.32; -0.03] 0.018 *
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.746				
< 65 years					
N"/N'/N	204 / 204 / 204	195 / 195 / 195			
Presence of SRF and/or IRF in the study eye, n (%)	116 (56.9)	140 (71.8)	0.51 [0.34; 0.78] 0.002 *	0.79 [0.68; 0.92] 0.002 *	-0.15 [-0.24; -0.06] 0.002 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N"/N'/N	164 / 164 / 164	173 / 173 / 173			
Presence of SRF and/or IRF in the study eye, n (%)	95 (57.9)	129 (74.6)	0.46 [0.29; 0.74] 0.001 *	0.78 [0.67; 0.91] 0.001 *	-0.17 [-0.27; -0.07] 0.001 *
Presence of SRF and/or IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.891				
< 65 years					
N"/N'/N	104 / 104 / 104	93 / 93 / 93			
Presence of SRF and/or IRF in the study eye, n (%)	44 (42.3)	50 (53.8)	0.62 [0.35; 1.09] 0.097	0.79 [0.59; 1.05] 0.109	-0.11 [-0.25; 0.02] 0.106
≥ 65 years					
N"/N'/N	85 / 85 / 85	94 / 94 / 94			
Presence of SRF and/or IRF in the study eye, n (%)	35 (41.2)	51 (54.3)	0.58 [0.32; 1.06] 0.076	0.76 [0.55; 1.04] 0.086	-0.13 [-0.28; 0.01] 0.078
KITE: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.847				
< 65 years					
N"/N'/N	100 / 100 / 100	102 / 102 / 102			
Presence of SRF and/or IRF in the study eye, n (%)	38 (38.0)	56 (54.9)	0.50 [0.28; 0.88] 0.016 *	0.69 [0.51; 0.94] 0.018 *	-0.17 [-0.30; -0.03] 0.015 *
≥ 65 years					
N"/N'/N	79 / 79 / 79	79 / 79 / 79			
Presence of SRF and/or IRF in the study eye, n (%)	35 (44.3)	47 (59.5)	0.54 [0.29; 1.02] 0.057	0.74 [0.55; 1.01] 0.060	-0.15 [-0.31; 0.00] 0.053
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 1.000				
< 65 years					
N"/N'/N	204 / 204 / 204	195 / 195 / 195			
Presence of SRF and/or IRF in the study eye, n (%)	82 (40.2)	106 (54.4)	0.57 [0.38; 0.84] 0.005 *	0.74 [0.60; 0.91] 0.005 *	-0.14 [-0.24; -0.05] 0.004 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by age (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N"/N'/N	164 / 164 / 164	173 / 173 / 173			
Presence of SRF and/or IRF in the study eye, n (%)	70 (42.7)	98 (56.6)	0.57 [0.37; 0.87] 0.010 *	0.75 [0.60; 0.94] 0.010 *	-0.14 [-0.25; -0.04] 0.009 *

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + baseline category + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + baseline category + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Presence of SRF in the study eye / KITE / Week 52: logit(proportion) = treatment [by age].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 11.3 Presence of SRF and/or IRF in the study eye by gender (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Presence of SRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.677**					
KESTREL: Presence of SRF in the study eye, Week 100					
Interaction Test:	N.E.				
Male					
N''/N'/N	85 / 110 / 110	95 / 126 / 126			
Presence of SRF in the study eye, n (%)	2 (1.8)	2 (1.6)	1.15 [0.16; 8.29] 0.891	1.15 [0.16; 8.00] 0.891	0.00 [-0.03; 0.04] 0.891
Female					
N''/N'/N	63 / 79 / 79	50 / 61 / 61			
Presence of SRF in the study eye, n (%)	1 (1.3)	0 (0.0)	N.E.	2.33 [0.10; 56.10] 0.603	0.01 [-0.01; 0.04] 0.314
KITE: Presence of SRF in the study eye, Week 100					
Interaction Test:	p = 0.938				
Male					
N''/N'/N	91 / 120 / 120	93 / 115 / 115			
Presence of SRF in the study eye, n (%)	3 (2.5)	3 (2.6)	0.95 [0.18; 4.94] 0.949	0.96 [0.20; 4.65] 0.958	-0.00 [-0.04; 0.04] 0.958
Female					
N''/N'/N	42 / 59 / 59	52 / 66 / 66			
Presence of SRF in the study eye, n (%)	1 (1.7)	2 (3.0)	0.84 [0.07; 10.04] 0.893	0.56 [0.05; 6.01] 0.632	-0.01 [-0.07; 0.04] 0.621
Pooled Analysis: Presence of SRF in the study eye, Week 100					
Interaction Test:	p = 0.913				
Male					
N''/N'/N	176 / 230 / 230	188 / 241 / 241			
Presence of SRF in the study eye, n (%)	5 (2.2)	5 (2.1)	1.14 [0.30; 4.32] 0.847	1.03 [0.30; 3.50] 0.963	0.00 [-0.03; 0.03] 0.963

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N"/N'/N	105 / 138 / 138	102 / 127 / 127			
Presence of SRF in the study eye, n (%)	2 (1.4)	2 (1.6)	1.30 [0.17; 10.26] 0.802	0.97 [0.16; 5.82] 0.969	0.00 [-0.03; 0.03] 0.984
Presence of IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.503**					
KESTREL: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.335				
Male					
N"/N'/N	88 / 110 / 110	104 / 126 / 126			
Presence of IRF in the study eye, n (%)	70 (63.6)	91 (72.2)	0.65 [0.37; 1.13] 0.124	0.88 [0.74; 1.05] 0.163	-0.09 [-0.21; 0.03] 0.158
Female					
N"/N'/N	66 / 79 / 79	57 / 61 / 61			
Presence of IRF in the study eye, n (%)	44 (55.7)	46 (75.4)	0.41 [0.20; 0.85] 0.017 *	0.74 [0.58; 0.94] 0.015 *	-0.20 [-0.35; -0.04] 0.012 *
KITE: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.401				
Male					
N"/N'/N	99 / 120 / 120	96 / 115 / 115			
Presence of IRF in the study eye, n (%)	61 (50.8)	78 (67.8)	0.49 [0.29; 0.84] 0.010 *	0.75 [0.60; 0.93] 0.009 *	-0.17 [-0.29; -0.05] 0.007 *
Female					
N"/N'/N	48 / 59 / 59	56 / 66 / 66			
Presence of IRF in the study eye, n (%)	35 (59.3)	54 (81.8)	0.32 [0.14; 0.73] 0.006 *	0.73 [0.57; 0.92] 0.009 *	-0.22 [-0.38; -0.07] 0.005 *
Pooled Analysis: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.189				
Male					
N"/N'/N	187 / 230 / 230	200 / 241 / 241			
Presence of IRF in the study eye, n (%)	131 (57.0)	169 (70.1)	0.55 [0.38; 0.82] 0.003 *	0.82 [0.71; 0.94] 0.004 *	-0.13 [-0.21; -0.04] 0.004 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N"/N'/N	114 / 138 / 138	113 / 127 / 127			
Presence of IRF in the study eye, n (%)	79 (57.2)	100 (78.7)	0.35 [0.21; 0.61] <.001 *	0.73 [0.62; 0.87] <.001 *	-0.21 [-0.32; -0.10] <.001 *
Presence of IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.733**					
KESTREL: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.362				
Male					
N"/N'/N	85 / 110 / 110	95 / 126 / 126			
Presence of IRF in the study eye, n (%)	47 (42.7)	74 (58.7)	0.51 [0.30; 0.86] 0.012 *	0.73 [0.56; 0.94] 0.017 *	-0.16 [-0.29; -0.03] 0.013 *
Female					
N"/N'/N	63 / 79 / 79	50 / 61 / 61			
Presence of IRF in the study eye, n (%)	31 (39.2)	28 (45.9)	0.76 [0.39; 1.50] 0.430	0.85 [0.58; 1.26] 0.427	-0.07 [-0.23; 0.10] 0.429
KITE: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.548				
Male					
N"/N'/N	91 / 120 / 120	93 / 115 / 115			
Presence of IRF in the study eye, n (%)	45 (37.5)	59 (51.3)	0.58 [0.34; 0.97] 0.040 *	0.73 [0.55; 0.98] 0.035 *	-0.14 [-0.26; -0.01] 0.032 *
Female					
N"/N'/N	42 / 59 / 59	52 / 66 / 66			
Presence of IRF in the study eye, n (%)	28 (47.5)	44 (66.7)	0.44 [0.21; 0.91] 0.027 *	0.71 [0.52; 0.98] 0.036 *	-0.19 [-0.36; -0.02] 0.027 *
Pooled Analysis: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.864				
Male					
N"/N'/N	176 / 230 / 230	188 / 241 / 241			
Presence of IRF in the study eye, n (%)	92 (40.0)	133 (55.2)	0.54 [0.37; 0.78] 0.001 *	0.73 [0.60; 0.89] 0.001 *	-0.15 [-0.24; -0.06] 0.001 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N"/N'/N	105 / 138 / 138	102 / 127 / 127			
Presence of IRF in the study eye, n (%)	59 (42.8)	72 (56.7)	0.57 [0.35; 0.93] 0.023 *	0.77 [0.60; 0.99] 0.039 *	-0.13 [-0.25; -0.01] 0.038 *
Presence of SRF and/or IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.574**					
KESTREL: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.335				
Male					
N"/N'/N	110 / 110 / 110	126 / 126 / 126			
Presence of SRF and/or IRF in the study eye, n (%)	70 (63.6)	91 (72.2)	0.65 [0.37; 1.13] 0.124	0.88 [0.74; 1.05] 0.163	-0.09 [-0.21; 0.03] 0.158
Female					
N"/N'/N	79 / 79 / 79	61 / 61 / 61			
Presence of SRF and/or IRF in the study eye, n (%)	44 (55.7)	46 (75.4)	0.41 [0.20; 0.85] 0.017 *	0.74 [0.58; 0.94] 0.015 *	-0.20 [-0.35; -0.04] 0.012 *
KITE: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.325				
Male					
N"/N'/N	120 / 120 / 120	115 / 115 / 115			
Presence of SRF and/or IRF in the study eye, n (%)	62 (51.7)	78 (67.8)	0.53 [0.31; 0.90] 0.018 *	0.76 [0.62; 0.94] 0.013 *	-0.16 [-0.29; -0.04] 0.010 *
Female					
N"/N'/N	59 / 59 / 59	66 / 66 / 66			
Presence of SRF and/or IRF in the study eye, n (%)	35 (59.3)	54 (81.8)	0.32 [0.14; 0.73] 0.007 *	0.73 [0.57; 0.92] 0.009 *	-0.22 [-0.38; -0.07] 0.005 *
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.155				
Male					
N"/N'/N	230 / 230 / 230	241 / 241 / 241			
Presence of SRF and/or IRF in the study eye, n (%)	132 (57.4)	169 (70.1)	0.57 [0.39; 0.84] 0.005 *	0.82 [0.72; 0.94] 0.005 *	-0.12 [-0.21; -0.04] 0.005 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N"/N'/N	138 / 138 / 138	127 / 127 / 127			
Presence of SRF and/or IRF in the study eye, n (%)	79 (57.2)	100 (78.7)	0.35 [0.21; 0.61] <.001 *	0.73 [0.62; 0.87] <.001 *	-0.21 [-0.32; -0.10] <.001 *
Presence of SRF and/or IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.450				
Male					
N"/N'/N	110 / 110 / 110	126 / 126 / 126			
Presence of SRF and/or IRF in the study eye, n (%)	48 (43.6)	73 (57.9)	0.55 [0.32; 0.92] 0.023 *	0.75 [0.58; 0.98] 0.032 *	-0.14 [-0.27; -0.02] 0.027 *
Female					
N"/N'/N	79 / 79 / 79	61 / 61 / 61			
Presence of SRF and/or IRF in the study eye, n (%)	31 (39.2)	28 (45.9)	0.76 [0.39; 1.50] 0.428	0.85 [0.58; 1.26] 0.427	-0.07 [-0.23; 0.10] 0.429
KITE: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.566				
Male					
N"/N'/N	120 / 120 / 120	115 / 115 / 115			
Presence of SRF and/or IRF in the study eye, n (%)	45 (37.5)	59 (51.3)	0.57 [0.34; 0.96] 0.035 *	0.73 [0.55; 0.98] 0.035 *	-0.14 [-0.26; -0.01] 0.032 *
Female					
N"/N'/N	59 / 59 / 59	66 / 66 / 66			
Presence of SRF and/or IRF in the study eye, n (%)	28 (47.5)	44 (66.7)	0.44 [0.21; 0.91] 0.026 *	0.71 [0.52; 0.98] 0.036 *	-0.19 [-0.36; -0.02] 0.027 *
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.976				
Male					
N"/N'/N	230 / 230 / 230	241 / 241 / 241			
Presence of SRF and/or IRF in the study eye, n (%)	93 (40.4)	132 (54.8)	0.56 [0.39; 0.81] 0.002 *	0.74 [0.61; 0.90] 0.002 *	-0.14 [-0.23; -0.05] 0.002 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by gender (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N"/N'/N	138 / 138 / 138	127 / 127 / 127			
Presence of SRF and/or IRF in the study eye, n (%)	59 (42.8)	72 (56.7)	0.57 [0.35; 0.93] 0.023 *	0.77 [0.60; 0.99] 0.039 *	-0.13 [-0.25; -0.01] 0.038 *

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Presence of SRF in the study eye / KESTREL / Week 100: logit(proportion) = treatment [by gender].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 11.4 Presence of SRF and/or IRF in the study eye by BCVA (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Presence of SRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.600**					
KESTREL: Presence of SRF in the study eye, Week 52					
Interaction Test:	p = 0.208				
≤ 65 letters					
N"/N'/N	56 / 74 / 74	55 / 64 / 64			
Presence of SRF in the study eye, n (%)	3 (4.1)	1 (1.6)	2.88 [0.28; 29.86] 0.376	2.59 [0.28; 24.33] 0.404	0.02 [-0.03; 0.08] 0.368
> 65 letters					
N"/N'/N	98 / 115 / 115	106 / 123 / 123			
Presence of SRF in the study eye, n (%)	1 (0.9)	3 (2.4)	0.34 [0.03; 3.47] 0.361	0.36 [0.04; 3.38] 0.369	-0.02 [-0.05; 0.02] 0.338
KITE: Presence of SRF in the study eye, Week 52					
Interaction Test:	N.E.				
≤ 65 letters					
N"/N'/N	52 / 65 / 65	75 / 91 / 91			
Presence of SRF in the study eye, n (%)	1 (1.5)	6 (6.6)	0.22 [0.03; 1.88] 0.168	0.23 [0.03; 1.89] 0.173	-0.05 [-0.11; 0.01] 0.094
> 65 letters					
N"/N'/N	95 / 114 / 114	77 / 90 / 90			
Presence of SRF in the study eye, n (%)	2 (1.8)	0 (0.0)	N.E.	3.96 [0.19; 81.39] 0.373	0.02 [-0.01; 0.04] 0.154
Pooled Analysis: Presence of SRF in the study eye, Week 52					
Interaction Test:	p = 0.585				
≤ 65 letters					
N"/N'/N	108 / 139 / 139	130 / 155 / 155			
Presence of SRF in the study eye, n (%)	4 (2.9)	7 (4.5)	0.60 [0.16; 2.21] 0.445	0.65 [0.18; 2.39] 0.511	-0.01 [-0.06; 0.03] 0.494

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N"/N'/N	193 / 229 / 229	183 / 213 / 213			
Presence of SRF in the study eye, n (%)	3 (1.3)	3 (1.4)	1.08 [0.21; 5.53] 0.928	0.94 [0.20; 4.35] 0.935	-0.00 [-0.02; 0.02] 0.966
Presence of IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.503**					
KESTREL: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.419				
≤ 65 letters					
N"/N'/N	56 / 74 / 74	55 / 64 / 64			
Presence of IRF in the study eye, n (%)	48 (64.9)	47 (73.4)	0.68 [0.33; 1.43] 0.312	0.88 [0.71; 1.10] 0.276	-0.09 [-0.24; 0.07] 0.273
> 65 letters					
N"/N'/N	98 / 115 / 115	106 / 123 / 123			
Presence of IRF in the study eye, n (%)	66 (57.4)	90 (73.2)	0.47 [0.27; 0.81] 0.007 *	0.78 [0.65; 0.95] 0.012 *	-0.16 [-0.28; -0.04] 0.010 *
KITE: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.757				
≤ 65 letters					
N"/N'/N	52 / 65 / 65	75 / 91 / 91			
Presence of IRF in the study eye, n (%)	38 (58.5)	69 (75.8)	0.41 [0.20; 0.82] 0.012 *	0.77 [0.61; 0.98] 0.030 *	-0.17 [-0.32; -0.02] 0.022 *
> 65 letters					
N"/N'/N	95 / 114 / 114	77 / 90 / 90			
Presence of IRF in the study eye, n (%)	58 (50.9)	63 (70.0)	0.47 [0.26; 0.84] 0.011 *	0.73 [0.58; 0.91] 0.006 *	-0.19 [-0.32; -0.06] 0.004 *
Pooled Analysis: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.699				
≤ 65 letters					
N"/N'/N	108 / 139 / 139	130 / 155 / 155			
Presence of IRF in the study eye, n (%)	86 (61.9)	116 (74.8)	0.52 [0.31; 0.86] 0.011 *	0.82 [0.70; 0.97] 0.016 *	-0.13 [-0.24; -0.03] 0.015 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N"/N'/N	193 / 229 / 229	183 / 213 / 213			
Presence of IRF in the study eye, n (%)	124 (54.1)	153 (71.8)	0.46 [0.31; 0.68] <.001 *	0.76 [0.66; 0.88] <.001 *	-0.17 [-0.26; -0.08] <.001 *
Presence of IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.733**					
KESTREL: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.305				
≤ 65 letters					
N"/N'/N	55 / 74 / 74	50 / 64 / 64			
Presence of IRF in the study eye, n (%)	32 (43.2)	32 (50.0)	0.77 [0.39; 1.52] 0.449	0.86 [0.60; 1.24] 0.427	-0.07 [-0.23; 0.10] 0.427
> 65 letters					
N"/N'/N	93 / 115 / 115	95 / 123 / 123			
Presence of IRF in the study eye, n (%)	46 (40.0)	70 (56.9)	0.49 [0.29; 0.83] 0.007 *	0.70 [0.54; 0.92] 0.011 *	-0.17 [-0.29; -0.04] 0.008 *
KITE: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.249				
≤ 65 letters					
N"/N'/N	49 / 65 / 65	68 / 91 / 91			
Presence of IRF in the study eye, n (%)	28 (43.1)	58 (63.7)	0.41 [0.21; 0.78] 0.007 *	0.68 [0.49; 0.93] 0.016 *	-0.21 [-0.36; -0.05] 0.009 *
> 65 letters					
N"/N'/N	84 / 114 / 114	77 / 90 / 90			
Presence of IRF in the study eye, n (%)	45 (39.5)	45 (50.0)	0.68 [0.39; 1.19] 0.174	0.79 [0.58; 1.07] 0.131	-0.11 [-0.24; 0.03] 0.132
Pooled Analysis: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.949				
≤ 65 letters					
N"/N'/N	104 / 139 / 139	118 / 155 / 155			
Presence of IRF in the study eye, n (%)	60 (43.2)	90 (58.1)	0.55 [0.34; 0.87] 0.011 *	0.75 [0.59; 0.96] 0.017 *	-0.14 [-0.25; -0.03] 0.016 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N"/N'/N	177 / 229 / 229	172 / 213 / 213			
Presence of IRF in the study eye, n (%)	91 (39.7)	115 (54.0)	0.56 [0.38; 0.82] 0.003 *	0.74 [0.60; 0.91] 0.003 *	-0.14 [-0.23; -0.05] 0.003 *
Presence of SRF and/or IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.574**					
KESTREL: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.419				
≤ 65 letters					
N"/N'/N	74 / 74 / 74	64 / 64 / 64			
Presence of SRF and/or IRF in the study eye, n (%)	48 (64.9)	47 (73.4)	0.68 [0.33; 1.43] 0.312	0.88 [0.71; 1.10] 0.276	-0.09 [-0.24; 0.07] 0.273
> 65 letters					
N"/N'/N	115 / 115 / 115	123 / 123 / 123			
Presence of SRF and/or IRF in the study eye, n (%)	66 (57.4)	90 (73.2)	0.47 [0.27; 0.81] 0.007 *	0.78 [0.65; 0.95] 0.012 *	-0.16 [-0.28; -0.04] 0.010 *
KITE: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.886				
≤ 65 letters					
N"/N'/N	65 / 65 / 65	91 / 91 / 91			
Presence of SRF and/or IRF in the study eye, n (%)	38 (58.5)	69 (75.8)	0.45 [0.22; 0.89] 0.022 *	0.77 [0.61; 0.98] 0.030 *	-0.17 [-0.32; -0.02] 0.022 *
> 65 letters					
N"/N'/N	114 / 114 / 114	90 / 90 / 90			
Presence of SRF and/or IRF in the study eye, n (%)	59 (51.8)	63 (70.0)	0.48 [0.27; 0.86] 0.013 *	0.74 [0.59; 0.92] 0.008 *	-0.18 [-0.31; -0.05] 0.007 *
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.649				
≤ 65 letters					
N"/N'/N	139 / 139 / 139	155 / 155 / 155			
Presence of SRF and/or IRF in the study eye, n (%)	86 (61.9)	116 (74.8)	0.54 [0.33; 0.89] 0.016 *	0.82 [0.70; 0.97] 0.016 *	-0.13 [-0.24; -0.03] 0.015 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N"/N'/N	229 / 229 / 229	213 / 213 / 213			
Presence of SRF and/or IRF in the study eye, n (%)	125 (54.6)	153 (71.8)	0.47 [0.31; 0.69] <.001 *	0.76 [0.66; 0.88] <.001 *	-0.17 [-0.26; -0.08] <.001 *
Presence of SRF and/or IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.401				
≤ 65 letters					
N"/N'/N	74 / 74 / 74	64 / 64 / 64			
Presence of SRF and/or IRF in the study eye, n (%)	32 (43.2)	32 (50.0)	0.76 [0.39; 1.50] 0.432	0.86 [0.60; 1.24] 0.427	-0.07 [-0.23; 0.10] 0.427
> 65 letters					
N"/N'/N	115 / 115 / 115	123 / 123 / 123			
Presence of SRF and/or IRF in the study eye, n (%)	47 (40.9)	69 (56.1)	0.53 [0.31; 0.89] 0.016 *	0.73 [0.56; 0.95] 0.021 *	-0.15 [-0.28; -0.03] 0.017 *
KITE: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.314				
≤ 65 letters					
N"/N'/N	65 / 65 / 65	91 / 91 / 91			
Presence of SRF and/or IRF in the study eye, n (%)	28 (43.1)	58 (63.7)	0.42 [0.22; 0.81] 0.009 *	0.68 [0.49; 0.93] 0.016 *	-0.21 [-0.36; -0.05] 0.009 *
> 65 letters					
N"/N'/N	114 / 114 / 114	90 / 90 / 90			
Presence of SRF and/or IRF in the study eye, n (%)	45 (39.5)	45 (50.0)	0.65 [0.37; 1.14] 0.137	0.79 [0.58; 1.07] 0.131	-0.11 [-0.24; 0.03] 0.132
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.891				
≤ 65 letters					
N"/N'/N	139 / 139 / 139	155 / 155 / 155			
Presence of SRF and/or IRF in the study eye, n (%)	60 (43.2)	90 (58.1)	0.56 [0.35; 0.88] 0.013 *	0.75 [0.59; 0.96] 0.017 *	-0.14 [-0.25; -0.03] 0.016 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N"/N'/N	229 / 229 / 229	213 / 213 / 213			
Presence of SRF and/or IRF in the study eye, n (%)	92 (40.2)	114 (53.5)	0.58 [0.40; 0.85] 0.005 *	0.75 [0.62; 0.92] 0.006 *	-0.13 [-0.22; -0.04] 0.006 *

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Presence of SRF in the study eye / KITE / Week 52: logit(proportion) = treatment [by BCVA].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 11.5 Presence of SRF and/or IRF in the study eye by region (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Presence of IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.503**					
KESTREL: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.122				
Region of the Americas					
N''/N'/N	72 / 90 / 90	73 / 83 / 83			
Presence of IRF in the study eye, n (%)	56 (62.2)	67 (80.7)	0.37 [0.19; 0.75] 0.006 *	0.77 [0.64; 0.93] 0.008 *	-0.19 [-0.32; -0.05] 0.006 *
European Region					
N''/N'/N	56 / 69 / 69	61 / 75 / 75			
Presence of IRF in the study eye, n (%)	42 (60.9)	47 (62.7)	0.91 [0.46; 1.80] 0.792	0.97 [0.75; 1.26] 0.825	-0.02 [-0.18; 0.14] 0.825
Western Pacific Region					
N''/N'/N	26 / 30 / 30	27 / 29 / 29			
Presence of IRF in the study eye, n (%)	16 (53.3)	23 (79.3)	0.31 [0.10; 1.00] 0.049 *	0.67 [0.46; 0.99] 0.042 *	-0.26 [-0.49; -0.03] 0.028 *
KITE: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.643				
South-East Asia Region and Eastern Mediterranean Region					
N''/N'/N	17 / 26 / 26	14 / 21 / 21			
Presence of IRF in the study eye, n (%)	11 (42.3)	11 (52.4)	0.60 [0.19; 1.94] 0.395	0.81 [0.44; 1.48] 0.490	-0.10 [-0.39; 0.19] 0.490
European Region					
N''/N'/N	114 / 135 / 135	114 / 132 / 132			
Presence of IRF in the study eye, n (%)	76 (56.3)	99 (75.0)	0.44 [0.26; 0.75] 0.002 *	0.75 [0.63; 0.90] 0.002 *	-0.19 [-0.30; -0.08] 0.001 *
Western Pacific Region					
N''/N'/N	16 / 18 / 18	24 / 28 / 28			
Presence of IRF in the study eye, n (%)	9 (50.0)	22 (78.6)	0.26 [0.07; 1.00] 0.049 *	0.64 [0.39; 1.05] 0.077	-0.29 [-0.56; -0.01] 0.043 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.205				
Region of the Americas					
N"/N'/N	72 / 90 / 90	73 / 83 / 83			
Presence of IRF in the study eye, n (%)	56 (62.2)	67 (80.7)	0.28 [0.13; 0.62] 0.002 *	0.77 [0.64; 0.93] 0.007 *	-0.19 [-0.32; -0.05] 0.006 *
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	17 / 26 / 26	14 / 21 / 21			
Presence of IRF in the study eye, n (%)	11 (42.3)	11 (52.4)	0.83 [0.24; 2.84] 0.761	0.81 [0.44; 1.48] 0.496	-0.10 [-0.39; 0.19] 0.490
European Region					
N"/N'/N	170 / 204 / 204	175 / 207 / 207			
Presence of IRF in the study eye, n (%)	118 (57.8)	146 (70.5)	0.62 [0.41; 0.95] 0.030 *	0.82 [0.71; 0.95] 0.007 *	-0.13 [-0.22; -0.04] 0.007 *
Western Pacific Region					
N"/N'/N	42 / 48 / 48	51 / 57 / 57			
Presence of IRF in the study eye, n (%)	25 (52.1)	45 (78.9)	0.28 [0.12; 0.66] 0.004 *	0.66 [0.48; 0.89] 0.004 *	-0.27 [-0.45; -0.09] 0.003 *
Presence of IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.733**					
KESTREL: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.773				
Region of the Americas					
N"/N'/N	66 / 90 / 90	65 / 83 / 83			
Presence of IRF in the study eye, n (%)	41 (45.6)	51 (61.4)	0.51 [0.28; 0.94] 0.032 *	0.74 [0.56; 0.98] 0.038 *	-0.16 [-0.31; -0.01] 0.034 *
European Region					
N"/N'/N	56 / 69 / 69	56 / 75 / 75			
Presence of IRF in the study eye, n (%)	26 (37.7)	35 (46.7)	0.69 [0.35; 1.35] 0.277	0.81 [0.55; 1.19] 0.280	-0.09 [-0.25; 0.07] 0.273
Western Pacific Region					
N"/N'/N	26 / 30 / 30	24 / 29 / 29			
Presence of IRF in the study eye, n (%)	11 (36.7)	16 (55.2)	0.49 [0.17; 1.39] 0.177	0.66 [0.37; 1.18] 0.163	-0.19 [-0.44; 0.06] 0.147

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.948				
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	13 / 26 / 26	15 / 21 / 21			
Presence of IRF in the study eye, n (%)	7 (26.9)	8 (38.1)	0.57 [0.17; 1.98] 0.378	0.71 [0.31; 1.63] 0.416	-0.11 [-0.38; 0.16] 0.415
European Region					
N"/N'/N	108 / 135 / 135	108 / 132 / 132			
Presence of IRF in the study eye, n (%)	58 (43.0)	77 (58.3)	0.55 [0.34; 0.89] 0.015 *	0.74 [0.58; 0.94] 0.013 *	-0.15 [-0.27; -0.04] 0.011 *
Western Pacific Region					
N"/N'/N	12 / 18 / 18	22 / 28 / 28			
Presence of IRF in the study eye, n (%)	8 (44.4)	18 (64.3)	0.45 [0.13; 1.51] 0.193	0.69 [0.38; 1.24] 0.217	-0.20 [-0.49; 0.09] 0.180
Pooled Analysis: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.892				
Region of the Americas					
N"/N'/N	66 / 90 / 90	65 / 83 / 83			
Presence of IRF in the study eye, n (%)	41 (45.6)	51 (61.4)	0.46 [0.23; 0.94] 0.032 *	0.74 [0.56; 0.98] 0.037 *	-0.16 [-0.31; -0.01] 0.034 *
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	13 / 26 / 26	15 / 21 / 21			
Presence of IRF in the study eye, n (%)	7 (26.9)	8 (38.1)	0.64 [0.17; 2.34] 0.499	0.71 [0.31; 1.63] 0.419	-0.11 [-0.38; 0.16] 0.415
European Region					
N"/N'/N	164 / 204 / 204	164 / 207 / 207			
Presence of IRF in the study eye, n (%)	84 (41.2)	112 (54.1)	0.61 [0.40; 0.92] 0.019 *	0.76 [0.62; 0.93] 0.008 *	-0.13 [-0.23; -0.04] 0.007 *
Western Pacific Region					
N"/N'/N	38 / 48 / 48	46 / 57 / 57			
Presence of IRF in the study eye, n (%)	19 (39.6)	34 (59.6)	0.46 [0.21; 1.02] 0.055	0.68 [0.45; 1.02] 0.054	-0.19 [-0.38; -0.00] 0.048 *
Presence of SRF and/or IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.574**					

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.122				
Region of the Americas					
N"/N'/N	90 / 90 / 90	83 / 83 / 83			
Presence of SRF and/or IRF in the study eye, n (%)	56 (62.2)	67 (80.7)	0.37 [0.19; 0.75] 0.006 *	0.77 [0.64; 0.93] 0.008 *	-0.19 [-0.32; -0.05] 0.006 *
European Region					
N"/N'/N	69 / 69 / 69	75 / 75 / 75			
Presence of SRF and/or IRF in the study eye, n (%)	42 (60.9)	47 (62.7)	0.91 [0.46; 1.80] 0.792	0.97 [0.75; 1.26] 0.825	-0.02 [-0.18; 0.14] 0.825
Western Pacific Region					
N"/N'/N	30 / 30 / 30	29 / 29 / 29			
Presence of SRF and/or IRF in the study eye, n (%)	16 (53.3)	23 (79.3)	0.31 [0.10; 1.00] 0.049 *	0.67 [0.46; 0.99] 0.042 *	-0.26 [-0.49; -0.03] 0.028 *
KITE: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.682				
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	26 / 26 / 26	21 / 21 / 21			
Presence of SRF and/or IRF in the study eye, n (%)	11 (42.3)	11 (52.4)	0.67 [0.21; 2.12] 0.492	0.81 [0.44; 1.48] 0.490	-0.10 [-0.39; 0.19] 0.490
European Region					
N"/N'/N	135 / 135 / 135	132 / 132 / 132			
Presence of SRF and/or IRF in the study eye, n (%)	77 (57.0)	99 (75.0)	0.45 [0.27; 0.76] 0.003 *	0.76 [0.64; 0.91] 0.002 *	-0.18 [-0.29; -0.07] 0.002 *
Western Pacific Region					
N"/N'/N	18 / 18 / 18	28 / 28 / 28			
Presence of SRF and/or IRF in the study eye, n (%)	9 (50.0)	22 (78.6)	0.31 [0.08; 1.14] 0.078	0.64 [0.39; 1.05] 0.077	-0.29 [-0.56; -0.01] 0.043 *
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.220				
Region of the Americas					
N"/N'/N	90 / 90 / 90	83 / 83 / 83			
Presence of SRF and/or IRF in the study eye, n (%)	56 (62.2)	67 (80.7)	0.28 [0.13; 0.63] 0.002 *	0.77 [0.64; 0.93] 0.007 *	-0.19 [-0.32; -0.05] 0.006 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	26 / 26 / 26	21 / 21 / 21			
Presence of SRF and/or IRF in the study eye, n (%)	11 (42.3)	11 (52.4)	0.89 [0.26; 3.02] 0.851	0.81 [0.44; 1.48] 0.496	-0.10 [-0.39; 0.19] 0.490
European Region					
N"/N'/N	204 / 204 / 204	207 / 207 / 207			
Presence of SRF and/or IRF in the study eye, n (%)	119 (58.3)	146 (70.5)	0.63 [0.41; 0.96] 0.033 *	0.83 [0.71; 0.96] 0.009 *	-0.12 [-0.22; -0.03] 0.009 *
Western Pacific Region					
N"/N'/N	48 / 48 / 48	57 / 57 / 57			
Presence of SRF and/or IRF in the study eye, n (%)	25 (52.1)	45 (78.9)	0.29 [0.12; 0.70] 0.005 *	0.66 [0.48; 0.89] 0.004 *	-0.27 [-0.45; -0.09] 0.003 *
Presence of SRF and/or IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.744				
Region of the Americas					
N"/N'/N	90 / 90 / 90	83 / 83 / 83			
Presence of SRF and/or IRF in the study eye, n (%)	42 (46.7)	51 (61.4)	0.54 [0.29; 0.99] 0.047 *	0.76 [0.57; 1.00] 0.053	-0.15 [-0.29; -0.00] 0.049 *
European Region					
N"/N'/N	69 / 69 / 69	75 / 75 / 75			
Presence of SRF and/or IRF in the study eye, n (%)	26 (37.7)	34 (45.3)	0.72 [0.37; 1.42] 0.345	0.83 [0.56; 1.23] 0.356	-0.08 [-0.24; 0.08] 0.350
Western Pacific Region					
N"/N'/N	30 / 30 / 30	29 / 29 / 29			
Presence of SRF and/or IRF in the study eye, n (%)	11 (36.7)	16 (55.2)	0.48 [0.17; 1.37] 0.171	0.66 [0.37; 1.18] 0.163	-0.19 [-0.44; 0.06] 0.147
KITE: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.928				
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	26 / 26 / 26	21 / 21 / 21			
Presence of SRF and/or IRF in the study eye, n (%)	7 (26.9)	8 (38.1)	0.60 [0.17; 2.07] 0.418	0.71 [0.31; 1.63] 0.416	-0.11 [-0.38; 0.16] 0.415

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
European Region					
N"/N'/N	135 / 135 / 135	132 / 132 / 132			
Presence of SRF and/or IRF in the study eye, n (%)	58 (43.0)	77 (58.3)	0.54 [0.33; 0.87] 0.012 *	0.74 [0.58; 0.94] 0.013 *	-0.15 [-0.27; -0.04] 0.011 *
Western Pacific Region					
N"/N'/N	18 / 18 / 18	28 / 28 / 28			
Presence of SRF and/or IRF in the study eye, n (%)	8 (44.4)	18 (64.3)	0.43 [0.13; 1.46] 0.178	0.69 [0.38; 1.24] 0.217	-0.20 [-0.49; 0.09] 0.180
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.874				
Region of the Americas					
N"/N'/N	90 / 90 / 90	83 / 83 / 83			
Presence of SRF and/or IRF in the study eye, n (%)	42 (46.7)	51 (61.4)	0.47 [0.23; 0.96] 0.038 *	0.76 [0.57; 1.00] 0.052	-0.15 [-0.29; -0.00] 0.049 *
South-East Asia Region and Eastern Mediterranean Region					
N"/N'/N	26 / 26 / 26	21 / 21 / 21			
Presence of SRF and/or IRF in the study eye, n (%)	7 (26.9)	8 (38.1)	0.69 [0.19; 2.50] 0.569	0.71 [0.31; 1.63] 0.419	-0.11 [-0.38; 0.16] 0.415
European Region					
N"/N'/N	204 / 204 / 204	207 / 207 / 207			
Presence of SRF and/or IRF in the study eye, n (%)	84 (41.2)	111 (53.6)	0.63 [0.42; 0.95] 0.027 *	0.76 [0.62; 0.94] 0.010 *	-0.13 [-0.22; -0.03] 0.009 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by region (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Western Pacific Region					
N''/N'/N	48 / 48 / 48	57 / 57 / 57			
Presence of SRF and/or IRF in the study eye, n (%)	19 (39.6)	34 (59.6)	0.46 [0.21; 1.02] 0.055	0.68 [0.45; 1.02] 0.054	-0.19 [-0.38; -0.00] 0.048 *

N: Number of patients
N': Number of patients in the analysis
N'': Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 11.6 Presence of SRF and/or IRF in the study eye by diabetes type (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Presence of SRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.600**					
KESTREL: Presence of SRF in the study eye, Week 52					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	9 / 12 / 12	6 / 6 / 6			
Presence of SRF in the study eye, n (%)	0 (0.0)	1 (16.7)	N.E.	0.18 [0.01; 3.85] 0.272	-0.17 [-0.46; 0.13] 0.273
Type 2					
N"/N'/N	145 / 177 / 177	155 / 181 / 181			
Presence of SRF in the study eye, n (%)	4 (2.3)	3 (1.7)	1.37 [0.30; 6.22] 0.682	1.36 [0.31; 6.00] 0.682	0.01 [-0.02; 0.03] 0.681
KITE: Presence of SRF in the study eye, Week 52					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	18 / 19 / 19	7 / 7 / 7			
Presence of SRF in the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N"/N'/N	129 / 160 / 160	145 / 174 / 174			
Presence of SRF in the study eye, n (%)	3 (1.9)	6 (3.4)	0.54 [0.13; 2.18] 0.382	0.54 [0.14; 2.14] 0.383	-0.02 [-0.05; 0.02] 0.369
Pooled Analysis: Presence of SRF in the study eye, Week 52					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	27 / 31 / 31	13 / 13 / 13			
Presence of SRF in the study eye, n (%)	0 (0.0)	1 (7.7)	N.E.	0.18 [0.01; 3.85] 0.223	-0.07 [-0.22; 0.07] 0.313
Type 2					
N"/N'/N	274 / 337 / 337	300 / 355 / 355			
Presence of SRF in the study eye, n (%)	7 (2.1)	9 (2.5)	0.86 [0.31; 2.43] 0.783	0.82 [0.31; 2.19] 0.696	-0.00 [-0.03; 0.02] 0.695

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Presence of SRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.677**					
KESTREL: Presence of SRF in the study eye, Week 100					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	10 / 12 / 12	4 / 6 / 6			
Presence of SRF in the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N"/N'/N	138 / 177 / 177	141 / 181 / 181			
Presence of SRF in the study eye, n (%)	3 (1.7)	2 (1.1)	1.54 [0.25; 9.35] 0.637	1.53 [0.26; 9.07] 0.637	0.01 [-0.02; 0.03] 0.635
KITE: Presence of SRF in the study eye, Week 100					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	17 / 19 / 19	5 / 7 / 7			
Presence of SRF in the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N"/N'/N	116 / 160 / 160	140 / 174 / 174			
Presence of SRF in the study eye, n (%)	4 (2.5)	5 (2.9)	0.87 [0.23; 3.29] 0.833	0.87 [0.24; 3.18] 0.833	-0.00 [-0.04; 0.03] 0.833
Pooled Analysis: Presence of SRF in the study eye, Week 100					
Interaction Test:	N.E.				
Type 1					
N"/N'/N	27 / 31 / 31	9 / 13 / 13			
Presence of SRF in the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N"/N'/N	254 / 337 / 337	281 / 355 / 355			
Presence of SRF in the study eye, n (%)	7 (2.1)	7 (2.0)	1.16 [0.38; 3.59] 0.793	1.06 [0.38; 3.01] 0.907	0.00 [-0.02; 0.02] 0.907
Presence of IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.503**					

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.600				
Type 1					
N"/N'/N	9 / 12 / 12	6 / 6 / 6			
Presence of IRF in the study eye, n (%)	7 (58.3)	5 (83.3)	0.28 [0.02; 3.24] 0.311	0.70 [0.39; 1.27] 0.242	-0.25 [-0.66; 0.16] 0.230
Type 2					
N"/N'/N	145 / 177 / 177	155 / 181 / 181			
Presence of IRF in the study eye, n (%)	107 (60.5)	132 (72.9)	0.55 [0.35; 0.86] 0.009 *	0.83 [0.71; 0.96] 0.013 *	-0.12 [-0.22; -0.03] 0.012 *
KITE: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.946				
Type 1					
N"/N'/N	18 / 19 / 19	7 / 7 / 7			
Presence of IRF in the study eye, n (%)	9 (47.4)	5 (71.4)	0.41 [0.06; 2.67] 0.348	0.66 [0.34; 1.29] 0.227	-0.24 [-0.64; 0.16] 0.242
Type 2					
N"/N'/N	129 / 160 / 160	145 / 174 / 174			
Presence of IRF in the study eye, n (%)	87 (54.4)	127 (73.0)	0.43 [0.27; 0.69] <.001 *	0.74 [0.63; 0.88] <.001 *	-0.19 [-0.29; -0.08] <.001 *
Pooled Analysis: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.680				
Type 1					
N"/N'/N	27 / 31 / 31	13 / 13 / 13			
Presence of IRF in the study eye, n (%)	16 (51.6)	10 (76.9)	0.35 [0.08; 1.55] 0.168	0.68 [0.43; 1.07] 0.138	-0.24 [-0.53; 0.04] 0.096
Type 2					
N"/N'/N	274 / 337 / 337	300 / 355 / 355			
Presence of IRF in the study eye, n (%)	194 (57.6)	259 (73.0)	0.49 [0.35; 0.67] <.001 *	0.79 [0.71; 0.88] <.001 *	-0.15 [-0.22; -0.08] <.001 *
Presence of IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.733**					

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.120				
Type 1					
N"/N'/N	10 / 12 / 12	4 / 6 / 6			
Presence of IRF in the study eye, n (%)	2 (16.7)	4 (66.7)	0.10 [0.01; 0.98] 0.048 *	0.25 [0.06; 1.00] 0.050 *	-0.50 [-0.93; -0.07] 0.023 *
Type 2					
N"/N'/N	138 / 177 / 177	141 / 181 / 181			
Presence of IRF in the study eye, n (%)	76 (42.9)	98 (54.1)	0.63 [0.41; 0.96] 0.030 *	0.79 [0.64; 0.98] 0.036 *	-0.11 [-0.21; -0.01] 0.033 *
KITE: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.317				
Type 1					
N"/N'/N	17 / 19 / 19	5 / 7 / 7			
Presence of IRF in the study eye, n (%)	6 (31.6)	5 (71.4)	0.20 [0.03; 1.38] 0.102	0.44 [0.20; 0.99] 0.049 *	-0.40 [-0.79; -0.00] 0.048 *
Type 2					
N"/N'/N	116 / 160 / 160	140 / 174 / 174			
Presence of IRF in the study eye, n (%)	67 (41.9)	98 (56.3)	0.55 [0.36; 0.86] 0.008 *	0.74 [0.59; 0.93] 0.010 *	-0.14 [-0.25; -0.04] 0.008 *
Pooled Analysis: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.082				
Type 1					
N"/N'/N	27 / 31 / 31	9 / 13 / 13			
Presence of IRF in the study eye, n (%)	8 (25.8)	9 (69.2)	0.16 [0.04; 0.68] 0.013 *	0.36 [0.18; 0.74] 0.007 *	-0.44 [-0.73; -0.15] 0.003 *
Type 2					
N"/N'/N	254 / 337 / 337	281 / 355 / 355			
Presence of IRF in the study eye, n (%)	143 (42.4)	196 (55.2)	0.59 [0.44; 0.80] <.001 *	0.77 [0.66; 0.90] <.001 *	-0.13 [-0.20; -0.05] <.001 *
Presence of SRF and/or IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.574**					

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.600				
Type 1					
N"/N'/N	12 / 12 / 12	6 / 6 / 6			
Presence of SRF and/or IRF in the study eye, n (%)	7 (58.3)	5 (83.3)	0.28 [0.02; 3.24] 0.311	0.70 [0.39; 1.27] 0.242	-0.25 [-0.66; 0.16] 0.230
Type 2					
N"/N'/N	177 / 177 / 177	181 / 181 / 181			
Presence of SRF and/or IRF in the study eye, n (%)	107 (60.5)	132 (72.9)	0.55 [0.35; 0.86] 0.009 *	0.83 [0.71; 0.96] 0.013 *	-0.12 [-0.22; -0.03] 0.012 *
KITE: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.900				
Type 1					
N"/N'/N	19 / 19 / 19	7 / 7 / 7			
Presence of SRF and/or IRF in the study eye, n (%)	9 (47.4)	5 (71.4)	0.40 [0.06; 2.67] 0.347	0.66 [0.34; 1.29] 0.227	-0.24 [-0.64; 0.16] 0.242
Type 2					
N"/N'/N	160 / 160 / 160	174 / 174 / 174			
Presence of SRF and/or IRF in the study eye, n (%)	88 (55.0)	127 (73.0)	0.46 [0.29; 0.72] <.001 *	0.75 [0.64; 0.89] <.001 *	-0.18 [-0.28; -0.08] <.001 *
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.646				
Type 1					
N"/N'/N	31 / 31 / 31	13 / 13 / 13			
Presence of SRF and/or IRF in the study eye, n (%)	16 (51.6)	10 (76.9)	0.35 [0.08; 1.54] 0.164	0.68 [0.43; 1.07] 0.138	-0.24 [-0.53; 0.04] 0.096
Type 2					
N"/N'/N	337 / 337 / 337	355 / 355 / 355			
Presence of SRF and/or IRF in the study eye, n (%)	195 (57.9)	259 (73.0)	0.50 [0.36; 0.69] <.001 *	0.79 [0.71; 0.89] <.001 *	-0.15 [-0.22; -0.08] <.001 *
Presence of SRF and/or IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.110				
Type 1					
N"/N'/N	12 / 12 / 12	6 / 6 / 6			
Presence of SRF and/or IRF in the study eye, n (%)	2 (16.7)	4 (66.7)	0.10 [0.01; 0.97] 0.047 *	0.25 [0.06; 1.00] 0.050 *	-0.50 [-0.93; -0.07] 0.023 *
Type 2					
N"/N'/N	177 / 177 / 177	181 / 181 / 181			
Presence of SRF and/or IRF in the study eye, n (%)	77 (43.5)	97 (53.6)	0.66 [0.43; 1.00] 0.049 *	0.81 [0.65; 1.01] 0.058	-0.10 [-0.20; 0.00] 0.055
KITE: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.283				
Type 1					
N"/N'/N	19 / 19 / 19	7 / 7 / 7			
Presence of SRF and/or IRF in the study eye, n (%)	6 (31.6)	5 (71.4)	0.19 [0.03; 1.28] 0.087	0.44 [0.20; 0.99] 0.049 *	-0.40 [-0.79; -0.00] 0.048 *
Type 2					
N"/N'/N	160 / 160 / 160	174 / 174 / 174			
Presence of SRF and/or IRF in the study eye, n (%)	67 (41.9)	98 (56.3)	0.55 [0.36; 0.85] 0.007 *	0.74 [0.59; 0.93] 0.010 *	-0.14 [-0.25; -0.04] 0.008 *
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.072				
Type 1					
N"/N'/N	31 / 31 / 31	13 / 13 / 13			
Presence of SRF and/or IRF in the study eye, n (%)	8 (25.8)	9 (69.2)	0.16 [0.04; 0.67] 0.012 *	0.36 [0.18; 0.74] 0.007 *	-0.44 [-0.73; -0.15] 0.003 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N"/N'/N	337 / 337 / 337	355 / 355 / 355			
Presence of SRF and/or IRF in the study eye, n (%)	144 (42.7)	195 (54.9)	0.61 [0.45; 0.83] 0.001 *	0.78 [0.67; 0.91] 0.001 *	-0.12 [-0.20; -0.05] 0.001 *

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Presence of SRF in the study eye / KESTREL / Week 52, Presence of SRF in the study eye / KITE / Week 52, Presence of SRF in the study eye / KESTREL / Week 100, Presence of SRF in the study eye / KITE / Week 100: logit(proportion) = treatment [by diabetes type].
Presence of SRF in the study eye / Pooled Analysis / Week 52, Presence of SRF in the study eye / Pooled Analysis / Week 100: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 11.7 Presence of SRF and/or IRF in the study eye by HbA1c (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Presence of SRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.600**					
KESTREL: Presence of SRF in the study eye, Week 52					
Interaction Test:	N.E.				
< 7.5 %					
N"/N'/N	63 / 76 / 76	95 / 107 / 107			
Presence of SRF in the study eye, n (%)	0 (0.0)	2 (1.9)	N.E.	0.28 [0.01; 5.76] 0.410	-0.02 [-0.04; 0.01] 0.153
≥ 7.5 %					
N"/N'/N	91 / 112 / 112	66 / 80 / 80			
Presence of SRF in the study eye, n (%)	4 (3.6)	2 (2.5)	1.44 [0.26; 8.08] 0.676	1.43 [0.27; 7.61] 0.676	0.01 [-0.04; 0.06] 0.665
KITE: Presence of SRF in the study eye, Week 52					
Interaction Test:	p = 0.390				
< 7.5 %					
N"/N'/N	66 / 82 / 82	80 / 96 / 96			
Presence of SRF in the study eye, n (%)	1 (1.2)	4 (4.2)	0.30 [0.03; 2.87] 0.295	0.29 [0.03; 2.57] 0.267	-0.03 [-0.08; 0.02] 0.214
≥ 7.5 %					
N"/N'/N	81 / 97 / 97	72 / 85 / 85			
Presence of SRF in the study eye, n (%)	2 (2.1)	2 (2.4)	1.14 [0.15; 8.67] 0.901	0.88 [0.13; 6.09] 0.894	-0.00 [-0.05; 0.04] 0.894
Pooled Analysis: Presence of SRF in the study eye, Week 52					
Interaction Test:	p = 0.176				
< 7.5 %					
N"/N'/N	129 / 158 / 158	175 / 203 / 203			
Presence of SRF in the study eye, n (%)	1 (0.6)	6 (3.0)	0.23 [0.03; 1.99] 0.183	0.29 [0.05; 1.68] 0.140	-0.02 [-0.05; 0.00] 0.074

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N"/N'/N	172 / 209 / 209	138 / 165 / 165			
Presence of SRF in the study eye, n (%)	6 (2.9)	4 (2.4)	1.32 [0.35; 4.95] 0.682	1.16 [0.33; 4.10] 0.812	0.00 [-0.03; 0.04] 0.810
Presence of IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.503**					
KESTREL: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.466				
< 7.5 %					
N"/N'/N	63 / 76 / 76	95 / 107 / 107			
Presence of IRF in the study eye, n (%)	47 (61.8)	76 (71.0)	0.64 [0.34; 1.19] 0.159	0.87 [0.70; 1.08] 0.205	-0.09 [-0.23; 0.05] 0.195
≥ 7.5 %					
N"/N'/N	91 / 112 / 112	66 / 80 / 80			
Presence of IRF in the study eye, n (%)	67 (59.8)	61 (76.3)	0.46 [0.24; 0.87] 0.017 *	0.78 [0.65; 0.95] 0.015 *	-0.16 [-0.29; -0.03] 0.013 *
KITE: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.715				
< 7.5 %					
N"/N'/N	66 / 82 / 82	80 / 96 / 96			
Presence of IRF in the study eye, n (%)	43 (52.4)	68 (70.8)	0.45 [0.24; 0.84] 0.012 *	0.74 [0.58; 0.94] 0.015 *	-0.18 [-0.33; -0.04] 0.011 *
≥ 7.5 %					
N"/N'/N	81 / 97 / 97	72 / 85 / 85			
Presence of IRF in the study eye, n (%)	53 (54.6)	64 (75.3)	0.38 [0.20; 0.74] 0.004 *	0.73 [0.58; 0.90] 0.004 *	-0.21 [-0.34; -0.07] 0.003 *
Pooled Analysis: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.453				
< 7.5 %					
N"/N'/N	129 / 158 / 158	175 / 203 / 203			
Presence of IRF in the study eye, n (%)	90 (57.0)	144 (70.9)	0.53 [0.34; 0.83] 0.005 *	0.81 [0.69; 0.95] 0.007 *	-0.14 [-0.24; -0.04] 0.007 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N"/N'/N	172 / 209 / 209	138 / 165 / 165			
Presence of IRF in the study eye, n (%)	120 (57.4)	125 (75.8)	0.42 [0.26; 0.66] <.001 *	0.76 [0.65; 0.87] <.001 *	-0.19 [-0.28; -0.09] <.001 *
Presence of IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.733**					
KESTREL: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = <.001 *				
< 7.5 %					
N"/N'/N	59 / 76 / 76	90 / 107 / 107			
Presence of IRF in the study eye, n (%)	37 (48.7)	48 (44.9)	1.15 [0.64; 2.08] 0.644	1.09 [0.79; 1.48] 0.607	0.04 [-0.11; 0.18] 0.609
≥ 7.5 %					
N"/N'/N	88 / 112 / 112	55 / 80 / 80			
Presence of IRF in the study eye, n (%)	41 (36.6)	54 (67.5)	0.27 [0.15; 0.50] <.001 *	0.54 [0.41; 0.72] <.001 *	-0.31 [-0.44; -0.17] <.001 *
KITE: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.496				
< 7.5 %					
N"/N'/N	61 / 82 / 82	74 / 96 / 96			
Presence of IRF in the study eye, n (%)	35 (42.7)	53 (55.2)	0.60 [0.33; 1.09] 0.095	0.77 [0.57; 1.05] 0.102	-0.13 [-0.27; 0.02] 0.093
≥ 7.5 %					
N"/N'/N	72 / 97 / 97	71 / 85 / 85			
Presence of IRF in the study eye, n (%)	38 (39.2)	50 (58.8)	0.45 [0.25; 0.82] 0.009 *	0.67 [0.49; 0.90] 0.009 *	-0.20 [-0.34; -0.05] 0.007 *
Pooled Analysis: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.005 *				
< 7.5 %					
N"/N'/N	120 / 158 / 158	164 / 203 / 203			
Presence of IRF in the study eye, n (%)	72 (45.6)	101 (49.8)	0.84 [0.55; 1.27] 0.400	0.91 [0.73; 1.14] 0.415	-0.04 [-0.15; 0.06] 0.415

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N"/N'/N	160 / 209 / 209	126 / 165 / 165			
Presence of IRF in the study eye, n (%)	79 (37.8)	104 (63.0)	0.36 [0.23; 0.54] <.001 *	0.60 [0.49; 0.74] <.001 *	-0.25 [-0.35; -0.15] <.001 *
Presence of SRF and/or IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.574**					
KESTREL: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.466				
< 7.5 %					
N"/N'/N	76 / 76 / 76	107 / 107 / 107			
Presence of SRF and/or IRF in the study eye, n (%)	47 (61.8)	76 (71.0)	0.64 [0.34; 1.19] 0.159	0.87 [0.70; 1.08] 0.205	-0.09 [-0.23; 0.05] 0.195
≥ 7.5 %					
N"/N'/N	112 / 112 / 112	80 / 80 / 80			
Presence of SRF and/or IRF in the study eye, n (%)	67 (59.8)	61 (76.3)	0.46 [0.24; 0.87] 0.017 *	0.78 [0.65; 0.95] 0.015 *	-0.16 [-0.29; -0.03] 0.013 *
KITE: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.912				
< 7.5 %					
N"/N'/N	82 / 82 / 82	96 / 96 / 96			
Presence of SRF and/or IRF in the study eye, n (%)	43 (52.4)	68 (70.8)	0.45 [0.24; 0.84] 0.012 *	0.74 [0.58; 0.94] 0.015 *	-0.18 [-0.33; -0.04] 0.011 *
≥ 7.5 %					
N"/N'/N	97 / 97 / 97	85 / 85 / 85			
Presence of SRF and/or IRF in the study eye, n (%)	54 (55.7)	64 (75.3)	0.43 [0.23; 0.82] 0.010 *	0.74 [0.60; 0.92] 0.006 *	-0.20 [-0.33; -0.06] 0.004 *
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.541				
< 7.5 %					
N"/N'/N	158 / 158 / 158	203 / 203 / 203			
Presence of SRF and/or IRF in the study eye, n (%)	90 (57.0)	144 (70.9)	0.53 [0.34; 0.83] 0.005 *	0.81 [0.69; 0.95] 0.007 *	-0.14 [-0.24; -0.04] 0.007 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N"/N'/N	209 / 209 / 209	165 / 165 / 165			
Presence of SRF and/or IRF in the study eye, n (%)	121 (57.9)	125 (75.8)	0.44 [0.28; 0.69] <.001 *	0.76 [0.66; 0.88] <.001 *	-0.18 [-0.27; -0.09] <.001 *
Presence of SRF and/or IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = <.001 *				
< 7.5 %					
N"/N'/N	76 / 76 / 76	107 / 107 / 107			
Presence of SRF and/or IRF in the study eye, n (%)	37 (48.7)	47 (43.9)	1.19 [0.66; 2.16] 0.556	1.11 [0.81; 1.52] 0.522	0.05 [-0.10; 0.19] 0.524
≥ 7.5 %					
N"/N'/N	112 / 112 / 112	80 / 80 / 80			
Presence of SRF and/or IRF in the study eye, n (%)	42 (37.5)	54 (67.5)	0.28 [0.15; 0.52] <.001 *	0.56 [0.42; 0.74] <.001 *	-0.30 [-0.44; -0.16] <.001 *
KITE: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.477				
< 7.5 %					
N"/N'/N	82 / 82 / 82	96 / 96 / 96			
Presence of SRF and/or IRF in the study eye, n (%)	35 (42.7)	53 (55.2)	0.60 [0.33; 1.09] 0.095	0.77 [0.57; 1.05] 0.102	-0.13 [-0.27; 0.02] 0.093
≥ 7.5 %					
N"/N'/N	97 / 97 / 97	85 / 85 / 85			
Presence of SRF and/or IRF in the study eye, n (%)	38 (39.2)	50 (58.8)	0.44 [0.24; 0.81] 0.008 *	0.67 [0.49; 0.90] 0.009 *	-0.20 [-0.34; -0.05] 0.007 *
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.005 *				
< 7.5 %					
N"/N'/N	158 / 158 / 158	203 / 203 / 203			
Presence of SRF and/or IRF in the study eye, n (%)	72 (45.6)	100 (49.3)	0.86 [0.57; 1.31] 0.478	0.92 [0.74; 1.15] 0.467	-0.04 [-0.14; 0.07] 0.468

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N"/N'/N	209 / 209 / 209	165 / 165 / 165			
Presence of SRF and/or IRF in the study eye, n (%)	80 (38.3)	104 (63.0)	0.37 [0.24; 0.56] <.001 *	0.61 [0.49; 0.75] <.001 *	-0.25 [-0.35; -0.15] <.001 *

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Presence of SRF in the study eye / KESTREL / Week 52: logit(proportion) = treatment [by HbA1c].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 11.8 Presence of SRF and/or IRF in the study eye by duration of DME (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Presence of IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.503**					
KESTREL: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.402				
≤ 3 months					
N"/N'/N	103 / 120 / 120	96 / 110 / 110			
Presence of IRF in the study eye, n (%)	68 (56.7)	82 (74.5)	0.42 [0.24; 0.75] 0.003 *	0.76 [0.63; 0.92] 0.005 *	-0.18 [-0.30; -0.06] 0.004 *
> 3 - < 12 months					
N"/N'/N	24 / 30 / 30	31 / 39 / 39			
Presence of IRF in the study eye, n (%)	19 (63.3)	26 (66.7)	0.86 [0.32; 2.34] 0.769	0.95 [0.67; 1.35] 0.775	-0.03 [-0.26; 0.19] 0.774
≥ 12 months					
N"/N'/N	27 / 39 / 39	34 / 38 / 38			
Presence of IRF in the study eye, n (%)	27 (69.2)	29 (76.3)	0.70 [0.25; 1.93] 0.490	0.91 [0.69; 1.19] 0.486	-0.07 [-0.27; 0.13] 0.483
KITE: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.039 *				
≤ 3 months					
N"/N'/N	68 / 85 / 85	76 / 92 / 92			
Presence of IRF in the study eye, n (%)	42 (49.4)	67 (72.8)	0.33 [0.18; 0.63] <.001 *	0.68 [0.53; 0.87] 0.002 *	-0.23 [-0.37; -0.09] 0.001 *
> 3 - < 12 months					
N"/N'/N	44 / 51 / 51	42 / 49 / 49			
Presence of IRF in the study eye, n (%)	33 (64.7)	32 (65.3)	1.04 [0.45; 2.38] 0.934	0.99 [0.74; 1.32] 0.950	-0.01 [-0.19; 0.18] 0.950
≥ 12 months					
N"/N'/N	35 / 43 / 43	34 / 40 / 40			
Presence of IRF in the study eye, n (%)	21 (48.8)	33 (82.5)	0.22 [0.08; 0.62] 0.004 *	0.59 [0.42; 0.83] 0.002 *	-0.34 [-0.53; -0.15] <.001 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.035 *				
≤ 3 months					
N"/N'/N	171 / 205 / 205	172 / 202 / 202			
Presence of IRF in the study eye, n (%)	110 (53.7)	149 (73.8)	0.37 [0.24; 0.57] <.001 *	0.73 [0.62; 0.84] <.001 *	-0.20 [-0.29; -0.11] <.001 *
> 3 - < 12 months					
N"/N'/N	68 / 81 / 81	73 / 88 / 88			
Presence of IRF in the study eye, n (%)	52 (64.2)	58 (65.9)	1.00 [0.53; 1.90] 0.997	0.97 [0.78; 1.22] 0.818	-0.02 [-0.16; 0.13] 0.817
≥ 12 months					
N"/N'/N	62 / 82 / 82	68 / 78 / 78			
Presence of IRF in the study eye, n (%)	48 (58.5)	62 (79.5)	0.39 [0.19; 0.79] 0.009 *	0.74 [0.59; 0.91] 0.005 *	-0.21 [-0.35; -0.07] 0.004 *
Presence of IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.733**					
KESTREL: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.761				
≤ 3 months					
N"/N'/N	98 / 120 / 120	85 / 110 / 110			
Presence of IRF in the study eye, n (%)	49 (40.8)	62 (56.4)	0.52 [0.31; 0.89] 0.017 *	0.72 [0.55; 0.95] 0.020 *	-0.16 [-0.28; -0.03] 0.017 *
> 3 - < 12 months					
N"/N'/N	22 / 30 / 30	27 / 39 / 39			
Presence of IRF in the study eye, n (%)	15 (50.0)	24 (61.5)	0.62 [0.24; 1.63] 0.333	0.81 [0.53; 1.26] 0.350	-0.12 [-0.35; 0.12] 0.336
≥ 12 months					
N"/N'/N	28 / 39 / 39	33 / 38 / 38			
Presence of IRF in the study eye, n (%)	14 (35.9)	16 (42.1)	0.77 [0.31; 1.94] 0.587	0.85 [0.49; 1.49] 0.577	-0.06 [-0.28; 0.16] 0.576

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.424				
≤ 3 months					
N"/N'/N	58 / 85 / 85	72 / 92 / 92			
Presence of IRF in the study eye, n (%)	37 (43.5)	51 (55.4)	0.59 [0.33; 1.08] 0.086	0.79 [0.58; 1.06] 0.119	-0.12 [-0.27; 0.03] 0.111
> 3 - < 12 months					
N"/N'/N	43 / 51 / 51	38 / 49 / 49			
Presence of IRF in the study eye, n (%)	21 (41.2)	26 (53.1)	0.64 [0.29; 1.41] 0.268	0.78 [0.51; 1.18] 0.237	-0.12 [-0.31; 0.08] 0.231
≥ 12 months					
N"/N'/N	32 / 43 / 43	35 / 40 / 40			
Presence of IRF in the study eye, n (%)	15 (34.9)	26 (65.0)	0.31 [0.12; 0.76] 0.011 *	0.54 [0.34; 0.86] 0.009 *	-0.30 [-0.51; -0.10] 0.004 *
Pooled Analysis: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.866				
≤ 3 months					
N"/N'/N	156 / 205 / 205	157 / 202 / 202			
Presence of IRF in the study eye, n (%)	86 (42.0)	113 (55.9)	0.55 [0.37; 0.82] 0.003 *	0.75 [0.61; 0.92] 0.005 *	-0.14 [-0.24; -0.04] 0.005 *
> 3 - < 12 months					
N"/N'/N	65 / 81 / 81	65 / 88 / 88			
Presence of IRF in the study eye, n (%)	36 (44.4)	50 (56.8)	0.62 [0.34; 1.14] 0.126	0.79 [0.58; 1.07] 0.129	-0.12 [-0.27; 0.03] 0.124
≥ 12 months					
N"/N'/N	60 / 82 / 82	68 / 78 / 78			
Presence of IRF in the study eye, n (%)	29 (35.4)	42 (53.8)	0.49 [0.26; 0.92] 0.027 *	0.66 [0.46; 0.94] 0.018 *	-0.19 [-0.34; -0.03] 0.016 *
Presence of SRF and/or IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.574**					

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.402				
≤ 3 months					
N"/N'/N	120 / 120 / 120	110 / 110 / 110			
Presence of SRF and/or IRF in the study eye, n (%)	68 (56.7)	82 (74.5)	0.42 [0.24; 0.75] 0.003 *	0.76 [0.63; 0.92] 0.005 *	-0.18 [-0.30; -0.06] 0.004 *
> 3 - < 12 months					
N"/N'/N	30 / 30 / 30	39 / 39 / 39			
Presence of SRF and/or IRF in the study eye, n (%)	19 (63.3)	26 (66.7)	0.86 [0.32; 2.34] 0.769	0.95 [0.67; 1.35] 0.775	-0.03 [-0.26; 0.19] 0.774
≥ 12 months					
N"/N'/N	39 / 39 / 39	38 / 38 / 38			
Presence of SRF and/or IRF in the study eye, n (%)	27 (69.2)	29 (76.3)	0.70 [0.25; 1.93] 0.490	0.91 [0.69; 1.19] 0.486	-0.07 [-0.27; 0.13] 0.483
KITE: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.074				
≤ 3 months					
N"/N'/N	85 / 85 / 85	92 / 92 / 92			
Presence of SRF and/or IRF in the study eye, n (%)	42 (49.4)	67 (72.8)	0.36 [0.19; 0.68] 0.002 *	0.68 [0.53; 0.87] 0.002 *	-0.23 [-0.37; -0.09] 0.001 *
> 3 - < 12 months					
N"/N'/N	51 / 51 / 51	49 / 49 / 49			
Presence of SRF and/or IRF in the study eye, n (%)	33 (64.7)	32 (65.3)	0.98 [0.43; 2.22] 0.955	0.99 [0.74; 1.32] 0.950	-0.01 [-0.19; 0.18] 0.950
≥ 12 months					
N"/N'/N	43 / 43 / 43	40 / 40 / 40			
Presence of SRF and/or IRF in the study eye, n (%)	22 (51.2)	33 (82.5)	0.25 [0.09; 0.69] 0.007 *	0.62 [0.45; 0.86] 0.004 *	-0.31 [-0.50; -0.12] 0.001 *
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.055				
≤ 3 months					
N"/N'/N	205 / 205 / 205	202 / 202 / 202			
Presence of SRF and/or IRF in the study eye, n (%)	110 (53.7)	149 (73.8)	0.39 [0.25; 0.59] <.001 *	0.73 [0.62; 0.84] <.001 *	-0.20 [-0.29; -0.11] <.001 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 3 - < 12 months					
N"/N'/N	81 / 81 / 81	88 / 88 / 88			
Presence of SRF and/or IRF in the study eye, n (%)	52 (64.2)	58 (65.9)	0.97 [0.51; 1.83] 0.923	0.97 [0.78; 1.22] 0.818	-0.02 [-0.16; 0.13] 0.817
≥ 12 months					
N"/N'/N	82 / 82 / 82	78 / 78 / 78			
Presence of SRF and/or IRF in the study eye, n (%)	49 (59.8)	62 (79.5)	0.41 [0.20; 0.83] 0.013 *	0.75 [0.61; 0.93] 0.007 *	-0.20 [-0.34; -0.06] 0.006 *
Presence of SRF and/or IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.768				
≤ 3 months					
N"/N'/N	120 / 120 / 120	110 / 110 / 110			
Presence of SRF and/or IRF in the study eye, n (%)	50 (41.7)	62 (56.4)	0.54 [0.32; 0.92] 0.022 *	0.74 [0.57; 0.97] 0.027 *	-0.15 [-0.27; -0.02] 0.024 *
> 3 - < 12 months					
N"/N'/N	30 / 30 / 30	39 / 39 / 39			
Presence of SRF and/or IRF in the study eye, n (%)	15 (50.0)	23 (59.0)	0.69 [0.27; 1.81] 0.456	0.85 [0.54; 1.32] 0.466	-0.09 [-0.33; 0.15] 0.457
≥ 12 months					
N"/N'/N	39 / 39 / 39	38 / 38 / 38			
Presence of SRF and/or IRF in the study eye, n (%)	14 (35.9)	16 (42.1)	0.77 [0.31; 1.93] 0.581	0.85 [0.49; 1.49] 0.577	-0.06 [-0.28; 0.16] 0.576
KITE: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.348				
≤ 3 months					
N"/N'/N	85 / 85 / 85	92 / 92 / 92			
Presence of SRF and/or IRF in the study eye, n (%)	37 (43.5)	51 (55.4)	0.61 [0.33; 1.10] 0.100	0.79 [0.58; 1.06] 0.119	-0.12 [-0.27; 0.03] 0.111
> 3 - < 12 months					
N"/N'/N	51 / 51 / 51	49 / 49 / 49			
Presence of SRF and/or IRF in the study eye, n (%)	21 (41.2)	26 (53.1)	0.63 [0.28; 1.38] 0.247	0.78 [0.51; 1.18] 0.237	-0.12 [-0.31; 0.08] 0.231

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months					
N"/N'/N	43 / 43 / 43	40 / 40 / 40			
Presence of SRF and/or IRF in the study eye, n (%)	15 (34.9)	26 (65.0)	0.29 [0.11; 0.71] 0.007 *	0.54 [0.34; 0.86] 0.009 *	-0.30 [-0.51; -0.10] 0.004 *
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.802				
≤ 3 months					
N"/N'/N	205 / 205 / 205	202 / 202 / 202			
Presence of SRF and/or IRF in the study eye, n (%)	87 (42.4)	113 (55.9)	0.57 [0.39; 0.85] 0.006 *	0.76 [0.62; 0.93] 0.007 *	-0.13 [-0.23; -0.04] 0.006 *
> 3 - < 12 months					
N"/N'/N	81 / 81 / 81	88 / 88 / 88			
Presence of SRF and/or IRF in the study eye, n (%)	36 (44.4)	49 (55.7)	0.64 [0.35; 1.19] 0.160	0.81 [0.59; 1.10] 0.167	-0.11 [-0.26; 0.04] 0.162
≥ 12 months					
N"/N'/N	82 / 82 / 82	78 / 78 / 78			
Presence of SRF and/or IRF in the study eye, n (%)	29 (35.4)	42 (53.8)	0.48 [0.25; 0.91] 0.024 *	0.66 [0.46; 0.94] 0.018 *	-0.19 [-0.34; -0.03] 0.016 *

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 11.9 Presence of SRF and/or IRF in the study eye by DME type (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Presence of SRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.600**					
KESTREL: Presence of SRF in the study eye, Week 52					
Interaction Test:	p = 0.610				
focal					
N''/N'/N	51 / 59 / 59	41 / 48 / 48			
Presence of SRF in the study eye, n (%)	1 (1.7)	2 (4.2)	0.63 [0.05; 8.36] 0.729	0.41 [0.04; 4.35] 0.457	-0.02 [-0.09; 0.04] 0.459
diffuse					
N''/N'/N	101 / 127 / 127	117 / 134 / 134			
Presence of SRF in the study eye, n (%)	3 (2.4)	2 (1.5)	1.45 [0.23; 9.06] 0.690	1.58 [0.27; 9.32] 0.612	0.01 [-0.02; 0.04] 0.610
KITE: Presence of SRF in the study eye, Week 52					
Interaction Test:	p = 0.172				
focal					
N''/N'/N	48 / 63 / 63	52 / 66 / 66			
Presence of SRF in the study eye, n (%)	2 (3.2)	1 (1.5)	2.32 [0.19; 28.32] 0.509	2.10 [0.19; 22.54] 0.542	0.02 [-0.04; 0.07] 0.535
diffuse					
N''/N'/N	98 / 115 / 115	96 / 109 / 109			
Presence of SRF in the study eye, n (%)	1 (0.9)	5 (4.6)	0.23 [0.03; 2.06] 0.188	0.19 [0.02; 1.60] 0.126	-0.04 [-0.08; 0.01] 0.089
Pooled Analysis: Presence of SRF in the study eye, Week 52					
Interaction Test:	p = 0.397				
focal					
N''/N'/N	99 / 122 / 122	93 / 114 / 114			
Presence of SRF in the study eye, n (%)	3 (2.5)	3 (2.6)	1.42 [0.26; 7.76] 0.687	0.93 [0.20; 4.34] 0.921	-0.00 [-0.04; 0.04] 0.922

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N"/N'/N	199 / 242 / 242	213 / 243 / 243			
Presence of SRF in the study eye, n (%)	4 (1.7)	7 (2.9)	0.56 [0.15; 2.04] 0.382	0.57 [0.17; 1.91] 0.357	-0.01 [-0.04; 0.01] 0.359
Presence of IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.503**					
KESTREL: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.045 *				
focal					
N"/N'/N	51 / 59 / 59	41 / 48 / 48			
Presence of IRF in the study eye, n (%)	39 (66.1)	30 (62.5)	1.07 [0.47; 2.42] 0.866	1.06 [0.80; 1.41] 0.700	0.04 [-0.15; 0.22] 0.699
diffuse					
N"/N'/N	101 / 127 / 127	117 / 134 / 134			
Presence of IRF in the study eye, n (%)	72 (56.7)	103 (76.9)	0.40 [0.23; 0.68] <.001 *	0.74 [0.62; 0.88] <.001 *	-0.20 [-0.31; -0.09] <.001 *
KITE: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.924				
focal					
N"/N'/N	48 / 63 / 63	52 / 66 / 66			
Presence of IRF in the study eye, n (%)	35 (55.6)	48 (72.7)	0.44 [0.21; 0.93] 0.032 *	0.76 [0.59; 1.00] 0.047 *	-0.17 [-0.33; -0.01] 0.039 *
diffuse					
N"/N'/N	98 / 115 / 115	96 / 109 / 109			
Presence of IRF in the study eye, n (%)	60 (52.2)	79 (72.5)	0.42 [0.24; 0.74] 0.003 *	0.72 [0.58; 0.89] 0.002 *	-0.20 [-0.33; -0.08] 0.001 *
Pooled Analysis: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.167				
focal					
N"/N'/N	99 / 122 / 122	93 / 114 / 114			
Presence of IRF in the study eye, n (%)	74 (60.7)	78 (68.4)	0.65 [0.38; 1.13] 0.127	0.89 [0.73; 1.07] 0.214	-0.08 [-0.20; 0.04] 0.213

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N"/N'/N	199 / 242 / 242	213 / 243 / 243			
Presence of IRF in the study eye, n (%)	132 (54.5)	182 (74.9)	0.41 [0.28; 0.60] <.001 *	0.73 [0.64; 0.84] <.001 *	-0.20 [-0.29; -0.12] <.001 *
Presence of IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.733**					
KESTREL: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.850				
focal					
N"/N'/N	50 / 59 / 59	35 / 48 / 48			
Presence of IRF in the study eye, n (%)	24 (40.7)	26 (54.2)	0.55 [0.25; 1.20] 0.133	0.75 [0.50; 1.12] 0.164	-0.13 [-0.32; 0.05] 0.161
diffuse					
N"/N'/N	96 / 127 / 127	106 / 134 / 134			
Presence of IRF in the study eye, n (%)	52 (40.9)	72 (53.7)	0.60 [0.37; 0.98] 0.041 *	0.76 [0.59; 0.99] 0.042 *	-0.13 [-0.25; -0.01] 0.037 *
KITE: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.563				
focal					
N"/N'/N	46 / 63 / 63	53 / 66 / 66			
Presence of IRF in the study eye, n (%)	26 (41.3)	35 (53.0)	0.61 [0.30; 1.23] 0.169	0.78 [0.54; 1.13] 0.186	-0.12 [-0.29; 0.05] 0.178
diffuse					
N"/N'/N	86 / 115 / 115	88 / 109 / 109			
Presence of IRF in the study eye, n (%)	46 (40.0)	64 (58.7)	0.47 [0.28; 0.81] 0.006 *	0.68 [0.52; 0.90] 0.006 *	-0.19 [-0.32; -0.06] 0.004 *
Pooled Analysis: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.796				
focal					
N"/N'/N	96 / 122 / 122	88 / 114 / 114			
Presence of IRF in the study eye, n (%)	50 (41.0)	61 (53.5)	0.59 [0.35; 0.99] 0.044 *	0.77 [0.58; 1.01] 0.055	-0.13 [-0.25; 0.00] 0.052

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N"/N'/N	182 / 242 / 242	194 / 243 / 243			
Presence of IRF in the study eye, n (%)	98 (40.5)	136 (56.0)	0.54 [0.38; 0.77] <.001 *	0.72 [0.60; 0.87] <.001 *	-0.16 [-0.24; -0.07] <.001 *
Presence of SRF and/or IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.574**					
KESTREL: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.045 *				
focal					
N"/N'/N	59 / 59 / 59	48 / 48 / 48			
Presence of SRF and/or IRF in the study eye, n (%)	39 (66.1)	30 (62.5)	1.07 [0.47; 2.42] 0.866	1.06 [0.80; 1.41] 0.700	0.04 [-0.15; 0.22] 0.699
diffuse					
N"/N'/N	127 / 127 / 127	134 / 134 / 134			
Presence of SRF and/or IRF in the study eye, n (%)	72 (56.7)	103 (76.9)	0.40 [0.23; 0.68] <.001 *	0.74 [0.62; 0.88] <.001 *	-0.20 [-0.31; -0.09] <.001 *
KITE: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.912				
focal					
N"/N'/N	63 / 63 / 63	66 / 66 / 66			
Presence of SRF and/or IRF in the study eye, n (%)	35 (55.6)	48 (72.7)	0.47 [0.22; 0.98] 0.043 *	0.76 [0.59; 1.00] 0.047 *	-0.17 [-0.33; -0.01] 0.039 *
diffuse					
N"/N'/N	115 / 115 / 115	109 / 109 / 109			
Presence of SRF and/or IRF in the study eye, n (%)	61 (53.0)	79 (72.5)	0.44 [0.25; 0.78] 0.005 *	0.73 [0.59; 0.90] 0.003 *	-0.19 [-0.32; -0.07] 0.002 *
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.155				
focal					
N"/N'/N	122 / 122 / 122	114 / 114 / 114			
Presence of SRF and/or IRF in the study eye, n (%)	74 (60.7)	78 (68.4)	0.67 [0.39; 1.16] 0.158	0.89 [0.73; 1.07] 0.214	-0.08 [-0.20; 0.04] 0.213

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N"/N'/N	242 / 242 / 242	243 / 243 / 243			
Presence of SRF and/or IRF in the study eye, n (%)	133 (55.0)	182 (74.9)	0.41 [0.28; 0.61] <.001 *	0.74 [0.64; 0.84] <.001 *	-0.20 [-0.28; -0.12] <.001 *
Presence of SRF and/or IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.760				
focal					
N"/N'/N	59 / 59 / 59	48 / 48 / 48			
Presence of SRF and/or IRF in the study eye, n (%)	24 (40.7)	26 (54.2)	0.55 [0.25; 1.20] 0.135	0.75 [0.50; 1.12] 0.164	-0.13 [-0.32; 0.05] 0.161
diffuse					
N"/N'/N	127 / 127 / 127	134 / 134 / 134			
Presence of SRF and/or IRF in the study eye, n (%)	53 (41.7)	71 (53.0)	0.63 [0.39; 1.04] 0.070	0.79 [0.61; 1.02] 0.072	-0.11 [-0.23; 0.01] 0.067
KITE: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.502				
focal					
N"/N'/N	63 / 63 / 63	66 / 66 / 66			
Presence of SRF and/or IRF in the study eye, n (%)	26 (41.3)	35 (53.0)	0.62 [0.31; 1.25] 0.183	0.78 [0.54; 1.13] 0.186	-0.12 [-0.29; 0.05] 0.178
diffuse					
N"/N'/N	115 / 115 / 115	109 / 109 / 109			
Presence of SRF and/or IRF in the study eye, n (%)	46 (40.0)	64 (58.7)	0.46 [0.27; 0.79] 0.005 *	0.68 [0.52; 0.90] 0.006 *	-0.19 [-0.32; -0.06] 0.004 *
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.786				
focal					
N"/N'/N	122 / 122 / 122	114 / 114 / 114			
Presence of SRF and/or IRF in the study eye, n (%)	50 (41.0)	61 (53.5)	0.60 [0.36; 1.02] 0.058	0.77 [0.58; 1.01] 0.055	-0.13 [-0.25; 0.00] 0.052

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N"/N'/N	242 / 242 / 242	243 / 243 / 243			
Presence of SRF and/or IRF in the study eye, n (%)	99 (40.9)	135 (55.6)	0.55 [0.39; 0.79] 0.001 *	0.74 [0.61; 0.89] 0.001 *	-0.15 [-0.24; -0.06] 0.001 *

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 11.10 Presence of SRF and/or IRF in the study eye by CSFT (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Presence of IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.503**					
KESTREL: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.224				
< 450 µm					
N"/N'/N	87 / 107 / 107	83 / 96 / 96			
Presence of IRF in the study eye, n (%)	58 (54.2)	65 (67.7)	0.54 [0.30; 0.97] 0.039 *	0.80 [0.64; 1.00] 0.050 *	-0.14 [-0.27; -0.00] 0.046 *
≥ 450 - < 650 µm					
N"/N'/N	58 / 70 / 70	61 / 71 / 71			
Presence of IRF in the study eye, n (%)	45 (64.3)	57 (80.3)	0.44 [0.21; 0.95] 0.037 *	0.80 [0.65; 0.99] 0.037 *	-0.16 [-0.31; -0.01] 0.031 *
≥ 650 µm					
N"/N'/N	9 / 12 / 12	17 / 20 / 20			
Presence of IRF in the study eye, n (%)	11 (91.7)	15 (75.0)	3.72 [0.38; 36.55] 0.260	1.22 [0.90; 1.66] 0.197	0.17 [-0.08; 0.41] 0.184
KITE: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.820				
< 450 µm					
N"/N'/N	65 / 85 / 85	63 / 82 / 82			
Presence of IRF in the study eye, n (%)	41 (48.2)	59 (72.0)	0.38 [0.19; 0.72] 0.003 *	0.67 [0.52; 0.87] 0.002 *	-0.24 [-0.38; -0.09] 0.001 *
≥ 450 - < 650 µm					
N"/N'/N	66 / 74 / 74	72 / 79 / 79			
Presence of IRF in the study eye, n (%)	41 (55.4)	58 (73.4)	0.42 [0.21; 0.85] 0.015 *	0.75 [0.59; 0.96] 0.024 *	-0.18 [-0.33; -0.03] 0.018 *
≥ 650 µm					
N"/N'/N	16 / 20 / 20	16 / 19 / 19			
Presence of IRF in the study eye, n (%)	14 (70.0)	15 (78.9)	0.62 [0.15; 2.69] 0.528	0.89 [0.61; 1.28] 0.523	-0.09 [-0.36; 0.18] 0.519

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.294				
< 450 µm					
N"/N'/N	152 / 192 / 192	146 / 178 / 178			
Presence of IRF in the study eye, n (%)	99 (51.6)	124 (69.7)	0.45 [0.29; 0.69] <.001 *	0.74 [0.63; 0.88] <.001 *	-0.18 [-0.28; -0.08] <.001 *
≥ 450 - < 650 µm					
N"/N'/N	124 / 144 / 144	133 / 150 / 150			
Presence of IRF in the study eye, n (%)	86 (59.7)	115 (76.7)	0.44 [0.27; 0.74] 0.002 *	0.78 [0.66; 0.91] 0.002 *	-0.17 [-0.27; -0.07] 0.001 *
≥ 650 µm					
N"/N'/N	25 / 32 / 32	33 / 39 / 39			
Presence of IRF in the study eye, n (%)	25 (78.1)	30 (76.9)	1.13 [0.37; 3.49] 0.826	1.03 [0.81; 1.31] 0.830	0.02 [-0.17; 0.22] 0.826
Presence of IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.733**					
KESTREL: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.171				
< 450 µm					
N"/N'/N	85 / 107 / 107	75 / 96 / 96			
Presence of IRF in the study eye, n (%)	39 (36.4)	51 (53.1)	0.50 [0.28; 0.87] 0.015 *	0.69 [0.50; 0.94] 0.018 *	-0.17 [-0.30; -0.03] 0.016 *
≥ 450 - < 650 µm					
N"/N'/N	55 / 70 / 70	54 / 71 / 71			
Presence of IRF in the study eye, n (%)	30 (42.9)	40 (56.3)	0.58 [0.30; 1.13] 0.112	0.76 [0.54; 1.07] 0.114	-0.13 [-0.30; 0.03] 0.106
≥ 650 µm					
N"/N'/N	8 / 12 / 12	16 / 20 / 20			
Presence of IRF in the study eye, n (%)	9 (75.0)	11 (55.0)	2.47 [0.51; 11.96] 0.261	1.36 [0.82; 2.28] 0.237	0.20 [-0.13; 0.53] 0.232

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.895				
< 450 µm					
N"/N'/N	62 / 85 / 85	63 / 82 / 82			
Presence of IRF in the study eye, n (%)	29 (34.1)	40 (48.8)	0.57 [0.30; 1.06] 0.078	0.70 [0.48; 1.01] 0.058	-0.15 [-0.29; 0.00] 0.052
≥ 450 - < 650 µm					
N"/N'/N	56 / 74 / 74	66 / 79 / 79			
Presence of IRF in the study eye, n (%)	33 (44.6)	49 (62.0)	0.47 [0.24; 0.90] 0.022 *	0.72 [0.53; 0.98] 0.035 *	-0.17 [-0.33; -0.02] 0.028 *
≥ 650 µm					
N"/N'/N	15 / 20 / 20	15 / 19 / 19			
Presence of IRF in the study eye, n (%)	11 (55.0)	14 (73.7)	0.44 [0.11; 1.71] 0.237	0.75 [0.46; 1.20] 0.231	-0.19 [-0.48; 0.11] 0.214
Pooled Analysis: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.520				
< 450 µm					
N"/N'/N	147 / 192 / 192	138 / 178 / 178			
Presence of IRF in the study eye, n (%)	68 (35.4)	91 (51.1)	0.52 [0.34; 0.80] 0.002 *	0.69 [0.54; 0.88] 0.002 *	-0.16 [-0.26; -0.06] 0.002 *
≥ 450 - < 650 µm					
N"/N'/N	111 / 144 / 144	120 / 150 / 150			
Presence of IRF in the study eye, n (%)	63 (43.8)	89 (59.3)	0.53 [0.33; 0.84] 0.007 *	0.74 [0.59; 0.93] 0.008 *	-0.16 [-0.27; -0.04] 0.007 *
≥ 650 µm					
N"/N'/N	23 / 32 / 32	31 / 39 / 39			
Presence of IRF in the study eye, n (%)	20 (62.5)	25 (64.1)	0.95 [0.36; 2.52] 0.922	0.97 [0.69; 1.37] 0.874	-0.02 [-0.25; 0.21] 0.874
Presence of SRF and/or IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.574**					

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.224				
< 450 µm					
N"/N'/N	107 / 107 / 107	96 / 96 / 96			
Presence of SRF and/or IRF in the study eye, n (%)	58 (54.2)	65 (67.7)	0.54 [0.30; 0.97] 0.039 *	0.80 [0.64; 1.00] 0.050 *	-0.14 [-0.27; -0.00] 0.046 *
≥ 450 - < 650 µm					
N"/N'/N	70 / 70 / 70	71 / 71 / 71			
Presence of SRF and/or IRF in the study eye, n (%)	45 (64.3)	57 (80.3)	0.44 [0.21; 0.95] 0.037 *	0.80 [0.65; 0.99] 0.037 *	-0.16 [-0.31; -0.01] 0.031 *
≥ 650 µm					
N"/N'/N	12 / 12 / 12	20 / 20 / 20			
Presence of SRF and/or IRF in the study eye, n (%)	11 (91.7)	15 (75.0)	3.72 [0.38; 36.55] 0.260	1.22 [0.90; 1.66] 0.197	0.17 [-0.08; 0.41] 0.184
KITE: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.861				
< 450 µm					
N"/N'/N	85 / 85 / 85	82 / 82 / 82			
Presence of SRF and/or IRF in the study eye, n (%)	42 (49.4)	59 (72.0)	0.40 [0.21; 0.77] 0.006 *	0.69 [0.53; 0.89] 0.004 *	-0.23 [-0.37; -0.08] 0.002 *
≥ 450 - < 650 µm					
N"/N'/N	74 / 74 / 74	79 / 79 / 79			
Presence of SRF and/or IRF in the study eye, n (%)	41 (55.4)	58 (73.4)	0.45 [0.23; 0.88] 0.020 *	0.75 [0.59; 0.96] 0.024 *	-0.18 [-0.33; -0.03] 0.018 *
≥ 650 µm					
N"/N'/N	20 / 20 / 20	19 / 19 / 19			
Presence of SRF and/or IRF in the study eye, n (%)	14 (70.0)	15 (78.9)	0.62 [0.15; 2.69] 0.527	0.89 [0.61; 1.28] 0.523	-0.09 [-0.36; 0.18] 0.519
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.317				
< 450 µm					
N"/N'/N	192 / 192 / 192	178 / 178 / 178			
Presence of SRF and/or IRF in the study eye, n (%)	100 (52.1)	124 (69.7)	0.46 [0.30; 0.71] <.001 *	0.75 [0.63; 0.88] <.001 *	-0.18 [-0.27; -0.08] <.001 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 450 - < 650 µm					
N"/N'/N	144 / 144 / 144	150 / 150 / 150			
Presence of SRF and/or IRF in the study eye, n (%)	86 (59.7)	115 (76.7)	0.45 [0.27; 0.75] 0.002 *	0.78 [0.66; 0.91] 0.002 *	-0.17 [-0.27; -0.07] 0.001 *
≥ 650 µm					
N"/N'/N	32 / 32 / 32	39 / 39 / 39			
Presence of SRF and/or IRF in the study eye, n (%)	25 (78.1)	30 (76.9)	1.13 [0.37; 3.49] 0.830	1.03 [0.81; 1.31] 0.830	0.02 [-0.17; 0.22] 0.826
Presence of SRF and/or IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.200				
< 450 µm					
N"/N'/N	107 / 107 / 107	96 / 96 / 96			
Presence of SRF and/or IRF in the study eye, n (%)	40 (37.4)	50 (52.1)	0.54 [0.31; 0.95] 0.031 *	0.72 [0.53; 0.98] 0.037 *	-0.15 [-0.28; -0.01] 0.034 *
≥ 450 - < 650 µm					
N"/N'/N	70 / 70 / 70	71 / 71 / 71			
Presence of SRF and/or IRF in the study eye, n (%)	30 (42.9)	40 (56.3)	0.58 [0.30; 1.13] 0.111	0.76 [0.54; 1.07] 0.114	-0.13 [-0.30; 0.03] 0.106
≥ 650 µm					
N"/N'/N	12 / 12 / 12	20 / 20 / 20			
Presence of SRF and/or IRF in the study eye, n (%)	9 (75.0)	11 (55.0)	2.46 [0.51; 11.91] 0.263	1.36 [0.82; 2.28] 0.237	0.20 [-0.13; 0.53] 0.232
KITE: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.933				
< 450 µm					
N"/N'/N	85 / 85 / 85	82 / 82 / 82			
Presence of SRF and/or IRF in the study eye, n (%)	29 (34.1)	40 (48.8)	0.55 [0.29; 1.03] 0.061	0.70 [0.48; 1.01] 0.058	-0.15 [-0.29; 0.00] 0.052
≥ 450 - < 650 µm					
N"/N'/N	74 / 74 / 74	79 / 79 / 79			
Presence of SRF and/or IRF in the study eye, n (%)	33 (44.6)	49 (62.0)	0.47 [0.25; 0.91] 0.024 *	0.72 [0.53; 0.98] 0.035 *	-0.17 [-0.33; -0.02] 0.028 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm					
N"/N'/N	20 / 20 / 20	19 / 19 / 19			
Presence of SRF and/or IRF in the study eye, n (%)	11 (55.0)	14 (73.7)	0.44 [0.11; 1.71] 0.238	0.75 [0.46; 1.20] 0.231	-0.19 [-0.48; 0.11] 0.214
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.548				
< 450 µm					
N"/N'/N	192 / 192 / 192	178 / 178 / 178			
Presence of SRF and/or IRF in the study eye, n (%)	69 (35.9)	90 (50.6)	0.55 [0.36; 0.83] 0.005 *	0.71 [0.56; 0.90] 0.004 *	-0.15 [-0.25; -0.05] 0.004 *
≥ 450 - < 650 µm					
N"/N'/N	144 / 144 / 144	150 / 150 / 150			
Presence of SRF and/or IRF in the study eye, n (%)	63 (43.8)	89 (59.3)	0.53 [0.33; 0.85] 0.008 *	0.74 [0.59; 0.93] 0.008 *	-0.16 [-0.27; -0.04] 0.007 *
≥ 650 µm					
N"/N'/N	32 / 32 / 32	39 / 39 / 39			
Presence of SRF and/or IRF in the study eye, n (%)	20 (62.5)	25 (64.1)	0.96 [0.36; 2.53] 0.928	0.97 [0.69; 1.37] 0.874	-0.02 [-0.25; 0.21] 0.874

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 11.11 Presence of SRF and/or IRF in the study eye by status of SRF (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Presence of SRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.600**					
KESTREL: Presence of SRF in the study eye, Week 52					
Interaction Test:	N.E.				
presence					
N"/N'/N	49 / 62 / 62	53 / 61 / 61			
Presence of SRF in the study eye, n (%)	3 (4.8)	4 (6.6)	0.72 [0.16; 3.38] 0.682	0.74 [0.17; 3.16] 0.682	-0.02 [-0.10; 0.06] 0.681
absence					
N"/N'/N	105 / 127 / 127	108 / 126 / 126			
Presence of SRF in the study eye, n (%)	1 (0.8)	0 (0.0)	N.E.	2.98 [0.12; 72.38] 0.503	0.01 [-0.01; 0.02] 0.315
KITE: Presence of SRF in the study eye, Week 52					
Interaction Test:	N.E.				
presence					
N"/N'/N	45 / 56 / 56	58 / 67 / 67			
Presence of SRF in the study eye, n (%)	3 (5.4)	5 (7.5)	0.70 [0.16; 3.08] 0.639	0.72 [0.18; 2.87] 0.639	-0.02 [-0.11; 0.07] 0.632
absence					
N"/N'/N	102 / 123 / 123	94 / 114 / 114			
Presence of SRF in the study eye, n (%)	0 (0.0)	1 (0.9)	N.E.	0.31 [0.01; 7.51] 0.471	-0.01 [-0.03; 0.01] 0.315
Pooled Analysis: Presence of SRF in the study eye, Week 52					
Interaction Test:	p = 0.870				
presence					
N"/N'/N	94 / 118 / 118	111 / 128 / 128			
Presence of SRF in the study eye, n (%)	6 (5.1)	9 (7.0)	0.73 [0.25; 2.15] 0.570	0.73 [0.27; 1.98] 0.533	-0.02 [-0.08; 0.04] 0.529

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N"/N'/N	207 / 250 / 250	202 / 240 / 240			
Presence of SRF in the study eye, n (%)	1 (0.4)	1 (0.4)	0.94 [0.06; 15.12] 0.963	0.96 [0.14; 6.66] 0.967	-0.00 [-0.01; 0.01] 0.977
Presence of SRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.677**					
KESTREL: Presence of SRF in the study eye, Week 100					
Interaction Test:	N.E.				
presence					
N"/N'/N	52 / 62 / 62	47 / 61 / 61			
Presence of SRF in the study eye, n (%)	3 (4.8)	2 (3.3)	1.50 [0.24; 9.30] 0.663	1.48 [0.26; 8.53] 0.664	0.02 [-0.05; 0.09] 0.661
absence					
N"/N'/N	96 / 127 / 127	98 / 126 / 126			
Presence of SRF in the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE: Presence of SRF in the study eye, Week 100					
Interaction Test:	N.E.				
presence					
N"/N'/N	39 / 56 / 56	54 / 67 / 67			
Presence of SRF in the study eye, n (%)	4 (7.1)	4 (6.0)	1.21 [0.29; 5.08] 0.793	1.20 [0.31; 4.57] 0.793	0.01 [-0.08; 0.10] 0.794
absence					
N"/N'/N	94 / 123 / 123	91 / 114 / 114			
Presence of SRF in the study eye, n (%)	0 (0.0)	1 (0.9)	N.E.	0.31 [0.01; 7.51] 0.471	-0.01 [-0.03; 0.01] 0.315
Pooled Analysis: Presence of SRF in the study eye, Week 100					
Interaction Test:	N.E.				
presence					
N"/N'/N	91 / 118 / 118	101 / 128 / 128			
Presence of SRF in the study eye, n (%)	7 (5.9)	6 (4.7)	1.35 [0.42; 4.34] 0.613	1.30 [0.45; 3.75] 0.633	0.01 [-0.04; 0.07] 0.633

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N"/N'/N	190 / 250 / 250	189 / 240 / 240			
Presence of SRF in the study eye, n (%)	0 (0.0)	1 (0.4)	N.E.	0.31 [0.01; 7.51] 0.446	-0.00 [-0.01; 0.00] 0.312
Presence of IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.503**					
KESTREL: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.506				
presence					
N"/N'/N	49 / 62 / 62	53 / 61 / 61			
Presence of IRF in the study eye, n (%)	38 (61.3)	43 (70.5)	0.66 [0.31; 1.40] 0.282	0.87 [0.67; 1.12] 0.284	-0.09 [-0.26; 0.07] 0.279
absence					
N"/N'/N	105 / 127 / 127	108 / 126 / 126			
Presence of IRF in the study eye, n (%)	76 (59.8)	94 (74.6)	0.48 [0.28; 0.83] 0.009 *	0.80 [0.67; 0.96] 0.014 *	-0.15 [-0.26; -0.03] 0.011 *
KITE: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.147				
presence					
N"/N'/N	45 / 56 / 56	58 / 67 / 67			
Presence of IRF in the study eye, n (%)	32 (57.1)	44 (65.7)	0.66 [0.31; 1.40] 0.281	0.87 [0.65; 1.16] 0.339	-0.09 [-0.26; 0.09] 0.332
absence					
N"/N'/N	102 / 123 / 123	94 / 114 / 114			
Presence of IRF in the study eye, n (%)	64 (52.0)	88 (77.2)	0.33 [0.19; 0.58] <.001 *	0.67 [0.55; 0.82] <.001 *	-0.25 [-0.37; -0.13] <.001 *
Pooled Analysis: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.120				
presence					
N"/N'/N	94 / 118 / 118	111 / 128 / 128			
Presence of IRF in the study eye, n (%)	70 (59.3)	87 (68.0)	0.67 [0.39; 1.13] 0.135	0.87 [0.72; 1.05] 0.150	-0.09 [-0.21; 0.03] 0.147

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N"/N'/N	207 / 250 / 250	202 / 240 / 240			
Presence of IRF in the study eye, n (%)	140 (56.0)	182 (75.8)	0.40 [0.27; 0.59] <.001 *	0.74 [0.65; 0.84] <.001 *	-0.20 [-0.28; -0.12] <.001 *
Presence of IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.733**					
KESTREL: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.522				
presence					
N"/N'/N	52 / 62 / 62	47 / 61 / 61			
Presence of IRF in the study eye, n (%)	27 (43.5)	32 (52.5)	0.70 [0.34; 1.42] 0.323	0.83 [0.57; 1.20] 0.325	-0.09 [-0.26; 0.09] 0.321
absence					
N"/N'/N	96 / 127 / 127	98 / 126 / 126			
Presence of IRF in the study eye, n (%)	51 (40.2)	70 (55.6)	0.53 [0.32; 0.87] 0.012 *	0.72 [0.56; 0.94] 0.016 *	-0.15 [-0.28; -0.03] 0.013 *
KITE: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.619				
presence					
N"/N'/N	39 / 56 / 56	54 / 67 / 67			
Presence of IRF in the study eye, n (%)	22 (39.3)	39 (58.2)	0.45 [0.22; 0.93] 0.032 *	0.67 [0.46; 0.99] 0.045 *	-0.19 [-0.36; -0.02] 0.033 *
absence					
N"/N'/N	94 / 123 / 123	91 / 114 / 114			
Presence of IRF in the study eye, n (%)	51 (41.5)	64 (56.1)	0.57 [0.34; 0.95] 0.030 *	0.74 [0.57; 0.96] 0.025 *	-0.15 [-0.27; -0.02] 0.022 *
Pooled Analysis: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.907				
presence					
N"/N'/N	91 / 118 / 118	101 / 128 / 128			
Presence of IRF in the study eye, n (%)	49 (41.5)	71 (55.5)	0.56 [0.34; 0.94] 0.027 *	0.75 [0.57; 0.98] 0.030 *	-0.14 [-0.26; -0.01] 0.028 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N"/N'/N	190 / 250 / 250	189 / 240 / 240			
Presence of IRF in the study eye, n (%)	102 (40.8)	134 (55.8)	0.54 [0.38; 0.78] <.001 *	0.73 [0.61; 0.88] <.001 *	-0.15 [-0.24; -0.06] <.001 *
Presence of SRF and/or IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.574**					
KESTREL: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.506				
presence					
N"/N'/N	62 / 62 / 62	61 / 61 / 61			
Presence of SRF and/or IRF in the study eye, n (%)	38 (61.3)	43 (70.5)	0.66 [0.31; 1.40] 0.282	0.87 [0.67; 1.12] 0.284	-0.09 [-0.26; 0.07] 0.279
absence					
N"/N'/N	127 / 127 / 127	126 / 126 / 126			
Presence of SRF and/or IRF in the study eye, n (%)	76 (59.8)	94 (74.6)	0.48 [0.28; 0.83] 0.009 *	0.80 [0.67; 0.96] 0.014 *	-0.15 [-0.26; -0.03] 0.011 *
KITE: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.085				
presence					
N"/N'/N	56 / 56 / 56	67 / 67 / 67			
Presence of SRF and/or IRF in the study eye, n (%)	33 (58.9)	44 (65.7)	0.75 [0.36; 1.56] 0.440	0.90 [0.68; 1.19] 0.446	-0.07 [-0.24; 0.10] 0.442
absence					
N"/N'/N	123 / 123 / 123	114 / 114 / 114			
Presence of SRF and/or IRF in the study eye, n (%)	64 (52.0)	88 (77.2)	0.33 [0.19; 0.58] <.001 *	0.67 [0.55; 0.82] <.001 *	-0.25 [-0.37; -0.13] <.001 *
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.085				
presence					
N"/N'/N	118 / 118 / 118	128 / 128 / 128			
Presence of SRF and/or IRF in the study eye, n (%)	71 (60.2)	87 (68.0)	0.71 [0.42; 1.20] 0.197	0.88 [0.73; 1.07] 0.194	-0.08 [-0.20; 0.04] 0.192

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N"/N'/N	250 / 250 / 250	240 / 240 / 240			
Presence of SRF and/or IRF in the study eye, n (%)	140 (56.0)	182 (75.8)	0.40 [0.27; 0.59] <.001 *	0.74 [0.65; 0.84] <.001 *	-0.20 [-0.28; -0.12] <.001 *
Presence of SRF and/or IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.471				
presence					
N"/N'/N	62 / 62 / 62	61 / 61 / 61			
Presence of SRF and/or IRF in the study eye, n (%)	28 (45.2)	32 (52.5)	0.75 [0.37; 1.52] 0.419	0.86 [0.60; 1.24] 0.420	-0.07 [-0.25; 0.10] 0.417
absence					
N"/N'/N	127 / 127 / 127	126 / 126 / 126			
Presence of SRF and/or IRF in the study eye, n (%)	51 (40.2)	69 (54.8)	0.54 [0.33; 0.90] 0.017 *	0.73 [0.56; 0.96] 0.022 *	-0.15 [-0.27; -0.02] 0.019 *
KITE: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.683				
presence					
N"/N'/N	56 / 56 / 56	67 / 67 / 67			
Presence of SRF and/or IRF in the study eye, n (%)	22 (39.3)	39 (58.2)	0.46 [0.22; 0.95] 0.035 *	0.67 [0.46; 0.99] 0.045 *	-0.19 [-0.36; -0.02] 0.033 *
absence					
N"/N'/N	123 / 123 / 123	114 / 114 / 114			
Presence of SRF and/or IRF in the study eye, n (%)	51 (41.5)	64 (56.1)	0.55 [0.33; 0.93] 0.025 *	0.74 [0.57; 0.96] 0.025 *	-0.15 [-0.27; -0.02] 0.022 *
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.849				
presence					
N"/N'/N	118 / 118 / 118	128 / 128 / 128			
Presence of SRF and/or IRF in the study eye, n (%)	50 (42.4)	71 (55.5)	0.59 [0.36; 0.98] 0.041 *	0.76 [0.59; 0.99] 0.041 *	-0.13 [-0.26; -0.01] 0.039 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N"/N'/N	250 / 250 / 250	240 / 240 / 240			
Presence of SRF and/or IRF in the study eye, n (%)	102 (40.8)	133 (55.4)	0.56 [0.39; 0.80] 0.001 *	0.74 [0.61; 0.89] 0.001 *	-0.15 [-0.23; -0.06] 0.001 *

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Presence of SRF in the study eye / KESTREL / Week 52, Presence of SRF in the study eye / KITE / Week 52, Presence of SRF in the study eye / KESTREL / Week 100, Presence of SRF in the study eye / KITE / Week 100: logit(proportion) = treatment [by status of SRF].
Presence of SRF in the study eye / Pooled Analysis / Week 100: logit(proportion) = treatment + study + treatment * study [by status of SRF].

Exceptionally applied model (due to redundance of status of SRF and baseline category):
Presence of SRF in the study eye / POOLED: logit(proportion) = treatment + age category + study + treatment * study + status of SRF + treatment * status of SRF.

Table 11.12 Presence of SRF and/or IRF in the study eye by exposure (week 52) (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by exposure (week 52) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Presence of SRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.600**					
KESTREL: Presence of SRF in the study eye, Week 52					
Interaction Test:	p = 0.527				
Non-exposed					
N''/N'/N	58 / 71 / 71	62 / 75 / 75			
Presence of SRF in the study eye, n (%)	3 (4.2)	2 (2.7)	1.39 [0.21; 9.18] 0.734	1.58 [0.27; 9.21] 0.608	0.02 [-0.04; 0.07] 0.607
Exposed					
N''/N'/N	96 / 118 / 118	99 / 112 / 112			
Presence of SRF in the study eye, n (%)	1 (0.8)	2 (1.8)	0.51 [0.04; 5.85] 0.588	0.47 [0.04; 5.16] 0.540	-0.01 [-0.04; 0.02] 0.534
KITE: Presence of SRF in the study eye, Week 52					
Interaction Test:	p = 0.668				
Non-exposed					
N''/N'/N	71 / 85 / 85	76 / 90 / 90			
Presence of SRF in the study eye, n (%)	2 (2.4)	3 (3.3)	0.76 [0.12; 4.94] 0.775	0.71 [0.12; 4.12] 0.699	-0.01 [-0.06; 0.04] 0.696
Exposed					
N''/N'/N	76 / 94 / 94	76 / 91 / 91			
Presence of SRF in the study eye, n (%)	1 (1.1)	3 (3.3)	0.40 [0.04; 4.05] 0.434	0.32 [0.03; 3.05] 0.323	-0.02 [-0.06; 0.02] 0.299
Pooled Analysis: Presence of SRF in the study eye, Week 52					
Interaction Test:	p = 0.394				
Non-exposed					
N''/N'/N	129 / 156 / 156	138 / 165 / 165			
Presence of SRF in the study eye, n (%)	5 (3.2)	5 (3.0)	1.08 [0.29; 4.05] 0.913	1.06 [0.31; 3.59] 0.929	0.00 [-0.04; 0.04] 0.928

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by exposure (week 52) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N''/N'/N	172 / 212 / 212	175 / 203 / 203			
Presence of SRF in the study eye, n (%)	2 (0.9)	5 (2.5)	0.42 [0.08; 2.28] 0.318	0.38 [0.08; 1.96] 0.232	-0.02 [-0.04; 0.01] 0.234
Presence of IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.503**					
KESTREL: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.905				
Non-exposed					
N''/N'/N	58 / 71 / 71	62 / 75 / 75			
Presence of IRF in the study eye, n (%)	40 (56.3)	52 (69.3)	0.55 [0.28; 1.10] 0.092	0.81 [0.63; 1.05] 0.109	-0.13 [-0.29; 0.03] 0.102
Exposed					
N''/N'/N	96 / 118 / 118	99 / 112 / 112			
Presence of IRF in the study eye, n (%)	74 (62.7)	85 (75.9)	0.52 [0.29; 0.93] 0.027 *	0.83 [0.69; 0.98] 0.032 *	-0.13 [-0.25; -0.01] 0.028 *
KITE: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.202				
Non-exposed					
N''/N'/N	71 / 85 / 85	76 / 90 / 90			
Presence of IRF in the study eye, n (%)	49 (57.6)	64 (71.1)	0.57 [0.31; 1.08] 0.085	0.81 [0.65; 1.02] 0.067	-0.13 [-0.28; 0.01] 0.061
Exposed					
N''/N'/N	76 / 94 / 94	76 / 91 / 91			
Presence of IRF in the study eye, n (%)	47 (50.0)	68 (74.7)	0.32 [0.17; 0.61] <.001 *	0.67 [0.53; 0.85] <.001 *	-0.25 [-0.38; -0.11] <.001 *
Pooled Analysis: Presence of IRF in the study eye, Week 52					
Interaction Test:	p = 0.341				
Non-exposed					
N''/N'/N	129 / 156 / 156	138 / 165 / 165			
Presence of IRF in the study eye, n (%)	89 (57.1)	116 (70.3)	0.56 [0.35; 0.90] 0.017 *	0.81 [0.69; 0.96] 0.014 *	-0.13 [-0.24; -0.03] 0.013 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by exposure (week 52) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N''/N'/N	172 / 212 / 212	175 / 203 / 203			
Presence of IRF in the study eye, n (%)	121 (57.1)	153 (75.4)	0.41 [0.27; 0.64] <.001 *	0.76 [0.66; 0.87] <.001 *	-0.18 [-0.27; -0.09] <.001 *
Presence of SRF and/or IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.574**					
KESTREL: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.905				
Non-exposed					
N''/N'/N	71 / 71 / 71	75 / 75 / 75			
Presence of SRF and/or IRF in the study eye, n (%)	40 (56.3)	52 (69.3)	0.55 [0.28; 1.10] 0.092	0.81 [0.63; 1.05] 0.109	-0.13 [-0.29; 0.03] 0.102
Exposed					
N''/N'/N	118 / 118 / 118	112 / 112 / 112			
Presence of SRF and/or IRF in the study eye, n (%)	74 (62.7)	85 (75.9)	0.52 [0.29; 0.93] 0.027 *	0.83 [0.69; 0.98] 0.032 *	-0.13 [-0.25; -0.01] 0.028 *
KITE: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.299				
Non-exposed					
N''/N'/N	85 / 85 / 85	90 / 90 / 90			
Presence of SRF and/or IRF in the study eye, n (%)	49 (57.6)	64 (71.1)	0.57 [0.31; 1.08] 0.084	0.81 [0.65; 1.02] 0.067	-0.13 [-0.28; 0.01] 0.061
Exposed					
N''/N'/N	94 / 94 / 94	91 / 91 / 91			
Presence of SRF and/or IRF in the study eye, n (%)	48 (51.1)	68 (74.7)	0.36 [0.19; 0.67] 0.001 *	0.68 [0.54; 0.86] 0.001 *	-0.24 [-0.37; -0.10] <.001 *
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 52					
Interaction Test:	p = 0.413				
Non-exposed					
N''/N'/N	156 / 156 / 156	165 / 165 / 165			
Presence of SRF and/or IRF in the study eye, n (%)	89 (57.1)	116 (70.3)	0.57 [0.35; 0.90] 0.017 *	0.81 [0.69; 0.96] 0.014 *	-0.13 [-0.24; -0.03] 0.013 *

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by exposure (week 52) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N"/N'/N	212 / 212 / 212	203 / 203 / 203			
Presence of SRF and/or IRF in the study eye, n (%)	122 (57.5)	153 (75.4)	0.43 [0.28; 0.66] <.001 *	0.76 [0.66; 0.88] <.001 *	-0.18 [-0.27; -0.09] <.001 *

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 11.13 Presence of SRF and/or IRF in the study eye by exposure (week 100) (FAS), binary analysis, week 100

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Presence of IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.733**					
KESTREL: Presence of IRF in the study eye, Week 100					
Interaction Test:	N.E.				
Non-exposed					
N"/N'/N	0 / 12 / 12	0 / 13 / 13			
Presence of IRF in the study eye, n (%)	9 (75.0)	13 (100.0)	N.E.	0.75 [0.54; 1.04] 0.084	-0.25 [-0.49; -0.01] 0.046 *
Exposed					
N"/N'/N	148 / 177 / 177	145 / 174 / 174			
Presence of IRF in the study eye, n (%)	69 (39.0)	89 (51.1)	0.61 [0.40; 0.93] 0.022 *	0.76 [0.60; 0.96] 0.023 *	-0.12 [-0.23; -0.02] 0.021 *
KITE: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.651				
Non-exposed					
N"/N'/N	0 / 17 / 17	0 / 12 / 12			
Presence of IRF in the study eye, n (%)	11 (64.7)	9 (75.0)	0.73 [0.14; 3.84] 0.707	0.86 [0.53; 1.39] 0.546	-0.10 [-0.44; 0.23] 0.546
Exposed					
N"/N'/N	133 / 162 / 162	145 / 169 / 169			
Presence of IRF in the study eye, n (%)	62 (38.3)	94 (55.6)	0.49 [0.31; 0.76] 0.001 *	0.69 [0.54; 0.87] 0.002 *	-0.17 [-0.28; -0.07] 0.001 *
Pooled Analysis: Presence of IRF in the study eye, Week 100					
Interaction Test:	p = 0.522				
Non-exposed					
N"/N'/N	0 / 29 / 29	0 / 25 / 25			
Presence of IRF in the study eye, n (%)	20 (69.0)	22 (88.0)	0.33 [0.08; 1.43] 0.140	0.80 [0.60; 1.07] 0.141	-0.17 [-0.38; 0.04] 0.111

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N"/N'/N	281 / 339 / 339	290 / 343 / 343			
Presence of IRF in the study eye, n (%)	131 (38.6)	183 (53.4)	0.54 [0.40; 0.74] <.001 *	0.72 [0.61; 0.86] <.001 *	-0.15 [-0.22; -0.07] <.001 *
Presence of SRF and/or IRF in the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	N.E.				
Non-exposed					
N"/N'/N	12 / 12 / 12	13 / 13 / 13			
Presence of SRF and/or IRF in the study eye, n (%)	9 (75.0)	13 (100.0)	N.E.	0.75 [0.54; 1.04] 0.084	-0.25 [-0.49; -0.01] 0.046 *
Exposed					
N"/N'/N	177 / 177 / 177	174 / 174 / 174			
Presence of SRF and/or IRF in the study eye, n (%)	70 (39.5)	88 (50.6)	0.64 [0.42; 0.98] 0.038 *	0.78 [0.62; 0.99] 0.039 *	-0.11 [-0.21; -0.01] 0.037 *
KITE: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.723				
Non-exposed					
N"/N'/N	17 / 17 / 17	12 / 12 / 12			
Presence of SRF and/or IRF in the study eye, n (%)	11 (64.7)	9 (75.0)	0.67 [0.13; 3.50] 0.631	0.86 [0.53; 1.39] 0.546	-0.10 [-0.44; 0.23] 0.546
Exposed					
N"/N'/N	162 / 162 / 162	169 / 169 / 169			
Presence of SRF and/or IRF in the study eye, n (%)	62 (38.3)	94 (55.6)	0.49 [0.31; 0.76] 0.001 *	0.69 [0.54; 0.87] 0.002 *	-0.17 [-0.28; -0.07] 0.001 *
Pooled Analysis: Presence of SRF and/or IRF in the study eye, Week 100					
Interaction Test:	p = 0.469				
Non-exposed					
N"/N'/N	29 / 29 / 29	25 / 25 / 25			
Presence of SRF and/or IRF in the study eye, n (%)	20 (69.0)	22 (88.0)	0.32 [0.08; 1.38] 0.128	0.80 [0.60; 1.07] 0.141	-0.17 [-0.38; 0.04] 0.111

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by exposure (week 100) (FAS)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N"/N'/N	339 / 339 / 339	343 / 343 / 343			
Presence of SRF and/or IRF in the study eye, n (%)	132 (38.9)	182 (53.1)	0.56 [0.41; 0.76] <.001 *	0.73 [0.62; 0.87] <.001 *	-0.14 [-0.22; -0.07] <.001 *

N: Number of patients
N': Number of patients in the analysis
N": Number of patients with available response value
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: Last observation carried forward (LOCF)

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age category + baseline category + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Presence of IRF in the study eye / KESTREL / Week 100, Presence of SRF and/or IRF in the study eye / KESTREL / Week 100: logit(proportion) = treatment [by exposure (week 100)].

12 Safety analysis: Any adverse event

Table 12-1.1 Any adverse event (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any AE, n (%)	155 (82.0)	148 (79.1)	1.20 [0.72; 2.00] 0.483	1.04 [0.94; 1.14] 0.483	0.03 [-0.05; 0.11] 0.482
KITE, N'/N	179 / 179	181 / 181			
Any AE, n (%)	136 (76.0)	146 (80.7)	0.76 [0.46; 1.25] 0.281	0.94 [0.84; 1.05] 0.282	-0.05 [-0.13; 0.04] 0.280
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any AE, n (%) p_H=0.209	291 (79.1)	294 (79.9)	0.96 [0.67; 1.37] 0.818	0.99 [0.92; 1.07] 0.781	-0.01 [-0.07; 0.05] 0.781
Any AE, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any AE, n (%)	168 (88.9)	163 (87.2)	1.18 [0.63; 2.20] 0.607	1.02 [0.95; 1.10] 0.607	0.02 [-0.05; 0.08] 0.607
KITE, N'/N	179 / 179	181 / 181			
Any AE, n (%)	159 (88.8)	161 (89.0)	0.99 [0.51; 1.91] 0.970	1.00 [0.93; 1.07] 0.970	-0.00 [-0.07; 0.06] 0.970

	Treatment Groups		Comparison		
Any adverse event (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any AE, n (%)	327 (88.9)	324 (88.0)	1.08 [0.69; 1.70] 0.738	1.01 [0.96; 1.06] 0.728	0.01 [-0.04; 0.05] 0.728
p_H=0.703					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-1.2 Any adverse event by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	p = 0.535				
< 65 years					
N'/N	104 / 104	93 / 93			
Any AE, n (%)	87 (83.7)	73 (78.5)	1.40 [0.68; 2.87] 0.356	1.07 [0.93; 1.22] 0.359	0.05 [-0.06; 0.16] 0.356
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any AE, n (%)	68 (80.0)	75 (79.8)	1.01 [0.49; 2.11] 0.972	1.00 [0.87; 1.16] 0.972	0.00 [-0.12; 0.12] 0.972
KITE					
Interaction Test:	p = 0.402				
< 65 years					
N'/N	100 / 100	102 / 102			
Any AE, n (%)	78 (78.0)	81 (79.4)	0.92 [0.47; 1.80] 0.806	0.98 [0.85; 1.13] 0.806	-0.01 [-0.13; 0.10] 0.806
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any AE, n (%)	58 (73.4)	65 (82.3)	0.59 [0.28; 1.28] 0.182	0.89 [0.75; 1.06] 0.183	-0.09 [-0.22; 0.04] 0.177
Pooled Analysis					
Interaction Test:	p = 0.305				
< 65 years					
N'/N	204 / 204	195 / 195			
Any AE, n (%)	165 (80.9)	154 (79.0)	1.14 [0.70; 1.87] 0.599	1.02 [0.93; 1.13] 0.649	0.02 [-0.06; 0.10] 0.649
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any AE, n (%)	126 (76.8)	140 (80.9)	0.78 [0.46; 1.33] 0.362	0.95 [0.85; 1.06] 0.364	-0.04 [-0.13; 0.05] 0.363

	Treatment Groups		Comparison		
Any adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.703**					
KESTREL					
Interaction Test:	p = 0.338				
< 65 years					
N'/N	104 / 104	93 / 93			
Any AE, n (%)	97 (93.3)	83 (89.2)	1.67 [0.61; 4.58] 0.320	1.05 [0.96; 1.14] 0.323	0.04 [-0.04; 0.12] 0.320
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any AE, n (%)	71 (83.5)	80 (85.1)	0.89 [0.40; 1.99] 0.772	0.98 [0.86; 1.11] 0.772	-0.02 [-0.12; 0.09] 0.772
KITE					
Interaction Test:	p = 0.974				
< 65 years					
N'/N	100 / 100	102 / 102			
Any AE, n (%)	88 (88.0)	90 (88.2)	0.98 [0.42; 2.29] 0.959	1.00 [0.90; 1.10] 0.959	-0.00 [-0.09; 0.09] 0.959
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any AE, n (%)	71 (89.9)	71 (89.9)	1.00 [0.36; 2.81] 1.000	1.00 [0.90; 1.11] 1.000	0.00 [-0.09; 0.09] 1.000
Pooled Analysis					
Interaction Test:	p = 0.537				
< 65 years					
N'/N	204 / 204	195 / 195			
Any AE, n (%)	185 (90.7)	173 (88.7)	1.24 [0.65; 2.37] 0.513	1.02 [0.95; 1.09] 0.541	0.02 [-0.04; 0.08] 0.541

	Treatment Groups		Comparison		
Any adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any AE, n (%)	142 (86.6)	151 (87.3)	0.93 [0.49; 1.76] 0.831	0.99 [0.91; 1.08] 0.820	-0.01 [-0.08; 0.06] 0.819

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-1.3 Any adverse event by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	p = 0.337				
Male					
N'/N	110 / 110	126 / 126			
Any AE, n (%)	87 (79.1)	100 (79.4)	0.98 [0.52; 1.85] 0.959	1.00 [0.87; 1.14] 0.959	-0.00 [-0.11; 0.10] 0.959
Female					
N'/N	79 / 79	61 / 61			
Any AE, n (%)	68 (86.1)	48 (78.7)	1.67 [0.69; 4.05] 0.253	1.09 [0.93; 1.28] 0.265	0.07 [-0.05; 0.20] 0.258
KITE					
Interaction Test:	p = 0.210				
Male					
N'/N	120 / 120	115 / 115			
Any AE, n (%)	93 (77.5)	90 (78.3)	0.96 [0.52; 1.77] 0.888	0.99 [0.86; 1.13] 0.888	-0.01 [-0.11; 0.10] 0.888
Female					
N'/N	59 / 59	66 / 66			
Any AE, n (%)	43 (72.9)	56 (84.8)	0.48 [0.20; 1.16] 0.104	0.86 [0.71; 1.03] 0.109	-0.12 [-0.26; 0.02] 0.100
Pooled Analysis					
Interaction Test:	p = 0.816				
Male					
N'/N	230 / 230	241 / 241			
Any AE, n (%)	180 (78.3)	190 (78.8)	0.98 [0.63; 1.53] 0.945	0.99 [0.90; 1.09] 0.892	-0.01 [-0.08; 0.07] 0.891
Female					
N'/N	138 / 138	127 / 127			
Any AE, n (%)	111 (80.4)	104 (81.9)	0.90 [0.48; 1.67] 0.737	0.98 [0.87; 1.10] 0.709	-0.02 [-0.11; 0.08] 0.712

	Treatment Groups		Comparison		
Any adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.703**					
KESTREL					
Interaction Test:	p = 0.316				
Male					
N'/N	110 / 110	126 / 126			
Any AE, n (%)	95 (86.4)	110 (87.3)	0.92 [0.43; 1.96] 0.832	0.99 [0.90; 1.09] 0.832	-0.01 [-0.10; 0.08] 0.832
Female					
N'/N	79 / 79	61 / 61			
Any AE, n (%)	73 (92.4)	53 (86.9)	1.84 [0.60; 5.61] 0.286	1.06 [0.95; 1.19] 0.299	0.06 [-0.05; 0.16] 0.293
KITE					
Interaction Test:	p = 0.547				
Male					
N'/N	120 / 120	115 / 115			
Any AE, n (%)	106 (88.3)	100 (87.0)	1.14 [0.52; 2.47] 0.748	1.02 [0.92; 1.12] 0.749	0.01 [-0.07; 0.10] 0.749
Female					
N'/N	59 / 59	66 / 66			
Any AE, n (%)	53 (89.8)	61 (92.4)	0.72 [0.21; 2.51] 0.611	0.97 [0.87; 1.09] 0.613	-0.03 [-0.13; 0.07] 0.612
Pooled Analysis					
Interaction Test:	p = 0.741				
Male					
N'/N	230 / 230	241 / 241			
Any AE, n (%)	201 (87.4)	210 (87.1)	1.02 [0.59; 1.75] 0.949	1.00 [0.94; 1.07] 0.943	0.00 [-0.06; 0.06] 0.943

	Treatment Groups		Comparison		
Any adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any AE, n (%)	126 (91.3)	114 (89.8)	1.20 [0.53; 2.75] 0.662	1.02 [0.94; 1.10] 0.646	0.02 [-0.06; 0.09] 0.649

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-1.4 Any adverse event by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	p = 0.174				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any AE, n (%)	58 (78.4)	53 (82.8)	0.75 [0.32; 1.77] 0.513	0.95 [0.80; 1.11] 0.510	-0.04 [-0.18; 0.09] 0.509
> 65 letters					
N'/N	115 / 115	123 / 123			
Any AE, n (%)	97 (84.3)	95 (77.2)	1.59 [0.82; 3.06] 0.167	1.09 [0.96; 1.24] 0.164	0.07 [-0.03; 0.17] 0.161
KITE					
Interaction Test:	p = 0.447				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any AE, n (%)	47 (72.3)	74 (81.3)	0.60 [0.28; 1.28] 0.186	0.89 [0.74; 1.06] 0.200	-0.09 [-0.23; 0.04] 0.191
> 65 letters					
N'/N	114 / 114	90 / 90			
Any AE, n (%)	89 (78.1)	72 (80.0)	0.89 [0.45; 1.76] 0.737	0.98 [0.85; 1.12] 0.736	-0.02 [-0.13; 0.09] 0.736
Pooled Analysis					
Interaction Test:	p = 0.134				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any AE, n (%)	105 (75.5)	127 (81.9)	0.69 [0.39; 1.21] 0.190	0.92 [0.81; 1.04] 0.155	-0.07 [-0.16; 0.03] 0.156
> 65 letters					
N'/N	229 / 229	213 / 213			
Any AE, n (%)	186 (81.2)	167 (78.4)	1.20 [0.75; 1.92] 0.440	1.04 [0.95; 1.14] 0.439	0.03 [-0.05; 0.10] 0.438

	Treatment Groups		Comparison		
Any adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.703**					
KESTREL					
Interaction Test:	p = 0.191				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any AE, n (%)	63 (85.1)	57 (89.1)	0.70 [0.26; 1.94] 0.496	0.96 [0.84; 1.09] 0.491	-0.04 [-0.15; 0.07] 0.490
> 65 letters					
N'/N	115 / 115	123 / 123			
Any AE, n (%)	105 (91.3)	106 (86.2)	1.68 [0.74; 3.85] 0.216	1.06 [0.97; 1.16] 0.211	0.05 [-0.03; 0.13] 0.208
KITE					
Interaction Test:	p = 0.050				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any AE, n (%)	54 (83.1)	83 (91.2)	0.47 [0.18; 1.25] 0.132	0.91 [0.80; 1.03] 0.149	-0.08 [-0.19; 0.03] 0.141
> 65 letters					
N'/N	114 / 114	90 / 90			
Any AE, n (%)	105 (92.1)	78 (86.7)	1.79 [0.72; 4.47] 0.209	1.06 [0.96; 1.17] 0.220	0.05 [-0.03; 0.14] 0.215
Pooled Analysis					
Interaction Test:	p = 0.021 *				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any AE, n (%)	117 (84.2)	140 (90.3)	0.58 [0.28; 1.16] 0.123	0.93 [0.85; 1.02] 0.117	-0.06 [-0.14; 0.02] 0.120

	Treatment Groups		Comparison		
Any adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any AE, n (%)	210 (91.7)	184 (86.4)	1.73 [0.93; 3.19] 0.081	1.06 [0.99; 1.13] 0.077	0.05 [-0.01; 0.11] 0.077

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-1.5 Any adverse event by region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	p = 0.321				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any AE, n (%)	76 (84.4)	71 (85.5)	0.92 [0.40; 2.12] 0.840	0.99 [0.87; 1.12] 0.840	-0.01 [-0.12; 0.10] 0.840
European Region					
N'/N	69 / 69	75 / 75			
Any AE, n (%)	53 (76.8)	57 (76.0)	1.05 [0.48; 2.26] 0.909	1.01 [0.84; 1.21] 0.909	0.01 [-0.13; 0.15] 0.909
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any AE, n (%)	26 (86.7)	20 (69.0)	2.93 [0.79; 10.89] 0.109	1.26 [0.95; 1.67] 0.112	0.18 [-0.03; 0.38] 0.095
KITE					
Interaction Test:	p = 0.463				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any AE, n (%)	18 (69.2)	13 (61.9)	1.38 [0.41; 4.65] 0.599	1.12 [0.73; 1.71] 0.604	0.07 [-0.20; 0.35] 0.599
European Region					
N'/N	135 / 135	132 / 132			
Any AE, n (%)	102 (75.6)	109 (82.6)	0.65 [0.36; 1.18] 0.161	0.91 [0.81; 1.04] 0.160	-0.07 [-0.17; 0.03] 0.157
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any AE, n (%)	16 (88.9)	24 (85.7)	1.33 [0.22; 8.16] 0.756	1.04 [0.83; 1.30] 0.749	0.03 [-0.16; 0.23] 0.749

	Treatment Groups		Comparison		
Any adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.290				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any AE, n (%)	76 (84.4)	71 (85.5)	0.69 [0.27; 1.78] 0.446	0.99 [0.87; 1.12] 0.840	-0.01 [-0.12; 0.10] 0.840
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any AE, n (%)	18 (69.2)	13 (61.9)	1.85 [0.51; 6.74] 0.350	1.12 [0.73; 1.71] 0.602	0.07 [-0.20; 0.35] 0.599
European Region					
N'/N	204 / 204	207 / 207			
Any AE, n (%)	155 (76.0)	166 (80.2)	0.83 [0.51; 1.35] 0.463	0.95 [0.85; 1.05] 0.295	-0.04 [-0.12; 0.04] 0.294
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any AE, n (%)	42 (87.5)	44 (77.2)	2.02 [0.70; 5.84] 0.193	1.15 [0.96; 1.38] 0.132	0.12 [-0.03; 0.26] 0.120
Any AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.703**					
KESTREL					
Interaction Test:	p = 0.719				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any AE, n (%)	81 (90.0)	76 (91.6)	0.83 [0.29; 2.34] 0.723	0.98 [0.89; 1.08] 0.722	-0.02 [-0.10; 0.07] 0.721
European Region					
N'/N	69 / 69	75 / 75			
Any AE, n (%)	61 (88.4)	63 (84.0)	1.45 [0.56; 3.80] 0.447	1.05 [0.92; 1.20] 0.443	0.04 [-0.07; 0.16] 0.442
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any AE, n (%)	26 (86.7)	24 (82.8)	1.35 [0.33; 5.64] 0.677	1.05 [0.84; 1.30] 0.678	0.04 [-0.14; 0.22] 0.676

	Treatment Groups		Comparison		
Any adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.687				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any AE, n (%)	20 (76.9)	14 (66.7)	1.67 [0.46; 6.03] 0.437	1.15 [0.80; 1.67] 0.447	0.10 [-0.16; 0.36] 0.437
European Region					
N'/N	135 / 135	132 / 132			
Any AE, n (%)	123 (91.1)	122 (92.4)	0.84 [0.35; 2.02] 0.697	0.99 [0.92; 1.06] 0.696	-0.01 [-0.08; 0.05] 0.696
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any AE, n (%)	16 (88.9)	25 (89.3)	0.96 [0.14; 6.39] 0.966	1.00 [0.81; 1.23] 0.966	-0.00 [-0.19; 0.18] 0.966
Pooled Analysis					
Interaction Test:	p = 0.711				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any AE, n (%)	81 (90.0)	76 (91.6)	0.65 [0.20; 2.11] 0.475	0.98 [0.89; 1.08] 0.723	-0.02 [-0.10; 0.07] 0.721
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any AE, n (%)	20 (76.9)	14 (66.7)	2.14 [0.52; 8.81] 0.290	1.15 [0.80; 1.67] 0.439	0.10 [-0.16; 0.36] 0.437
European Region					
N'/N	204 / 204	207 / 207			
Any AE, n (%)	184 (90.2)	185 (89.4)	1.11 [0.58; 2.13] 0.745	1.01 [0.94; 1.08] 0.818	0.01 [-0.05; 0.07] 0.817

	Treatment Groups		Comparison		
Any adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any AE, n (%)	42 (87.5)	49 (86.0)	1.13 [0.36; 3.57] 0.838	1.02 [0.88; 1.19] 0.759	0.02 [-0.11; 0.15] 0.757

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-1.6 Any adverse event by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any AE, n (%)	8 (66.7)	6 (100.0)	N.E.	0.67 [0.45; 0.99] 0.047 *	-0.33 [-0.60; -0.07] 0.014 *
Type 2					
N'/N	177 / 177	181 / 181			
Any AE, n (%)	147 (83.1)	142 (78.5)	1.35 [0.79; 2.28] 0.271	1.06 [0.96; 1.17] 0.270	0.05 [-0.04; 0.13] 0.269
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any AE, n (%)	19 (100.0)	7 (100.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	160 / 160	174 / 174			
Any AE, n (%)	117 (73.1)	139 (79.9)	0.69 [0.41; 1.14] 0.146	0.92 [0.81; 1.03] 0.148	-0.07 [-0.16; 0.02] 0.145
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any AE, n (%)	27 (87.1)	13 (100.0)	N.E.	0.70 [0.45; 1.10] 0.187	-0.15 [-0.27; -0.02] 0.021 *
Type 2					
N'/N	337 / 337	355 / 355			
Any AE, n (%)	264 (78.3)	281 (79.2)	0.97 [0.67; 1.40] 0.856	0.99 [0.91; 1.07] 0.777	-0.01 [-0.07; 0.05] 0.778
Any AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.703**					

	Treatment Groups		Comparison		
Any adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any AE, n (%)	10 (83.3)	6 (100.0)	N.E.	0.83 [0.65; 1.07] 0.158	-0.17 [-0.38; 0.04] 0.121
Type 2					
N'/N	177 / 177	181 / 181			
Any AE, n (%)	158 (89.3)	157 (86.7)	1.27 [0.67; 2.41] 0.463	1.03 [0.95; 1.11] 0.462	0.03 [-0.04; 0.09] 0.462
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any AE, n (%)	19 (100.0)	7 (100.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	160 / 160	174 / 174			
Any AE, n (%)	140 (87.5)	154 (88.5)	0.91 [0.47; 1.76] 0.777	0.99 [0.91; 1.07] 0.778	-0.01 [-0.08; 0.06] 0.778
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any AE, n (%)	29 (93.5)	13 (100.0)	N.E.	0.87 [0.62; 1.22] 0.482	-0.07 [-0.16; 0.02] 0.118

	Treatment Groups		Comparison		
Any adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any AE, n (%)	298 (88.4)	311 (87.6)	1.08 [0.68; 1.71] 0.747	1.01 [0.96; 1.07] 0.740	0.01 [-0.04; 0.06] 0.739

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE, Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by diabetes type].
Week 52 / Pooled Analysis, Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 12-1.7 Any adverse event by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	p = 0.378				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any AE, n (%)	63 (82.9)	82 (76.6)	1.48 [0.70; 3.12] 0.305	1.08 [0.93; 1.25] 0.293	0.06 [-0.05; 0.18] 0.293
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any AE, n (%)	91 (81.3)	66 (82.5)	0.92 [0.44; 1.94] 0.825	0.98 [0.86; 1.13] 0.824	-0.01 [-0.12; 0.10] 0.824
KITE					
Interaction Test:	p = 0.698				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any AE, n (%)	59 (72.0)	76 (79.2)	0.67 [0.34; 1.34] 0.263	0.91 [0.77; 1.08] 0.270	-0.07 [-0.20; 0.05] 0.264
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any AE, n (%)	77 (79.4)	70 (82.4)	0.83 [0.39; 1.74] 0.612	0.96 [0.84; 1.11] 0.610	-0.03 [-0.14; 0.08] 0.610
Pooled Analysis					
Interaction Test:	p = 0.758				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any AE, n (%)	122 (77.2)	158 (77.8)	0.98 [0.59; 1.62] 0.941	0.99 [0.89; 1.11] 0.917	-0.00 [-0.09; 0.08] 0.917
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any AE, n (%)	168 (80.4)	136 (82.4)	0.88 [0.52; 1.48] 0.621	0.97 [0.88; 1.07] 0.607	-0.02 [-0.10; 0.06] 0.604

	Treatment Groups		Comparison		
Any adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.703**					
KESTREL					
Interaction Test:	p = 0.665				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any AE, n (%)	66 (86.8)	93 (86.9)	0.99 [0.42; 2.37] 0.988	1.00 [0.89; 1.12] 0.988	-0.00 [-0.10; 0.10] 0.988
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any AE, n (%)	101 (90.2)	70 (87.5)	1.31 [0.53; 3.25] 0.559	1.03 [0.93; 1.14] 0.566	0.03 [-0.06; 0.12] 0.564
KITE					
Interaction Test:	p = 0.627				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any AE, n (%)	72 (87.8)	86 (89.6)	0.84 [0.33; 2.12] 0.708	0.98 [0.88; 1.09] 0.710	-0.02 [-0.11; 0.08] 0.709
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any AE, n (%)	87 (89.7)	75 (88.2)	1.16 [0.46; 2.94] 0.754	1.02 [0.92; 1.13] 0.755	0.01 [-0.08; 0.11] 0.755
Pooled Analysis					
Interaction Test:	p = 0.522				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any AE, n (%)	138 (87.3)	179 (88.2)	0.92 [0.49; 1.73] 0.796	0.99 [0.92; 1.07] 0.791	-0.01 [-0.08; 0.06] 0.791

	Treatment Groups		Comparison		
Any adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any AE, n (%)	188 (90.0)	145 (87.9)	1.24 [0.65; 2.37] 0.521	1.02 [0.95; 1.10] 0.525	0.02 [-0.04; 0.09] 0.528

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-1.8 Any adverse event by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	p = 0.494				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any AE, n (%)	102 (85.0)	91 (82.7)	1.18 [0.59; 2.39] 0.640	1.03 [0.92; 1.15] 0.641	0.02 [-0.07; 0.12] 0.640
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any AE, n (%)	22 (73.3)	31 (79.5)	0.71 [0.23; 2.18] 0.549	0.92 [0.71; 1.21] 0.556	-0.06 [-0.26; 0.14] 0.552
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any AE, n (%)	31 (79.5)	26 (68.4)	1.79 [0.64; 5.04] 0.271	1.16 [0.89; 1.52] 0.274	0.11 [-0.08; 0.31] 0.265
KITE					
Interaction Test:	p = 0.560				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any AE, n (%)	61 (71.8)	75 (81.5)	0.58 [0.28; 1.17] 0.126	0.88 [0.75; 1.04] 0.130	-0.10 [-0.22; 0.03] 0.124
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any AE, n (%)	39 (76.5)	37 (75.5)	1.05 [0.42; 2.64] 0.911	1.01 [0.81; 1.26] 0.911	0.01 [-0.16; 0.18] 0.911
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any AE, n (%)	36 (83.7)	34 (85.0)	0.91 [0.28; 2.97] 0.873	0.98 [0.82; 1.19] 0.873	-0.01 [-0.17; 0.14] 0.873

	Treatment Groups		Comparison		
Any adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.551				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any AE, n (%)	163 (79.5)	166 (82.2)	0.82 [0.50; 1.35] 0.441	0.96 [0.88; 1.06] 0.448	-0.03 [-0.11; 0.05] 0.448
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any AE, n (%)	61 (75.3)	68 (77.3)	0.96 [0.47; 1.96] 0.901	0.98 [0.82; 1.16] 0.772	-0.02 [-0.15; 0.11] 0.771
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any AE, n (%)	67 (81.7)	60 (76.9)	1.37 [0.63; 2.97] 0.422	1.06 [0.91; 1.24] 0.465	0.05 [-0.08; 0.17] 0.464
Any AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.703**					
KESTREL					
Interaction Test:	p = 0.487				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any AE, n (%)	112 (93.3)	100 (90.9)	1.40 [0.53; 3.69] 0.496	1.03 [0.95; 1.11] 0.497	0.02 [-0.05; 0.09] 0.496
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any AE, n (%)	23 (76.7)	33 (84.6)	0.60 [0.18; 2.01] 0.405	0.91 [0.71; 1.15] 0.418	-0.08 [-0.27; 0.11] 0.410
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any AE, n (%)	33 (84.6)	30 (78.9)	1.47 [0.46; 4.72] 0.521	1.07 [0.87; 1.32] 0.521	0.06 [-0.12; 0.23] 0.519

	Treatment Groups		Comparison		
Any adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.708				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any AE, n (%)	76 (89.4)	82 (89.1)	1.03 [0.40; 2.67] 0.952	1.00 [0.91; 1.11] 0.952	0.00 [-0.09; 0.09] 0.952
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any AE, n (%)	44 (86.3)	41 (83.7)	1.23 [0.41; 3.68] 0.716	1.03 [0.87; 1.22] 0.716	0.03 [-0.11; 0.17] 0.716
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any AE, n (%)	39 (90.7)	38 (95.0)	0.51 [0.09; 2.97] 0.456	0.95 [0.85; 1.08] 0.446	-0.04 [-0.15; 0.07] 0.443
Pooled Analysis					
Interaction Test:	p = 0.860				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any AE, n (%)	188 (91.7)	182 (90.1)	1.21 [0.61; 2.41] 0.577	1.02 [0.96; 1.08] 0.601	0.01 [-0.04; 0.07] 0.601
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any AE, n (%)	67 (82.7)	74 (84.1)	0.90 [0.40; 2.03] 0.800	0.98 [0.85; 1.12] 0.773	-0.02 [-0.13; 0.10] 0.773

	Treatment Groups		Comparison		
Any adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any AE, n (%)	72 (87.8)	68 (87.2)	1.06 [0.41; 2.70] 0.909	1.01 [0.90; 1.13] 0.923	0.00 [-0.10; 0.11] 0.923

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-1.9 Any adverse event by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	p = 0.339				
focal					
N'/N	59 / 59	48 / 48			
Any AE, n (%)	46 (78.0)	32 (66.7)	1.77 [0.75; 4.18] 0.193	1.17 [0.92; 1.49] 0.204	0.11 [-0.06; 0.28] 0.193
diffuse					
N'/N	127 / 127	134 / 134			
Any AE, n (%)	106 (83.5)	111 (82.8)	1.05 [0.55; 2.00] 0.892	1.01 [0.90; 1.12] 0.892	0.01 [-0.08; 0.10] 0.892
KITE					
Interaction Test:	p = 0.357				
focal					
N'/N	63 / 63	66 / 66			
Any AE, n (%)	45 (71.4)	54 (81.8)	0.56 [0.24; 1.27] 0.165	0.87 [0.72; 1.06] 0.168	-0.10 [-0.25; 0.04] 0.161
diffuse					
N'/N	115 / 115	109 / 109			
Any AE, n (%)	90 (78.3)	87 (79.8)	0.91 [0.48; 1.73] 0.775	0.98 [0.86; 1.12] 0.775	-0.02 [-0.12; 0.09] 0.775
Pooled Analysis					
Interaction Test:	p = 0.955				
focal					
N'/N	122 / 122	114 / 114			
Any AE, n (%)	91 (74.6)	86 (75.4)	0.98 [0.54; 1.78] 0.958	0.99 [0.85; 1.15] 0.914	-0.01 [-0.12; 0.11] 0.915
diffuse					
N'/N	242 / 242	243 / 243			
Any AE, n (%)	196 (81.0)	198 (81.5)	0.96 [0.61; 1.52] 0.873	1.00 [0.91; 1.08] 0.915	-0.00 [-0.07; 0.07] 0.915

	Treatment Groups		Comparison		
Any adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.703**					
KESTREL					
Interaction Test:	p = 0.288				
focal					
N'/N	59 / 59	48 / 48			
Any AE, n (%)	51 (86.4)	37 (77.1)	1.90 [0.69; 5.17] 0.212	1.12 [0.93; 1.35] 0.223	0.09 [-0.05; 0.24] 0.214
diffuse					
N'/N	127 / 127	134 / 134			
Any AE, n (%)	114 (89.8)	121 (90.3)	0.94 [0.42; 2.12] 0.885	0.99 [0.92; 1.08] 0.885	-0.01 [-0.08; 0.07] 0.885
KITE					
Interaction Test:	p = 0.588				
focal					
N'/N	63 / 63	66 / 66			
Any AE, n (%)	57 (90.5)	58 (87.9)	1.31 [0.43; 4.01] 0.636	1.03 [0.91; 1.16] 0.635	0.03 [-0.08; 0.13] 0.634
diffuse					
N'/N	115 / 115	109 / 109			
Any AE, n (%)	101 (87.8)	97 (89.0)	0.89 [0.39; 2.03] 0.786	0.99 [0.90; 1.09] 0.785	-0.01 [-0.10; 0.07] 0.785
Pooled Analysis					
Interaction Test:	p = 0.249				
focal					
N'/N	122 / 122	114 / 114			
Any AE, n (%)	108 (88.5)	95 (83.3)	1.57 [0.74; 3.30] 0.236	1.07 [0.96; 1.19] 0.212	0.06 [-0.03; 0.15] 0.212

	Treatment Groups		Comparison		
Any adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any AE, n (%)	215 (88.8)	218 (89.7)	0.90 [0.50; 1.60] 0.720	0.99 [0.93; 1.05] 0.769	-0.01 [-0.06; 0.05] 0.769

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-1.10 Any adverse event by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	p = 0.220				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any AE, n (%)	87 (81.3)	73 (76.0)	1.37 [0.70; 2.69] 0.360	1.07 [0.93; 1.24] 0.363	0.05 [-0.06; 0.17] 0.361
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any AE, n (%)	59 (84.3)	56 (78.9)	1.44 [0.61; 3.39] 0.409	1.07 [0.91; 1.25] 0.408	0.05 [-0.07; 0.18] 0.406
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any AE, n (%)	9 (75.0)	19 (95.0)	0.16 [0.01; 1.74] 0.131	0.79 [0.56; 1.11] 0.175	-0.20 [-0.46; 0.06] 0.136
KITE					
Interaction Test:	p = 0.317				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any AE, n (%)	68 (80.0)	64 (78.0)	1.12 [0.53; 2.37] 0.757	1.03 [0.88; 1.20] 0.757	0.02 [-0.10; 0.14] 0.757
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any AE, n (%)	55 (74.3)	65 (82.3)	0.62 [0.29; 1.36] 0.234	0.90 [0.76; 1.07] 0.237	-0.08 [-0.21; 0.05] 0.232
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any AE, n (%)	13 (65.0)	16 (84.2)	0.35 [0.07; 1.62] 0.179	0.77 [0.53; 1.12] 0.177	-0.19 [-0.46; 0.07] 0.156

	Treatment Groups		Comparison		
Any adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.086				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any AE, n (%)	155 (80.7)	137 (77.0)	1.24 [0.75; 2.05] 0.398	1.05 [0.94; 1.17] 0.376	0.04 [-0.05; 0.12] 0.376
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any AE, n (%)	114 (79.2)	121 (80.7)	0.93 [0.52; 1.65] 0.797	0.98 [0.87; 1.10] 0.742	-0.02 [-0.11; 0.08] 0.743
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any AE, n (%)	22 (68.8)	35 (89.7)	0.26 [0.07; 0.95] 0.042 *	0.78 [0.60; 1.01] 0.042 *	-0.20 [-0.38; -0.01] 0.042 *
Any AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.703**					
KESTREL					
Interaction Test:	N.E.				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any AE, n (%)	96 (89.7)	81 (84.4)	1.62 [0.70; 3.71] 0.258	1.06 [0.96; 1.18] 0.262	0.05 [-0.04; 0.15] 0.258
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any AE, n (%)	61 (87.1)	62 (87.3)	0.98 [0.37; 2.65] 0.974	1.00 [0.88; 1.13] 0.974	-0.00 [-0.11; 0.11] 0.974
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any AE, n (%)	11 (91.7)	20 (100.0)	N.E.	0.92 [0.77; 1.09] 0.317	-0.08 [-0.24; 0.07] 0.296

	Treatment Groups		Comparison		
Any adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.342				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any AE, n (%)	77 (90.6)	70 (85.4)	1.65 [0.64; 4.27] 0.302	1.06 [0.95; 1.19] 0.302	0.05 [-0.05; 0.15] 0.299
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any AE, n (%)	66 (89.2)	74 (93.7)	0.56 [0.17; 1.79] 0.326	0.95 [0.86; 1.05] 0.326	-0.04 [-0.13; 0.04] 0.323
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any AE, n (%)	16 (80.0)	16 (84.2)	0.75 [0.14; 3.90] 0.732	0.95 [0.71; 1.27] 0.732	-0.04 [-0.28; 0.20] 0.731
Pooled Analysis					
Interaction Test:	p = 0.159				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any AE, n (%)	173 (90.1)	151 (84.8)	1.62 [0.87; 3.04] 0.131	1.06 [0.98; 1.15] 0.124	0.05 [-0.01; 0.12] 0.125
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any AE, n (%)	127 (88.2)	136 (90.7)	0.77 [0.36; 1.63] 0.495	0.97 [0.90; 1.05] 0.500	-0.02 [-0.09; 0.05] 0.500

	Treatment Groups		Comparison		
Any adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any AE, n (%)	27 (84.4)	36 (92.3)	0.45 [0.10; 2.04] 0.299	0.93 [0.77; 1.11] 0.410	-0.06 [-0.21; 0.09] 0.436

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL: logit(proportion) = treatment [by CSFT].

Table 12-1.11 Any adverse event by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	p = 0.069				
presence					
N'/N	62 / 62	61 / 61			
Any AE, n (%)	49 (79.0)	53 (86.9)	0.57 [0.22; 1.49] 0.251	0.91 [0.77; 1.07] 0.249	-0.08 [-0.21; 0.05] 0.244
absence					
N'/N	127 / 127	126 / 126			
Any AE, n (%)	106 (83.5)	95 (75.4)	1.65 [0.89; 3.06] 0.114	1.11 [0.98; 1.26] 0.115	0.08 [-0.02; 0.18] 0.111
KITE					
Interaction Test:	p = 0.500				
presence					
N'/N	56 / 56	67 / 67			
Any AE, n (%)	44 (78.6)	53 (79.1)	0.97 [0.41; 2.31] 0.943	0.99 [0.83; 1.19] 0.943	-0.01 [-0.15; 0.14] 0.943
absence					
N'/N	123 / 123	114 / 114			
Any AE, n (%)	92 (74.8)	93 (81.6)	0.67 [0.36; 1.25] 0.209	0.92 [0.80; 1.05] 0.206	-0.07 [-0.17; 0.04] 0.204
Pooled Analysis					
Interaction Test:	p = 0.427				
presence					
N'/N	118 / 118	128 / 128			
Any AE, n (%)	93 (78.8)	106 (82.8)	0.78 [0.41; 1.47] 0.438	0.95 [0.84; 1.07] 0.403	-0.04 [-0.14; 0.06] 0.402
absence					
N'/N	250 / 250	240 / 240			
Any AE, n (%)	198 (79.2)	188 (78.3)	1.06 [0.69; 1.64] 0.785	1.01 [0.92; 1.11] 0.810	0.01 [-0.06; 0.08] 0.810

	Treatment Groups		Comparison		
Any adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.703**					
KESTREL					
Interaction Test:	p = 0.046 *				
presence					
N'/N	62 / 62	61 / 61			
Any AE, n (%)	53 (85.5)	57 (93.4)	0.41 [0.12; 1.42] 0.161	0.91 [0.81; 1.03] 0.153	-0.08 [-0.19; 0.03] 0.147
absence					
N'/N	127 / 127	126 / 126			
Any AE, n (%)	115 (90.6)	106 (84.1)	1.81 [0.84; 3.88] 0.128	1.08 [0.98; 1.18] 0.126	0.06 [-0.02; 0.15] 0.123
KITE					
Interaction Test:	p = 0.767				
presence					
N'/N	56 / 56	67 / 67			
Any AE, n (%)	50 (89.3)	59 (88.1)	1.13 [0.37; 3.48] 0.831	1.01 [0.89; 1.15] 0.830	0.01 [-0.10; 0.12] 0.830
absence					
N'/N	123 / 123	114 / 114			
Any AE, n (%)	109 (88.6)	102 (89.5)	0.92 [0.40; 2.07] 0.833	0.99 [0.91; 1.08] 0.833	-0.01 [-0.09; 0.07] 0.833
Pooled Analysis					
Interaction Test:	p = 0.215				
presence					
N'/N	118 / 118	128 / 128			
Any AE, n (%)	103 (87.3)	116 (90.6)	0.71 [0.32; 1.59] 0.408	0.96 [0.88; 1.05] 0.399	-0.03 [-0.11; 0.04] 0.398

	Treatment Groups		Comparison		
Any adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any AE, n (%)	224 (89.6)	208 (86.7)	1.32 [0.76; 2.29] 0.324	1.03 [0.97; 1.10] 0.320	0.03 [-0.03; 0.09] 0.320

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-1.12 Any adverse event by exposure (week 52) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	p = 0.952				
Non-exposed					
N'/N	71 / 71	75 / 75			
Any AE, n (%)	59 (83.1)	60 (80.0)	1.23 [0.53; 2.85] 0.630	1.04 [0.89; 1.21] 0.629	0.03 [-0.09; 0.16] 0.629
Exposed					
N'/N	118 / 118	112 / 112			
Any AE, n (%)	96 (81.4)	88 (78.6)	1.19 [0.62; 2.27] 0.598	1.04 [0.91; 1.18] 0.599	0.03 [-0.08; 0.13] 0.598
KITE					
Interaction Test:	p = 0.639				
Non-exposed					
N'/N	85 / 85	90 / 90			
Any AE, n (%)	67 (78.8)	73 (81.1)	0.87 [0.41; 1.82] 0.706	0.97 [0.84; 1.13] 0.706	-0.02 [-0.14; 0.10] 0.706
Exposed					
N'/N	94 / 94	91 / 91			
Any AE, n (%)	69 (73.4)	73 (80.2)	0.68 [0.34; 1.36] 0.274	0.92 [0.78; 1.07] 0.273	-0.07 [-0.19; 0.05] 0.270
Pooled Analysis					
Interaction Test:	p = 0.693				
Non-exposed					
N'/N	156 / 156	165 / 165			
Any AE, n (%)	126 (80.8)	133 (80.6)	1.05 [0.60; 1.83] 0.868	1.00 [0.90; 1.12] 0.971	0.00 [-0.08; 0.09] 0.971
Exposed					
N'/N	212 / 212	203 / 203			
Any AE, n (%)	165 (77.8)	161 (79.3)	0.90 [0.56; 1.45] 0.677	0.98 [0.89; 1.09] 0.711	-0.01 [-0.09; 0.06] 0.711

	Treatment Groups		Comparison		
Any adverse event by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-1.13 Any adverse event by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.703**					
KESTREL					
Interaction Test:	p = 0.487				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any AE, n (%)	10 (83.3)	9 (69.2)	2.22 [0.33; 15.18] 0.415	1.20 [0.77; 1.87] 0.411	0.14 [-0.19; 0.47] 0.399
Exposed					
N'/N	177 / 177	174 / 174			
Any AE, n (%)	158 (89.3)	154 (88.5)	1.08 [0.55; 2.10] 0.821	1.01 [0.94; 1.09] 0.821	0.01 [-0.06; 0.07] 0.821
KITE					
Interaction Test:	p = 0.336				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any AE, n (%)	15 (88.2)	9 (75.0)	2.50 [0.35; 17.95] 0.362	1.18 [0.81; 1.70] 0.389	0.13 [-0.16; 0.42] 0.369
Exposed					
N'/N	162 / 162	169 / 169			
Any AE, n (%)	144 (88.9)	152 (89.9)	0.89 [0.44; 1.80] 0.756	0.99 [0.92; 1.06] 0.756	-0.01 [-0.08; 0.06] 0.756
Pooled Analysis					
Interaction Test:	p = 0.225				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any AE, n (%)	25 (86.2)	18 (72.0)	2.42 [0.61; 9.55] 0.206	1.19 [0.89; 1.58] 0.225	0.14 [-0.08; 0.35] 0.218

	Treatment Groups		Comparison		
Any adverse event by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any AE, n (%)	302 (89.1)	306 (89.2)	0.98 [0.61; 1.60] 0.950	1.00 [0.95; 1.05] 0.960	-0.00 [-0.05; 0.05] 0.960

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-2.1 Any ocular adverse event (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular AE, n (%)	102 (54.0)	89 (47.6)	1.29 [0.86; 1.94] 0.217	1.13 [0.93; 1.38] 0.218	0.06 [-0.04; 0.16] 0.215
KITE, N'/N	179 / 179	181 / 181			
Any ocular AE, n (%)	79 (44.1)	74 (40.9)	1.14 [0.75; 1.74] 0.533	1.08 [0.85; 1.37] 0.533	0.03 [-0.07; 0.13] 0.533
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular AE, n (%)	181 (49.2)	163 (44.3)	1.22 [0.91; 1.63] 0.188	1.11 [0.95; 1.29] 0.187	0.05 [-0.02; 0.12] 0.186
p_H=0.680					
Any ocular AE, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular AE, n (%)	123 (65.1)	113 (60.4)	1.22 [0.80; 1.86] 0.351	1.08 [0.92; 1.26] 0.352	0.05 [-0.05; 0.14] 0.350
KITE, N'/N	179 / 179	181 / 181			
Any ocular AE, n (%)	101 (56.4)	99 (54.7)	1.07 [0.71; 1.63] 0.741	1.03 [0.86; 1.24] 0.741	0.02 [-0.09; 0.12] 0.741
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular AE, n (%)	224 (60.9)	212 (57.6)	1.15 [0.85; 1.54] 0.367	1.06 [0.94; 1.19] 0.373	0.03 [-0.04; 0.10] 0.372
p_H=0.668					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-2.2 Any ocular adverse event by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.680**					
KESTREL					
Interaction Test:	p = 0.700				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular AE, n (%)	57 (54.8)	47 (50.5)	1.19 [0.68; 2.08] 0.549	1.08 [0.83; 1.42] 0.550	0.04 [-0.10; 0.18] 0.549
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular AE, n (%)	45 (52.9)	42 (44.7)	1.39 [0.77; 2.51] 0.270	1.18 [0.88; 1.60] 0.270	0.08 [-0.06; 0.23] 0.268
KITE					
Interaction Test:	p = 0.104				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular AE, n (%)	46 (46.0)	36 (35.3)	1.56 [0.89; 2.75] 0.122	1.30 [0.93; 1.83] 0.124	0.11 [-0.03; 0.24] 0.119
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular AE, n (%)	33 (41.8)	38 (48.1)	0.77 [0.41; 1.45] 0.424	0.87 [0.61; 1.23] 0.425	-0.06 [-0.22; 0.09] 0.423
Pooled Analysis					
Interaction Test:	p = 0.395				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular AE, n (%)	103 (50.5)	83 (42.6)	1.37 [0.92; 2.03] 0.123	1.18 [0.95; 1.45] 0.130	0.08 [-0.02; 0.17] 0.128
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular AE, n (%)	78 (47.6)	80 (46.2)	1.06 [0.69; 1.63] 0.791	1.03 [0.82; 1.29] 0.796	0.01 [-0.09; 0.12] 0.796

	Treatment Groups		Comparison		
Any ocular adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.888				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular AE, n (%)	71 (68.3)	59 (63.4)	1.24 [0.69; 2.24] 0.475	1.08 [0.88; 1.32] 0.478	0.05 [-0.08; 0.18] 0.475
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular AE, n (%)	52 (61.2)	54 (57.4)	1.17 [0.64; 2.12] 0.612	1.06 [0.84; 1.36] 0.612	0.04 [-0.11; 0.18] 0.612
KITE					
Interaction Test:	p = 0.355				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular AE, n (%)	55 (55.0)	50 (49.0)	1.27 [0.73; 2.21] 0.395	1.12 [0.86; 1.46] 0.396	0.06 [-0.08; 0.20] 0.394
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular AE, n (%)	46 (58.2)	49 (62.0)	0.85 [0.45; 1.61] 0.626	0.94 [0.73; 1.21] 0.626	-0.04 [-0.19; 0.11] 0.626
Pooled Analysis					
Interaction Test:	p = 0.462				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular AE, n (%)	126 (61.8)	109 (55.9)	1.27 [0.85; 1.90] 0.244	1.10 [0.93; 1.29] 0.269	0.05 [-0.04; 0.15] 0.267

	Treatment Groups		Comparison		
Any ocular adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular AE, n (%)	98 (59.8)	103 (59.5)	1.02 [0.66; 1.57] 0.944	1.00 [0.84; 1.20] 0.971	0.00 [-0.10; 0.11] 0.971

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-2.3 Any ocular adverse event by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.680**					
KESTREL					
Interaction Test:	p = 0.702				
Male					
N'/N	110 / 110	126 / 126			
Any ocular AE, n (%)	62 (56.4)	64 (50.8)	1.25 [0.75; 2.09] 0.392	1.11 [0.87; 1.41] 0.391	0.06 [-0.07; 0.18] 0.391
Female					
N'/N	79 / 79	61 / 61			
Any ocular AE, n (%)	40 (50.6)	25 (41.0)	1.48 [0.75; 2.90] 0.257	1.24 [0.85; 1.79] 0.265	0.10 [-0.07; 0.26] 0.253
KITE					
Interaction Test:	p = 0.657				
Male					
N'/N	120 / 120	115 / 115			
Any ocular AE, n (%)	51 (42.5)	47 (40.9)	1.07 [0.64; 1.80] 0.800	1.04 [0.77; 1.41] 0.800	0.02 [-0.11; 0.14] 0.800
Female					
N'/N	59 / 59	66 / 66			
Any ocular AE, n (%)	28 (47.5)	27 (40.9)	1.30 [0.64; 2.65] 0.462	1.16 [0.78; 1.72] 0.461	0.07 [-0.11; 0.24] 0.461
Pooled Analysis					
Interaction Test:	p = 0.594				
Male					
N'/N	230 / 230	241 / 241			
Any ocular AE, n (%)	113 (49.1)	111 (46.1)	1.15 [0.80; 1.65] 0.451	1.08 [0.89; 1.30] 0.432	0.04 [-0.05; 0.13] 0.431
Female					
N'/N	138 / 138	127 / 127			
Any ocular AE, n (%)	68 (49.3)	52 (40.9)	1.36 [0.83; 2.21] 0.220	1.20 [0.92; 1.57] 0.185	0.08 [-0.04; 0.20] 0.182

	Treatment Groups		Comparison		
Any ocular adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.218				
Male					
N'/N	110 / 110	126 / 126			
Any ocular AE, n (%)	71 (64.5)	81 (64.3)	1.01 [0.59; 1.73] 0.967	1.00 [0.83; 1.21] 0.967	0.00 [-0.12; 0.13] 0.967
Female					
N'/N	79 / 79	61 / 61			
Any ocular AE, n (%)	52 (65.8)	32 (52.5)	1.75 [0.88; 3.46] 0.111	1.25 [0.94; 1.67] 0.121	0.13 [-0.03; 0.30] 0.109
KITE					
Interaction Test:	p = 0.677				
Male					
N'/N	120 / 120	115 / 115			
Any ocular AE, n (%)	66 (55.0)	63 (54.8)	1.01 [0.60; 1.69] 0.973	1.00 [0.80; 1.27] 0.973	0.00 [-0.13; 0.13] 0.973
Female					
N'/N	59 / 59	66 / 66			
Any ocular AE, n (%)	35 (59.3)	36 (54.5)	1.22 [0.60; 2.47] 0.591	1.09 [0.80; 1.48] 0.590	0.05 [-0.13; 0.22] 0.590
Pooled Analysis					
Interaction Test:	p = 0.255				
Male					
N'/N	230 / 230	241 / 241			
Any ocular AE, n (%)	137 (59.6)	144 (59.8)	1.01 [0.70; 1.46] 0.965	1.00 [0.87; 1.16] 0.958	0.00 [-0.09; 0.09] 0.958

	Treatment Groups		Comparison		
Any ocular adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any ocular AE, n (%)	87 (63.0)	68 (53.5)	1.44 [0.88; 2.36] 0.145	1.17 [0.95; 1.45] 0.128	0.09 [-0.03; 0.21] 0.126

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-2.4 Any ocular adverse event by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.680**					
KESTREL					
Interaction Test:	p = 0.328				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any ocular AE, n (%)	39 (52.7)	34 (53.1)	0.98 [0.50; 1.92] 0.960	0.99 [0.72; 1.36] 0.960	-0.00 [-0.17; 0.16] 0.960
> 65 letters					
N'/N	115 / 115	123 / 123			
Any ocular AE, n (%)	63 (54.8)	55 (44.7)	1.50 [0.90; 2.50] 0.121	1.23 [0.95; 1.58] 0.122	0.10 [-0.03; 0.23] 0.119
KITE					
Interaction Test:	p = 0.334				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any ocular AE, n (%)	27 (41.5)	40 (44.0)	0.91 [0.48; 1.72] 0.764	0.95 [0.65; 1.37] 0.765	-0.02 [-0.18; 0.13] 0.763
> 65 letters					
N'/N	114 / 114	90 / 90			
Any ocular AE, n (%)	52 (45.6)	34 (37.8)	1.38 [0.79; 2.43] 0.261	1.21 [0.87; 1.68] 0.266	0.08 [-0.06; 0.21] 0.257
Pooled Analysis					
Interaction Test:	p = 0.171				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any ocular AE, n (%)	66 (47.5)	74 (47.7)	0.95 [0.60; 1.51] 0.828	0.97 [0.76; 1.23] 0.802	-0.01 [-0.13; 0.10] 0.801
> 65 letters					
N'/N	229 / 229	213 / 213			
Any ocular AE, n (%)	115 (50.2)	89 (41.8)	1.44 [0.99; 2.11] 0.057	1.22 [0.99; 1.49] 0.057	0.09 [-0.00; 0.18] 0.055

	Treatment Groups		Comparison		
Any ocular adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.150				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any ocular AE, n (%)	45 (60.8)	42 (65.6)	0.81 [0.41; 1.63] 0.559	0.93 [0.72; 1.20] 0.558	-0.05 [-0.21; 0.11] 0.558
> 65 letters					
N'/N	115 / 115	123 / 123			
Any ocular AE, n (%)	78 (67.8)	71 (57.7)	1.54 [0.91; 2.62] 0.108	1.18 [0.97; 1.43] 0.108	0.10 [-0.02; 0.22] 0.105
KITE					
Interaction Test:	p = 0.296				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any ocular AE, n (%)	35 (53.8)	53 (58.2)	0.84 [0.44; 1.59] 0.585	0.92 [0.70; 1.23] 0.589	-0.04 [-0.20; 0.11] 0.585
> 65 letters					
N'/N	114 / 114	90 / 90			
Any ocular AE, n (%)	66 (57.9)	46 (51.1)	1.32 [0.75; 2.29] 0.334	1.13 [0.88; 1.46] 0.339	0.07 [-0.07; 0.21] 0.333
Pooled Analysis					
Interaction Test:	p = 0.079				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any ocular AE, n (%)	80 (57.6)	95 (61.3)	0.83 [0.52; 1.32] 0.426	0.93 [0.76; 1.12] 0.427	-0.05 [-0.16; 0.07] 0.425

	Treatment Groups		Comparison		
Any ocular adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any ocular AE, n (%)	144 (62.9)	117 (54.9)	1.43 [0.97; 2.09] 0.069	1.16 [0.99; 1.35] 0.067	0.09 [-0.01; 0.18] 0.066

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-2.5 Any ocular adverse event by region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.680**					
KESTREL					
Interaction Test:	p = 0.346				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE, n (%)	56 (62.2)	41 (49.4)	1.69 [0.92; 3.09] 0.090	1.26 [0.96; 1.65] 0.095	0.13 [-0.02; 0.28] 0.087
European Region					
N'/N	69 / 69	75 / 75			
Any ocular AE, n (%)	33 (47.8)	33 (44.0)	1.17 [0.61; 2.25] 0.645	1.09 [0.76; 1.55] 0.645	0.04 [-0.12; 0.20] 0.645
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any ocular AE, n (%)	13 (43.3)	15 (51.7)	0.71 [0.26; 1.99] 0.519	0.84 [0.49; 1.44] 0.520	-0.08 [-0.34; 0.17] 0.517
KITE					
Interaction Test:	p = 0.403				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE, n (%)	13 (50.0)	6 (28.6)	2.50 [0.74; 8.46] 0.141	1.75 [0.80; 3.81] 0.159	0.21 [-0.06; 0.49] 0.123
European Region					
N'/N	135 / 135	132 / 132			
Any ocular AE, n (%)	57 (42.2)	53 (40.2)	1.09 [0.67; 1.77] 0.731	1.05 [0.79; 1.40] 0.731	0.02 [-0.10; 0.14] 0.731
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any ocular AE, n (%)	9 (50.0)	15 (53.6)	0.87 [0.26; 2.84] 0.813	0.93 [0.52; 1.66] 0.815	-0.04 [-0.33; 0.26] 0.813

	Treatment Groups		Comparison		
Any ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.255				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE, n (%)	56 (62.2)	41 (49.4)	1.67 [0.83; 3.36] 0.154	1.26 [0.96; 1.65] 0.090	0.13 [-0.02; 0.28] 0.087
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE, n (%)	13 (50.0)	6 (28.6)	2.53 [0.71; 9.05] 0.153	1.75 [0.80; 3.81] 0.141	0.21 [-0.06; 0.49] 0.123
European Region					
N'/N	204 / 204	207 / 207			
Any ocular AE, n (%)	90 (44.1)	86 (41.5)	1.12 [0.74; 1.68] 0.591	1.06 [0.85; 1.33] 0.583	0.03 [-0.07; 0.12] 0.582
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any ocular AE, n (%)	22 (45.8)	30 (52.6)	0.75 [0.35; 1.62] 0.466	0.88 [0.59; 1.30] 0.524	-0.06 [-0.26; 0.13] 0.520
Any ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.507				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE, n (%)	63 (70.0)	52 (62.7)	1.39 [0.74; 2.62] 0.307	1.12 [0.90; 1.38] 0.310	0.07 [-0.07; 0.21] 0.306
European Region					
N'/N	69 / 69	75 / 75			
Any ocular AE, n (%)	42 (60.9)	41 (54.7)	1.29 [0.66; 2.50] 0.452	1.11 [0.84; 1.47] 0.451	0.06 [-0.10; 0.22] 0.450
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any ocular AE, n (%)	18 (60.0)	20 (69.0)	0.68 [0.23; 1.97] 0.473	0.87 [0.59; 1.27] 0.473	-0.09 [-0.33; 0.15] 0.470

	Treatment Groups		Comparison		
Any ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.295				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE, n (%)	16 (61.5)	8 (38.1)	2.60 [0.80; 8.49] 0.113	1.62 [0.87; 3.02] 0.132	0.23 [-0.05; 0.51] 0.100
European Region					
N'/N	135 / 135	132 / 132			
Any ocular AE, n (%)	75 (55.6)	75 (56.8)	0.95 [0.59; 1.54] 0.835	0.98 [0.79; 1.21] 0.835	-0.01 [-0.13; 0.11] 0.835
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any ocular AE, n (%)	10 (55.6)	16 (57.1)	0.94 [0.28; 3.09] 0.916	0.97 [0.58; 1.64] 0.916	-0.02 [-0.31; 0.28] 0.916
Pooled Analysis					
Interaction Test:	p = 0.361				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE, n (%)	63 (70.0)	52 (62.7)	1.28 [0.62; 2.65] 0.505	1.12 [0.90; 1.38] 0.308	0.07 [-0.07; 0.21] 0.306
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE, n (%)	16 (61.5)	8 (38.1)	2.83 [0.82; 9.79] 0.100	1.62 [0.87; 3.02] 0.114	0.23 [-0.05; 0.51] 0.100
European Region					
N'/N	204 / 204	207 / 207			
Any ocular AE, n (%)	117 (57.4)	116 (56.0)	1.09 [0.72; 1.64] 0.686	1.02 [0.86; 1.21] 0.783	0.01 [-0.08; 0.11] 0.783

	Treatment Groups		Comparison		
Any ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any ocular AE, n (%)	28 (58.3)	36 (63.2)	0.80 [0.36; 1.76] 0.574	0.91 [0.67; 1.24] 0.548	-0.06 [-0.25; 0.13] 0.544

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-2.6 Any ocular adverse event by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.680**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular AE, n (%)	5 (41.7)	6 (100.0)	N.E.	0.42 [0.21; 0.81] 0.010 *	-0.58 [-0.86; -0.30] <.001 *
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular AE, n (%)	97 (54.8)	83 (45.9)	1.43 [0.94; 2.17] 0.091	1.20 [0.97; 1.47] 0.092	0.09 [-0.01; 0.19] 0.089
KITE					
Interaction Test:	p = 0.089				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular AE, n (%)	13 (68.4)	2 (28.6)	5.41 [0.81; 36.34] 0.082	2.39 [0.71; 8.03] 0.157	0.40 [0.00; 0.79] 0.048 *
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular AE, n (%)	66 (41.3)	72 (41.4)	0.99 [0.64; 1.54] 0.981	1.00 [0.77; 1.29] 0.981	-0.00 [-0.11; 0.10] 0.981
Pooled Analysis					
Interaction Test:	p = 0.678				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular AE, n (%)	18 (58.1)	8 (61.5)	0.90 [0.24; 3.41] 0.876	0.95 [0.52; 1.74] 0.867	-0.03 [-0.38; 0.32] 0.856
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular AE, n (%)	163 (48.4)	155 (43.7)	1.20 [0.89; 1.62] 0.231	1.10 [0.94; 1.30] 0.227	0.05 [-0.03; 0.12] 0.226

	Treatment Groups		Comparison		
Any ocular adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular AE, n (%)	7 (58.3)	6 (100.0)	N.E.	0.58 [0.36; 0.94] 0.027 *	-0.42 [-0.70; -0.14] 0.003 *
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular AE, n (%)	116 (65.5)	107 (59.1)	1.32 [0.86; 2.02] 0.211	1.11 [0.94; 1.30] 0.211	0.06 [-0.04; 0.16] 0.209
KITE					
Interaction Test:	p = 0.156				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular AE, n (%)	14 (73.7)	3 (42.9)	3.73 [0.61; 22.86] 0.154	1.72 [0.70; 4.21] 0.236	0.31 [-0.11; 0.72] 0.147
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular AE, n (%)	87 (54.4)	96 (55.2)	0.97 [0.63; 1.49] 0.884	0.99 [0.81; 1.20] 0.884	-0.01 [-0.11; 0.10] 0.884
Pooled Analysis					
Interaction Test:	p = 0.834				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular AE, n (%)	21 (67.7)	9 (69.2)	0.97 [0.24; 3.95] 0.966	1.00 [0.62; 1.61] 0.988	-0.01 [-0.33; 0.31] 0.952

	Treatment Groups		Comparison		
Any ocular adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular AE, n (%)	203 (60.2)	203 (57.2)	1.13 [0.83; 1.53] 0.428	1.05 [0.93; 1.19] 0.432	0.03 [-0.04; 0.10] 0.431

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 100 / KESTREL: logit(proportion) = treatment [by diabetes type].

Table 12-2.7 Any ocular adverse event by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.680**					
KESTREL					
Interaction Test:	p = 0.203				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any ocular AE, n (%)	42 (55.3)	46 (43.0)	1.64 [0.91; 2.96] 0.102	1.29 [0.95; 1.73] 0.098	0.12 [-0.02; 0.27] 0.099
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any ocular AE, n (%)	59 (52.7)	43 (53.8)	0.96 [0.54; 1.70] 0.883	0.98 [0.75; 1.28] 0.883	-0.01 [-0.15; 0.13] 0.883
KITE					
Interaction Test:	p = 0.530				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any ocular AE, n (%)	33 (40.2)	39 (40.6)	0.98 [0.54; 1.79] 0.959	0.99 [0.69; 1.42] 0.959	-0.00 [-0.15; 0.14] 0.959
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any ocular AE, n (%)	46 (47.4)	35 (41.2)	1.29 [0.72; 2.32] 0.398	1.15 [0.83; 1.60] 0.401	0.06 [-0.08; 0.21] 0.396
Pooled Analysis					
Interaction Test:	p = 0.638				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any ocular AE, n (%)	75 (47.5)	85 (41.9)	1.28 [0.84; 1.94] 0.257	1.14 [0.91; 1.44] 0.258	0.06 [-0.04; 0.16] 0.258
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any ocular AE, n (%)	105 (50.2)	78 (47.3)	1.11 [0.74; 1.67] 0.625	1.05 [0.85; 1.30] 0.627	0.03 [-0.08; 0.13] 0.626

	Treatment Groups		Comparison		
Any ocular adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.724				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any ocular AE, n (%)	49 (64.5)	66 (61.7)	1.13 [0.61; 2.08] 0.700	1.05 [0.84; 1.31] 0.698	0.03 [-0.11; 0.17] 0.699
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any ocular AE, n (%)	73 (65.2)	47 (58.8)	1.31 [0.73; 2.37] 0.365	1.11 [0.88; 1.39] 0.372	0.06 [-0.08; 0.20] 0.366
KITE					
Interaction Test:	p = 0.302				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any ocular AE, n (%)	40 (48.8)	51 (53.1)	0.84 [0.47; 1.52] 0.563	0.92 [0.69; 1.23] 0.565	-0.04 [-0.19; 0.10] 0.563
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any ocular AE, n (%)	61 (62.9)	48 (56.5)	1.31 [0.72; 2.37] 0.379	1.11 [0.87; 1.42] 0.382	0.06 [-0.08; 0.21] 0.378
Pooled Analysis					
Interaction Test:	p = 0.320				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any ocular AE, n (%)	89 (56.3)	117 (57.6)	0.96 [0.63; 1.47] 0.858	0.99 [0.82; 1.18] 0.883	-0.01 [-0.11; 0.09] 0.883

	Treatment Groups		Comparison		
Any ocular adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any ocular AE, n (%)	134 (64.1)	95 (57.6)	1.30 [0.86; 1.98] 0.219	1.11 [0.94; 1.31] 0.207	0.06 [-0.04; 0.16] 0.207

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-2.8 Any ocular adverse event by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.680**					
KESTREL					
Interaction Test:	p = 0.189				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any ocular AE, n (%)	72 (60.0)	55 (50.0)	1.50 [0.89; 2.53] 0.128	1.20 [0.95; 1.52] 0.132	0.10 [-0.03; 0.23] 0.126
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any ocular AE, n (%)	12 (40.0)	21 (53.8)	0.57 [0.22; 1.50] 0.255	0.74 [0.44; 1.26] 0.268	-0.14 [-0.37; 0.10] 0.248
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any ocular AE, n (%)	18 (46.2)	13 (34.2)	1.65 [0.66; 4.13] 0.287	1.35 [0.77; 2.35] 0.291	0.12 [-0.10; 0.34] 0.281
KITE					
Interaction Test:	p = 0.427				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any ocular AE, n (%)	38 (44.7)	35 (38.0)	1.32 [0.72; 2.40] 0.369	1.18 [0.83; 1.67] 0.369	0.07 [-0.08; 0.21] 0.368
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any ocular AE, n (%)	20 (39.2)	23 (46.9)	0.73 [0.33; 1.61] 0.436	0.84 [0.53; 1.31] 0.437	-0.08 [-0.27; 0.12] 0.434
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any ocular AE, n (%)	21 (48.8)	16 (40.0)	1.43 [0.60; 3.42] 0.419	1.22 [0.75; 1.99] 0.422	0.09 [-0.12; 0.30] 0.416

	Treatment Groups		Comparison		
Any ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.093				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any ocular AE, n (%)	110 (53.7)	90 (44.6)	1.42 [0.96; 2.11] 0.079	1.19 [0.98; 1.45] 0.083	0.09 [-0.01; 0.18] 0.081
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any ocular AE, n (%)	32 (39.5)	44 (50.0)	0.67 [0.36; 1.24] 0.200	0.79 [0.56; 1.12] 0.186	-0.10 [-0.25; 0.05] 0.181
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any ocular AE, n (%)	39 (47.6)	29 (37.2)	1.54 [0.82; 2.91] 0.180	1.28 [0.89; 1.84] 0.189	0.10 [-0.05; 0.26] 0.183
Any ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.070				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any ocular AE, n (%)	87 (72.5)	70 (63.6)	1.51 [0.86; 2.63] 0.150	1.14 [0.95; 1.36] 0.154	0.09 [-0.03; 0.21] 0.149
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any ocular AE, n (%)	13 (43.3)	25 (64.1)	0.43 [0.16; 1.13] 0.088	0.68 [0.42; 1.08] 0.104	-0.21 [-0.44; 0.02] 0.080
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any ocular AE, n (%)	23 (59.0)	18 (47.4)	1.60 [0.65; 3.93] 0.309	1.25 [0.81; 1.90] 0.312	0.12 [-0.11; 0.34] 0.304

	Treatment Groups		Comparison		
Any ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.641				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any ocular AE, n (%)	49 (57.6)	48 (52.2)	1.25 [0.69; 2.26] 0.465	1.10 [0.85; 1.44] 0.465	0.05 [-0.09; 0.20] 0.464
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any ocular AE, n (%)	26 (51.0)	28 (57.1)	0.78 [0.35; 1.72] 0.537	0.89 [0.62; 1.28] 0.537	-0.06 [-0.26; 0.13] 0.536
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any ocular AE, n (%)	26 (60.5)	23 (57.5)	1.13 [0.47; 2.71] 0.784	1.05 [0.73; 1.51] 0.784	0.03 [-0.18; 0.24] 0.784
Pooled Analysis					
Interaction Test:	p = 0.090				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any ocular AE, n (%)	136 (66.3)	118 (58.4)	1.39 [0.93; 2.08] 0.112	1.13 [0.97; 1.31] 0.122	0.07 [-0.02; 0.17] 0.120
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any ocular AE, n (%)	39 (48.1)	53 (60.2)	0.63 [0.34; 1.16] 0.135	0.80 [0.60; 1.06] 0.119	-0.12 [-0.27; 0.03] 0.115

	Treatment Groups		Comparison		
Any ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any ocular AE, n (%)	49 (59.8)	41 (52.6)	1.35 [0.72; 2.52] 0.352	1.14 [0.86; 1.50] 0.366	0.07 [-0.08; 0.22] 0.362

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-2.9 Any ocular adverse event by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.680**					
KESTREL					
Interaction Test:	p = 0.682				
focal					
N'/N	59 / 59	48 / 48			
Any ocular AE, n (%)	32 (54.2)	21 (43.8)	1.52 [0.71; 3.28] 0.281	1.24 [0.83; 1.84] 0.289	0.10 [-0.08; 0.29] 0.278
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular AE, n (%)	68 (53.5)	64 (47.8)	1.26 [0.78; 2.05] 0.351	1.12 [0.88; 1.43] 0.351	0.06 [-0.06; 0.18] 0.350
KITE					
Interaction Test:	p = 0.682				
focal					
N'/N	63 / 63	66 / 66			
Any ocular AE, n (%)	27 (42.9)	24 (36.4)	1.31 [0.65; 2.66] 0.451	1.18 [0.77; 1.81] 0.452	0.06 [-0.10; 0.23] 0.450
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular AE, n (%)	51 (44.3)	46 (42.2)	1.09 [0.64; 1.85] 0.746	1.05 [0.78; 1.42] 0.746	0.02 [-0.11; 0.15] 0.746
Pooled Analysis					
Interaction Test:	p = 0.557				
focal					
N'/N	122 / 122	114 / 114			
Any ocular AE, n (%)	59 (48.4)	45 (39.5)	1.42 [0.84; 2.39] 0.186	1.21 [0.90; 1.62] 0.200	0.08 [-0.04; 0.21] 0.197
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular AE, n (%)	119 (49.2)	110 (45.3)	1.18 [0.82; 1.68] 0.377	1.09 [0.90; 1.32] 0.365	0.04 [-0.05; 0.13] 0.364

	Treatment Groups		Comparison		
Any ocular adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.769				
focal					
N'/N	59 / 59	48 / 48			
Any ocular AE, n (%)	37 (62.7)	26 (54.2)	1.42 [0.66; 3.09] 0.372	1.16 [0.84; 1.60] 0.379	0.09 [-0.10; 0.27] 0.371
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular AE, n (%)	84 (66.1)	82 (61.2)	1.24 [0.75; 2.05] 0.407	1.08 [0.90; 1.30] 0.406	0.05 [-0.07; 0.17] 0.405
KITE					
Interaction Test:	p = 0.500				
focal					
N'/N	63 / 63	66 / 66			
Any ocular AE, n (%)	36 (57.1)	33 (50.0)	1.33 [0.67; 2.67] 0.417	1.14 [0.83; 1.58] 0.417	0.07 [-0.10; 0.24] 0.415
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular AE, n (%)	64 (55.7)	61 (56.0)	0.99 [0.58; 1.67] 0.963	0.99 [0.79; 1.26] 0.963	-0.00 [-0.13; 0.13] 0.963
Pooled Analysis					
Interaction Test:	p = 0.494				
focal					
N'/N	122 / 122	114 / 114			
Any ocular AE, n (%)	73 (59.8)	59 (51.8)	1.38 [0.82; 2.32] 0.221	1.15 [0.91; 1.45] 0.232	0.08 [-0.05; 0.20] 0.229

	Treatment Groups		Comparison		
Any ocular adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular AE, n (%)	148 (61.2)	143 (58.8)	1.11 [0.77; 1.59] 0.584	1.04 [0.90; 1.21] 0.571	0.03 [-0.06; 0.11] 0.570

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-2.10 Any ocular adverse event by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.680**					
KESTREL					
Interaction Test:	p = 0.484				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any ocular AE, n (%)	56 (52.3)	47 (49.0)	1.14 [0.66; 1.99] 0.631	1.07 [0.81; 1.40] 0.632	0.03 [-0.10; 0.17] 0.631
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any ocular AE, n (%)	38 (54.3)	28 (39.4)	1.82 [0.93; 3.56] 0.078	1.38 [0.96; 1.97] 0.082	0.15 [-0.01; 0.31] 0.074
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any ocular AE, n (%)	8 (66.7)	14 (70.0)	0.86 [0.18; 3.98] 0.844	0.95 [0.58; 1.56] 0.846	-0.03 [-0.37; 0.30] 0.845
KITE					
Interaction Test:	p = 0.490				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any ocular AE, n (%)	40 (47.1)	32 (39.0)	1.39 [0.75; 2.57] 0.295	1.21 [0.85; 1.71] 0.297	0.08 [-0.07; 0.23] 0.293
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any ocular AE, n (%)	31 (41.9)	32 (40.5)	1.06 [0.56; 2.02] 0.862	1.03 [0.71; 1.51] 0.862	0.01 [-0.14; 0.17] 0.862
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any ocular AE, n (%)	8 (40.0)	10 (52.6)	0.60 [0.17; 2.14] 0.430	0.76 [0.38; 1.51] 0.433	-0.13 [-0.44; 0.18] 0.425

	Treatment Groups		Comparison		
Any ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.388				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any ocular AE, n (%)	96 (50.0)	79 (44.4)	1.24 [0.82; 1.87] 0.305	1.12 [0.90; 1.39] 0.291	0.05 [-0.05; 0.16] 0.289
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any ocular AE, n (%)	69 (47.9)	60 (40.0)	1.38 [0.87; 2.20] 0.172	1.20 [0.92; 1.55] 0.176	0.08 [-0.03; 0.19] 0.174
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any ocular AE, n (%)	16 (50.0)	24 (61.5)	0.66 [0.25; 1.71] 0.390	0.86 [0.57; 1.30] 0.467	-0.09 [-0.31; 0.14] 0.462
Any ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.592				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any ocular AE, n (%)	66 (61.7)	58 (60.4)	1.05 [0.60; 1.86] 0.854	1.02 [0.82; 1.27] 0.854	0.01 [-0.12; 0.15] 0.854
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any ocular AE, n (%)	47 (67.1)	39 (54.9)	1.68 [0.85; 3.32] 0.138	1.22 [0.94; 1.60] 0.140	0.12 [-0.04; 0.28] 0.134
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any ocular AE, n (%)	10 (83.3)	16 (80.0)	1.25 [0.19; 8.13] 0.815	1.04 [0.75; 1.46] 0.811	0.03 [-0.24; 0.31] 0.812

	Treatment Groups		Comparison		
Any ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.441				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any ocular AE, n (%)	50 (58.8)	41 (50.0)	1.43 [0.78; 2.63] 0.253	1.18 [0.89; 1.56] 0.256	0.09 [-0.06; 0.24] 0.251
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any ocular AE, n (%)	40 (54.1)	47 (59.5)	0.80 [0.42; 1.52] 0.497	0.91 [0.69; 1.20] 0.499	-0.05 [-0.21; 0.10] 0.497
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any ocular AE, n (%)	11 (55.0)	10 (52.6)	1.10 [0.31; 3.88] 0.882	1.05 [0.58; 1.87] 0.882	0.02 [-0.29; 0.34] 0.882
Pooled Analysis					
Interaction Test:	p = 0.942				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any ocular AE, n (%)	116 (60.4)	99 (55.6)	1.21 [0.80; 1.83] 0.371	1.08 [0.91; 1.29] 0.362	0.05 [-0.05; 0.15] 0.361
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any ocular AE, n (%)	87 (60.4)	86 (57.3)	1.14 [0.71; 1.82] 0.586	1.05 [0.87; 1.28] 0.599	0.03 [-0.08; 0.14] 0.599

	Treatment Groups		Comparison		
Any ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any ocular AE, n (%)	21 (65.6)	26 (66.7)	1.01 [0.37; 2.72] 0.987	1.04 [0.75; 1.44] 0.802	0.03 [-0.19; 0.24] 0.798

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-2.11 Any ocular adverse event by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.680**					
KESTREL					
Interaction Test:	p = 0.231				
presence					
N'/N	62 / 62	61 / 61			
Any ocular AE, n (%)	32 (51.6)	33 (54.1)	0.91 [0.45; 1.84] 0.783	0.95 [0.68; 1.33] 0.783	-0.02 [-0.20; 0.15] 0.782
absence					
N'/N	127 / 127	126 / 126			
Any ocular AE, n (%)	70 (55.1)	56 (44.4)	1.54 [0.94; 2.52] 0.090	1.24 [0.97; 1.59] 0.092	0.11 [-0.02; 0.23] 0.088
KITE					
Interaction Test:	p = 0.677				
presence					
N'/N	56 / 56	67 / 67			
Any ocular AE, n (%)	28 (50.0)	29 (43.3)	1.31 [0.64; 2.67] 0.457	1.16 [0.79; 1.69] 0.456	0.07 [-0.11; 0.24] 0.456
absence					
N'/N	123 / 123	114 / 114			
Any ocular AE, n (%)	51 (41.5)	45 (39.5)	1.09 [0.65; 1.83] 0.755	1.05 [0.77; 1.43] 0.755	0.02 [-0.11; 0.14] 0.755
Pooled Analysis					
Interaction Test:	p = 0.568				
presence					
N'/N	118 / 118	128 / 128			
Any ocular AE, n (%)	60 (50.8)	62 (48.4)	1.08 [0.66; 1.79] 0.751	1.04 [0.81; 1.34] 0.743	0.02 [-0.10; 0.15] 0.742

	Treatment Groups		Comparison		
Any ocular adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular AE, n (%)	121 (48.4)	101 (42.1)	1.30 [0.91; 1.86] 0.153	1.15 [0.95; 1.40] 0.149	0.06 [-0.02; 0.15] 0.148
Any ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.428				
presence					
N'/N	62 / 62	61 / 61			
Any ocular AE, n (%)	39 (62.9)	39 (63.9)	0.96 [0.46; 1.99] 0.906	0.98 [0.75; 1.29] 0.905	-0.01 [-0.18; 0.16] 0.905
absence					
N'/N	127 / 127	126 / 126			
Any ocular AE, n (%)	84 (66.1)	74 (58.7)	1.37 [0.82; 2.29] 0.224	1.13 [0.93; 1.36] 0.225	0.07 [-0.04; 0.19] 0.222
KITE					
Interaction Test:	p = 0.780				
presence					
N'/N	56 / 56	67 / 67			
Any ocular AE, n (%)	34 (60.7)	38 (56.7)	1.18 [0.57; 2.43] 0.654	1.07 [0.80; 1.44] 0.653	0.04 [-0.13; 0.21] 0.653
absence					
N'/N	123 / 123	114 / 114			
Any ocular AE, n (%)	67 (54.5)	61 (53.5)	1.04 [0.62; 1.73] 0.882	1.02 [0.80; 1.29] 0.882	0.01 [-0.12; 0.14] 0.882
Pooled Analysis					
Interaction Test:	p = 0.715				
presence					
N'/N	118 / 118	128 / 128			
Any ocular AE, n (%)	73 (61.9)	77 (60.2)	1.06 [0.63; 1.78] 0.818	1.02 [0.84; 1.25] 0.814	0.01 [-0.11; 0.14] 0.813

	Treatment Groups		Comparison		
Any ocular adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular AE, n (%)	151 (60.4)	135 (56.3)	1.19 [0.83; 1.71] 0.334	1.08 [0.93; 1.25] 0.334	0.04 [-0.04; 0.13] 0.333

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-2.12 Any ocular adverse event by exposure (week 52) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.680**					
KESTREL					
Interaction Test:	p = 0.578				
Non-exposed					
N'/N	71 / 71	75 / 75			
Any ocular AE, n (%)	37 (52.1)	37 (49.3)	1.12 [0.58; 2.14] 0.737	1.06 [0.77; 1.45] 0.737	0.03 [-0.13; 0.19] 0.737
Exposed					
N'/N	118 / 118	112 / 112			
Any ocular AE, n (%)	65 (55.1)	52 (46.4)	1.42 [0.84; 2.38] 0.190	1.19 [0.92; 1.53] 0.193	0.09 [-0.04; 0.22] 0.188
KITE					
Interaction Test:	p = 0.876				
Non-exposed					
N'/N	85 / 85	90 / 90			
Any ocular AE, n (%)	39 (45.9)	39 (43.3)	1.11 [0.61; 2.01] 0.735	1.06 [0.76; 1.47] 0.735	0.03 [-0.12; 0.17] 0.735
Exposed					
N'/N	94 / 94	91 / 91			
Any ocular AE, n (%)	40 (42.6)	35 (38.5)	1.19 [0.66; 2.13] 0.571	1.11 [0.78; 1.57] 0.572	0.04 [-0.10; 0.18] 0.570
Pooled Analysis					
Interaction Test:	p = 0.616				
Non-exposed					
N'/N	156 / 156	165 / 165			
Any ocular AE, n (%)	76 (48.7)	76 (46.1)	1.12 [0.72; 1.74] 0.617	1.06 [0.84; 1.33] 0.635	0.03 [-0.08; 0.14] 0.633

	Treatment Groups		Comparison		
Any ocular adverse event by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	212 / 212	203 / 203			
Any ocular AE, n (%)	105 (49.5)	87 (42.9)	1.30 [0.88; 1.92] 0.185	1.15 [0.94; 1.42] 0.175	0.07 [-0.03; 0.16] 0.173

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-2.13 Any ocular adverse event by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.937				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any ocular AE, n (%)	5 (41.7)	5 (38.5)	1.14 [0.23; 5.67] 0.870	1.08 [0.41; 2.83] 0.870	0.03 [-0.35; 0.42] 0.870
Exposed					
N'/N	177 / 177	174 / 174			
Any ocular AE, n (%)	118 (66.7)	108 (62.1)	1.22 [0.79; 1.89] 0.369	1.07 [0.92; 1.26] 0.369	0.05 [-0.05; 0.15] 0.368
KITE					
Interaction Test:	p = 0.333				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any ocular AE, n (%)	9 (52.9)	4 (33.3)	2.25 [0.49; 10.41] 0.300	1.59 [0.63; 3.97] 0.323	0.20 [-0.16; 0.55] 0.282
Exposed					
N'/N	162 / 162	169 / 169			
Any ocular AE, n (%)	92 (56.8)	95 (56.2)	1.02 [0.66; 1.58] 0.916	1.01 [0.84; 1.22] 0.916	0.01 [-0.10; 0.11] 0.916
Pooled Analysis					
Interaction Test:	p = 0.459				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any ocular AE, n (%)	14 (48.3)	9 (36.0)	1.72 [0.57; 5.16] 0.331	1.33 [0.69; 2.58] 0.389	0.12 [-0.14; 0.38] 0.377

	Treatment Groups		Comparison		
Any ocular adverse event by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any ocular AE, n (%)	210 (61.9)	203 (59.2)	1.12 [0.82; 1.52] 0.472	1.04 [0.93; 1.18] 0.479	0.03 [-0.05; 0.10] 0.478

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-3.1 Any ocular adverse event at the study eye (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the study eye, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular AE at the study eye, n (%)	76 (40.2)	73 (39.0)	1.05 [0.69; 1.59] 0.816	1.03 [0.80; 1.32] 0.816	0.01 [-0.09; 0.11] 0.816
KITE, N'/N	179 / 179	181 / 181			
Any ocular AE at the study eye, n (%)	53 (29.6)	52 (28.7)	1.04 [0.66; 1.64] 0.854	1.03 [0.75; 1.42] 0.854	0.01 [-0.09; 0.10] 0.854
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular AE at the study eye, n (%)	129 (35.1)	125 (34.0)	1.05 [0.77; 1.42] 0.769	1.03 [0.85; 1.26] 0.768	0.01 [-0.06; 0.08] 0.767
p_H=0.983					
Any ocular AE at the study eye, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular AE at the study eye, n (%)	93 (49.2)	94 (50.3)	0.96 [0.64; 1.44] 0.837	0.98 [0.80; 1.20] 0.837	-0.01 [-0.11; 0.09] 0.837
KITE, N'/N	179 / 179	181 / 181			
Any ocular AE at the study eye, n (%)	73 (40.8)	74 (40.9)	1.00 [0.65; 1.52] 0.984	1.00 [0.78; 1.28] 0.984	-0.00 [-0.10; 0.10] 0.984
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular AE at the study eye, n (%)	166 (45.1)	168 (45.7)	0.98 [0.73; 1.31] 0.873	0.99 [0.84; 1.16] 0.872	-0.01 [-0.08; 0.07] 0.871
p_H=0.898					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-3.2 Any ocular adverse event at the study eye by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.983**					
KESTREL					
Interaction Test:	p = 0.243				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular AE at the study eye, n (%)	40 (38.5)	40 (43.0)	0.83 [0.47; 1.46] 0.516	0.89 [0.64; 1.25] 0.516	-0.05 [-0.18; 0.09] 0.516
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular AE at the study eye, n (%)	36 (42.4)	33 (35.1)	1.36 [0.74; 2.48] 0.320	1.21 [0.83; 1.75] 0.320	0.07 [-0.07; 0.22] 0.319
KITE					
Interaction Test:	p = 0.528				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular AE at the study eye, n (%)	29 (29.0)	26 (25.5)	1.19 [0.64; 2.22] 0.576	1.14 [0.72; 1.79] 0.576	0.04 [-0.09; 0.16] 0.575
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular AE at the study eye, n (%)	24 (30.4)	26 (32.9)	0.89 [0.45; 1.74] 0.732	0.92 [0.58; 1.46] 0.732	-0.03 [-0.17; 0.12] 0.732
Pooled Analysis					
Interaction Test:	p = 0.660				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular AE at the study eye, n (%)	69 (33.8)	66 (33.8)	0.98 [0.65; 1.49] 0.938	0.99 [0.75; 1.29] 0.922	-0.00 [-0.10; 0.09] 0.921

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular AE at the study eye, n (%)	60 (36.6)	59 (34.1)	1.13 [0.72; 1.77] 0.598	1.08 [0.81; 1.44] 0.610	0.03 [-0.08; 0.13] 0.610
Any ocular AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.898**					
KESTREL					
Interaction Test:	p = 0.479				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular AE at the study eye, n (%)	51 (49.0)	50 (53.8)	0.83 [0.47; 1.45] 0.509	0.91 [0.69; 1.20] 0.507	-0.05 [-0.19; 0.09] 0.507
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular AE at the study eye, n (%)	42 (49.4)	44 (46.8)	1.11 [0.62; 2.00] 0.728	1.06 [0.78; 1.43] 0.728	0.03 [-0.12; 0.17] 0.728
KITE					
Interaction Test:	p = 0.534				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular AE at the study eye, n (%)	37 (37.0)	35 (34.3)	1.12 [0.63; 2.00] 0.690	1.08 [0.74; 1.56] 0.690	0.03 [-0.11; 0.16] 0.690
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular AE at the study eye, n (%)	36 (45.6)	39 (49.4)	0.86 [0.46; 1.60] 0.633	0.92 [0.66; 1.28] 0.633	-0.04 [-0.19; 0.12] 0.632
Pooled Analysis					
Interaction Test:	p = 0.938				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular AE at the study eye, n (%)	88 (43.1)	85 (43.6)	0.97 [0.65; 1.44] 0.881	0.98 [0.78; 1.22] 0.844	-0.01 [-0.11; 0.09] 0.844

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular AE at the study eye, n (%)	78 (47.6)	83 (48.0)	0.99 [0.65; 1.53] 0.974	0.99 [0.79; 1.24] 0.941	-0.00 [-0.11; 0.10] 0.941

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-3.3 Any ocular adverse event at the study eye by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.983**					
KESTREL					
Interaction Test:	p = 0.480				
Male					
N'/N	110 / 110	126 / 126			
Any ocular AE at the study eye, n (%)	44 (40.0)	52 (41.3)	0.95 [0.56; 1.60] 0.843	0.97 [0.71; 1.32] 0.843	-0.01 [-0.14; 0.11] 0.843
Female					
N'/N	79 / 79	61 / 61			
Any ocular AE at the study eye, n (%)	32 (40.5)	21 (34.4)	1.30 [0.65; 2.59] 0.462	1.18 [0.76; 1.82] 0.466	0.06 [-0.10; 0.22] 0.459
KITE					
Interaction Test:	p = 0.546				
Male					
N'/N	120 / 120	115 / 115			
Any ocular AE at the study eye, n (%)	35 (29.2)	35 (30.4)	0.94 [0.54; 1.65] 0.832	0.96 [0.65; 1.42] 0.832	-0.01 [-0.13; 0.10] 0.832
Female					
N'/N	59 / 59	66 / 66			
Any ocular AE at the study eye, n (%)	18 (30.5)	17 (25.8)	1.27 [0.58; 2.77] 0.555	1.18 [0.68; 2.08] 0.555	0.05 [-0.11; 0.21] 0.555
Pooled Analysis					
Interaction Test:	p = 0.356				
Male					
N'/N	230 / 230	241 / 241			
Any ocular AE at the study eye, n (%)	79 (34.3)	87 (36.1)	0.94 [0.64; 1.38] 0.768	0.96 [0.76; 1.23] 0.772	-0.01 [-0.10; 0.07] 0.772

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any ocular AE at the study eye, n (%)	50 (36.2)	38 (29.9)	1.28 [0.76; 2.15] 0.353	1.18 [0.83; 1.67] 0.348	0.05 [-0.06; 0.17] 0.345
Any ocular AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.898**					
KESTREL					
Interaction Test:	p = 0.378				
Male					
N'/N	110 / 110	126 / 126			
Any ocular AE at the study eye, n (%)	55 (50.0)	68 (54.0)	0.85 [0.51; 1.42] 0.543	0.93 [0.72; 1.19] 0.544	-0.04 [-0.17; 0.09] 0.542
Female					
N'/N	79 / 79	61 / 61			
Any ocular AE at the study eye, n (%)	38 (48.1)	26 (42.6)	1.25 [0.64; 2.44] 0.519	1.13 [0.78; 1.63] 0.522	0.05 [-0.11; 0.22] 0.518
KITE					
Interaction Test:	p = 0.830				
Male					
N'/N	120 / 120	115 / 115			
Any ocular AE at the study eye, n (%)	48 (40.0)	47 (40.9)	0.96 [0.57; 1.62] 0.892	0.98 [0.72; 1.33] 0.892	-0.01 [-0.13; 0.12] 0.892
Female					
N'/N	59 / 59	66 / 66			
Any ocular AE at the study eye, n (%)	25 (42.4)	27 (40.9)	1.06 [0.52; 2.17] 0.868	1.04 [0.68; 1.57] 0.868	0.01 [-0.16; 0.19] 0.868
Pooled Analysis					
Interaction Test:	p = 0.457				
Male					
N'/N	230 / 230	241 / 241			
Any ocular AE at the study eye, n (%)	103 (44.8)	115 (47.7)	0.90 [0.63; 1.30] 0.579	0.95 [0.78; 1.15] 0.597	-0.02 [-0.11; 0.07] 0.596

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any ocular AE at the study eye, n (%)	63 (45.7)	53 (41.7)	1.14 [0.70; 1.85] 0.607	1.09 [0.82; 1.43] 0.561	0.04 [-0.08; 0.16] 0.559

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-3.4 Any ocular adverse event at the study eye by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.983**					
KESTREL					
Interaction Test:	p = 0.196				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any ocular AE at the study eye, n (%)	29 (39.2)	30 (46.9)	0.73 [0.37; 1.44] 0.363	0.84 [0.57; 1.23] 0.363	-0.08 [-0.24; 0.09] 0.362
> 65 letters					
N'/N	115 / 115	123 / 123			
Any ocular AE at the study eye, n (%)	47 (40.9)	43 (35.0)	1.29 [0.76; 2.17] 0.348	1.17 [0.84; 1.62] 0.348	0.06 [-0.06; 0.18] 0.347
KITE					
Interaction Test:	p = 0.817				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any ocular AE at the study eye, n (%)	21 (32.3)	27 (29.7)	1.13 [0.57; 2.25] 0.725	1.09 [0.68; 1.75] 0.724	0.03 [-0.12; 0.17] 0.726
> 65 letters					
N'/N	114 / 114	90 / 90			
Any ocular AE at the study eye, n (%)	32 (28.1)	25 (27.8)	1.01 [0.55; 1.88] 0.963	1.01 [0.65; 1.58] 0.963	0.00 [-0.12; 0.13] 0.963
Pooled Analysis					
Interaction Test:	p = 0.431				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any ocular AE at the study eye, n (%)	50 (36.0)	57 (36.8)	0.91 [0.56; 1.47] 0.699	0.94 [0.70; 1.27] 0.688	-0.02 [-0.13; 0.09] 0.687

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any ocular AE at the study eye, n (%)	79 (34.5)	68 (31.9)	1.17 [0.78; 1.75] 0.442	1.11 [0.85; 1.44] 0.457	0.03 [-0.05; 0.12] 0.456
Any ocular AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.898**					
KESTREL					
Interaction Test:	p = 0.046 *				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any ocular AE at the study eye, n (%)	33 (44.6)	38 (59.4)	0.55 [0.28; 1.08] 0.084	0.75 [0.54; 1.04] 0.084	-0.15 [-0.31; 0.02] 0.080
> 65 letters					
N'/N	115 / 115	123 / 123			
Any ocular AE at the study eye, n (%)	60 (52.2)	56 (45.5)	1.31 [0.78; 2.17] 0.306	1.15 [0.88; 1.49] 0.306	0.07 [-0.06; 0.19] 0.304
KITE					
Interaction Test:	p = 0.806				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any ocular AE at the study eye, n (%)	28 (43.1)	40 (44.0)	0.96 [0.51; 1.83] 0.913	0.98 [0.68; 1.41] 0.913	-0.01 [-0.17; 0.15] 0.913
> 65 letters					
N'/N	114 / 114	90 / 90			
Any ocular AE at the study eye, n (%)	45 (39.5)	34 (37.8)	1.07 [0.61; 1.90] 0.805	1.04 [0.74; 1.48] 0.805	0.02 [-0.12; 0.15] 0.805
Pooled Analysis					
Interaction Test:	p = 0.108				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any ocular AE at the study eye, n (%)	61 (43.9)	78 (50.3)	0.73 [0.46; 1.16] 0.187	0.85 [0.67; 1.09] 0.203	-0.07 [-0.19; 0.04] 0.201

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any ocular AE at the study eye, n (%)	105 (45.9)	90 (42.3)	1.20 [0.82; 1.75] 0.348	1.10 [0.90; 1.36] 0.355	0.04 [-0.05; 0.14] 0.353

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-3.5 Any ocular adverse event at the study eye by region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.983**					
KESTREL					
Interaction Test:	p = 0.948				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE at the study eye, n (%)	39 (43.3)	34 (41.0)	1.10 [0.60; 2.02] 0.753	1.06 [0.75; 1.50] 0.753	0.02 [-0.12; 0.17] 0.752
European Region					
N'/N	69 / 69	75 / 75			
Any ocular AE at the study eye, n (%)	25 (36.2)	28 (37.3)	0.95 [0.48; 1.88] 0.891	0.97 [0.63; 1.49] 0.891	-0.01 [-0.17; 0.15] 0.891
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any ocular AE at the study eye, n (%)	12 (40.0)	11 (37.9)	1.09 [0.38; 3.11] 0.871	1.05 [0.56; 2.00] 0.871	0.02 [-0.23; 0.27] 0.871
KITE					
Interaction Test:	p = 0.890				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE at the study eye, n (%)	8 (30.8)	5 (23.8)	1.42 [0.39; 5.24] 0.597	1.29 [0.50; 3.37] 0.600	0.07 [-0.18; 0.32] 0.592
European Region					
N'/N	135 / 135	132 / 132			
Any ocular AE at the study eye, n (%)	37 (27.4)	34 (25.8)	1.09 [0.63; 1.87] 0.760	1.06 [0.71; 1.59] 0.760	0.02 [-0.09; 0.12] 0.760
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any ocular AE at the study eye, n (%)	8 (44.4)	13 (46.4)	0.92 [0.28; 3.03] 0.895	0.96 [0.50; 1.84] 0.896	-0.02 [-0.31; 0.27] 0.895

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.959				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE at the study eye, n (%)	39 (43.3)	34 (41.0)	1.12 [0.55; 2.28] 0.752	1.06 [0.75; 1.50] 0.753	0.02 [-0.12; 0.17] 0.752
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE at the study eye, n (%)	8 (30.8)	5 (23.8)	1.40 [0.36; 5.45] 0.631	1.29 [0.50; 3.37] 0.600	0.07 [-0.18; 0.32] 0.592
European Region					
N'/N	204 / 204	207 / 207			
Any ocular AE at the study eye, n (%)	62 (30.4)	62 (30.0)	1.02 [0.66; 1.58] 0.915	1.02 [0.76; 1.37] 0.879	0.01 [-0.08; 0.10] 0.879
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any ocular AE at the study eye, n (%)	20 (41.7)	24 (42.1)	0.95 [0.43; 2.08] 0.900	1.01 [0.64; 1.59] 0.972	0.00 [-0.19; 0.19] 0.972
Any ocular AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.898**					
KESTREL					
Interaction Test:	p = 0.510				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE at the study eye, n (%)	50 (55.6)	42 (50.6)	1.22 [0.67; 2.22] 0.514	1.10 [0.83; 1.46] 0.516	0.05 [-0.10; 0.20] 0.514
European Region					
N'/N	69 / 69	75 / 75			
Any ocular AE at the study eye, n (%)	27 (39.1)	35 (46.7)	0.73 [0.38; 1.43] 0.362	0.84 [0.57; 1.23] 0.365	-0.08 [-0.24; 0.09] 0.360
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any ocular AE at the study eye, n (%)	16 (53.3)	17 (58.6)	0.81 [0.29; 2.26] 0.683	0.91 [0.58; 1.43] 0.683	-0.05 [-0.31; 0.20] 0.682

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.653				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE at the study eye, n (%)	12 (46.2)	7 (33.3)	1.71 [0.52; 5.64] 0.375	1.38 [0.66; 2.88] 0.385	0.13 [-0.15; 0.41] 0.366
European Region					
N'/N	135 / 135	132 / 132			
Any ocular AE at the study eye, n (%)	52 (38.5)	52 (39.4)	0.96 [0.59; 1.58] 0.883	0.98 [0.72; 1.32] 0.883	-0.01 [-0.13; 0.11] 0.883
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any ocular AE at the study eye, n (%)	9 (50.0)	15 (53.6)	0.87 [0.26; 2.84] 0.813	0.93 [0.52; 1.66] 0.815	-0.04 [-0.33; 0.26] 0.813
Pooled Analysis					
Interaction Test:	p = 0.541				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE at the study eye, n (%)	50 (55.6)	42 (50.6)	1.36 [0.68; 2.74] 0.382	1.10 [0.83; 1.46] 0.515	0.05 [-0.10; 0.20] 0.514
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE at the study eye, n (%)	12 (46.2)	7 (33.3)	1.53 [0.44; 5.31] 0.507	1.38 [0.66; 2.88] 0.378	0.13 [-0.15; 0.41] 0.366
European Region					
N'/N	204 / 204	207 / 207			
Any ocular AE at the study eye, n (%)	79 (38.7)	87 (42.0)	0.84 [0.56; 1.27] 0.421	0.92 [0.73; 1.17] 0.509	-0.03 [-0.13; 0.06] 0.507

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any ocular AE at the study eye, n (%)	25 (52.1)	32 (56.1)	0.84 [0.39; 1.83] 0.666	0.92 [0.64; 1.31] 0.646	-0.05 [-0.24; 0.15] 0.642

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-3.6 Any ocular adverse event at the study eye by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.983**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular AE at the study eye, n (%)	4 (33.3)	6 (100.0)	N.E.	0.33 [0.15; 0.74] 0.007 *	-0.67 [-0.93; -0.40] <.001 *
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular AE at the study eye, n (%)	72 (40.7)	67 (37.0)	1.17 [0.76; 1.79] 0.477	1.10 [0.85; 1.43] 0.478	0.04 [-0.06; 0.14] 0.477
KITE					
Interaction Test:	p = 0.202				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular AE at the study eye, n (%)	8 (42.1)	1 (14.3)	4.36 [0.44; 43.72] 0.210	2.95 [0.45; 19.50] 0.262	0.28 [-0.06; 0.62] 0.110
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular AE at the study eye, n (%)	45 (28.1)	51 (29.3)	0.94 [0.59; 1.52] 0.811	0.96 [0.68; 1.35] 0.811	-0.01 [-0.11; 0.09] 0.811
Pooled Analysis					
Interaction Test:	p = 0.352				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular AE at the study eye, n (%)	12 (38.7)	7 (53.8)	0.56 [0.15; 2.08] 0.384	0.75 [0.37; 1.55] 0.427	-0.14 [-0.47; 0.20] 0.424

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular AE at the study eye, n (%)	117 (34.7)	118 (33.2)	1.06 [0.77; 1.46] 0.716	1.04 [0.85; 1.28] 0.712	0.01 [-0.06; 0.08] 0.712
Any ocular AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.898**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular AE at the study eye, n (%)	6 (50.0)	6 (100.0)	N.E.	0.50 [0.28; 0.88] 0.016 *	-0.50 [-0.78; -0.22] <.001 *
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular AE at the study eye, n (%)	87 (49.2)	88 (48.6)	1.02 [0.67; 1.55] 0.920	1.01 [0.82; 1.25] 0.920	0.01 [-0.10; 0.11] 0.920
KITE					
Interaction Test:	p = 0.376				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular AE at the study eye, n (%)	9 (47.4)	2 (28.6)	2.25 [0.35; 14.61] 0.396	1.66 [0.47; 5.87] 0.433	0.19 [-0.22; 0.59] 0.361
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular AE at the study eye, n (%)	64 (40.0)	72 (41.4)	0.94 [0.61; 1.46] 0.798	0.97 [0.75; 1.25] 0.798	-0.01 [-0.12; 0.09] 0.798
Pooled Analysis					
Interaction Test:	p = 0.473				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular AE at the study eye, n (%)	15 (48.4)	8 (61.5)	0.60 [0.16; 2.25] 0.447	0.83 [0.46; 1.47] 0.522	-0.11 [-0.43; 0.20] 0.482

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular AE at the study eye, n (%)	151 (44.8)	160 (45.1)	0.98 [0.73; 1.33] 0.918	0.99 [0.84; 1.17] 0.918	-0.00 [-0.08; 0.07] 0.918

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 100 / KESTREL: logit(proportion) = treatment [by diabetes type].

Table 12-3.7 Any ocular adverse event at the study eye by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.983**					
KESTREL					
Interaction Test:	p = 0.341				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any ocular AE at the study eye, n (%)	31 (40.8)	38 (35.5)	1.25 [0.68; 2.29] 0.468	1.15 [0.79; 1.67] 0.466	0.05 [-0.09; 0.20] 0.469
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any ocular AE at the study eye, n (%)	44 (39.3)	35 (43.8)	0.83 [0.46; 1.49] 0.536	0.90 [0.64; 1.26] 0.533	-0.04 [-0.19; 0.10] 0.536
KITE					
Interaction Test:	p = 0.443				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any ocular AE at the study eye, n (%)	24 (29.3)	24 (25.0)	1.24 [0.64; 2.41] 0.523	1.17 [0.72; 1.90] 0.522	0.04 [-0.09; 0.17] 0.524
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any ocular AE at the study eye, n (%)	29 (29.9)	28 (32.9)	0.87 [0.46; 1.63] 0.659	0.91 [0.59; 1.40] 0.658	-0.03 [-0.17; 0.10] 0.659
Pooled Analysis					
Interaction Test:	p = 0.223				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any ocular AE at the study eye, n (%)	55 (34.8)	62 (30.5)	1.24 [0.80; 1.95] 0.336	1.16 [0.86; 1.56] 0.335	0.05 [-0.05; 0.14] 0.335

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any ocular AE at the study eye, n (%)	73 (34.9)	63 (38.2)	0.85 [0.55; 1.30] 0.448	0.90 [0.69; 1.18] 0.452	-0.04 [-0.14; 0.06] 0.451
Any ocular AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.898**					
KESTREL					
Interaction Test:	p = 0.932				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any ocular AE at the study eye, n (%)	37 (48.7)	54 (50.5)	0.93 [0.52; 1.68] 0.812	0.96 [0.72; 1.30] 0.813	-0.02 [-0.16; 0.13] 0.812
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any ocular AE at the study eye, n (%)	55 (49.1)	40 (50.0)	0.96 [0.54; 1.71] 0.903	0.98 [0.74; 1.31] 0.903	-0.01 [-0.15; 0.13] 0.903
KITE					
Interaction Test:	p = 0.871				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any ocular AE at the study eye, n (%)	31 (37.8)	36 (37.5)	1.01 [0.55; 1.86] 0.967	1.01 [0.69; 1.47] 0.967	0.00 [-0.14; 0.15] 0.967
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any ocular AE at the study eye, n (%)	42 (43.3)	38 (44.7)	0.94 [0.53; 1.70] 0.849	0.97 [0.70; 1.34] 0.849	-0.01 [-0.16; 0.13] 0.849
Pooled Analysis					
Interaction Test:	p = 0.957				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any ocular AE at the study eye, n (%)	68 (43.0)	90 (44.3)	0.96 [0.63; 1.47] 0.866	0.98 [0.78; 1.24] 0.888	-0.01 [-0.11; 0.10] 0.887

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any ocular AE at the study eye, n (%)	97 (46.4)	78 (47.3)	0.95 [0.63; 1.43] 0.802	0.98 [0.79; 1.21] 0.826	-0.01 [-0.11; 0.09] 0.825

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-3.8 Any ocular adverse event at the study eye by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.983**					
KESTREL					
Interaction Test:	p = 0.159				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any ocular AE at the study eye, n (%)	51 (42.5)	43 (39.1)	1.15 [0.68; 1.95] 0.599	1.09 [0.80; 1.49] 0.600	0.03 [-0.09; 0.16] 0.599
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any ocular AE at the study eye, n (%)	10 (33.3)	20 (51.3)	0.48 [0.18; 1.27] 0.139	0.65 [0.36; 1.17] 0.153	-0.18 [-0.41; 0.05] 0.127
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any ocular AE at the study eye, n (%)	15 (38.5)	10 (26.3)	1.75 [0.66; 4.61] 0.257	1.46 [0.75; 2.84] 0.263	0.12 [-0.09; 0.33] 0.251
KITE					
Interaction Test:	p = 0.237				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any ocular AE at the study eye, n (%)	30 (35.3)	31 (33.7)	1.07 [0.58; 2.00] 0.823	1.05 [0.70; 1.57] 0.823	0.02 [-0.12; 0.16] 0.823
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any ocular AE at the study eye, n (%)	10 (19.6)	14 (28.6)	0.61 [0.24; 1.54] 0.296	0.69 [0.34; 1.40] 0.299	-0.09 [-0.26; 0.08] 0.293
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any ocular AE at the study eye, n (%)	13 (30.2)	7 (17.5)	2.04 [0.72; 5.80] 0.180	1.73 [0.77; 3.89] 0.187	0.13 [-0.05; 0.31] 0.168

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.035 *				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any ocular AE at the study eye, n (%)	81 (39.5)	74 (36.6)	1.12 [0.75; 1.68] 0.589	1.07 [0.84; 1.37] 0.586	0.03 [-0.07; 0.12] 0.585
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any ocular AE at the study eye, n (%)	20 (24.7)	34 (38.6)	0.53 [0.27; 1.04] 0.063	0.67 [0.42; 1.05] 0.075	-0.13 [-0.26; 0.01] 0.071
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any ocular AE at the study eye, n (%)	28 (34.1)	17 (21.8)	1.88 [0.93; 3.83] 0.080	1.57 [0.94; 2.63] 0.081	0.12 [-0.01; 0.26] 0.075
Any ocular AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.898**					
KESTREL					
Interaction Test:	p = 0.122				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any ocular AE at the study eye, n (%)	63 (52.5)	56 (50.9)	1.07 [0.64; 1.79] 0.809	1.03 [0.80; 1.32] 0.810	0.02 [-0.11; 0.15] 0.809
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any ocular AE at the study eye, n (%)	10 (33.3)	22 (56.4)	0.39 [0.14; 1.04] 0.059	0.59 [0.33; 1.05] 0.074	-0.23 [-0.46; -0.00] 0.049 *
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any ocular AE at the study eye, n (%)	20 (51.3)	16 (42.1)	1.45 [0.59; 3.56] 0.420	1.22 [0.75; 1.97] 0.423	0.09 [-0.13; 0.31] 0.418

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.802				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any ocular AE at the study eye, n (%)	37 (43.5)	38 (41.3)	1.10 [0.60; 1.99] 0.765	1.05 [0.75; 1.49] 0.765	0.02 [-0.12; 0.17] 0.765
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any ocular AE at the study eye, n (%)	18 (35.3)	20 (40.8)	0.79 [0.35; 1.78] 0.570	0.86 [0.52; 1.43] 0.570	-0.06 [-0.25; 0.13] 0.569
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any ocular AE at the study eye, n (%)	18 (41.9)	16 (40.0)	1.08 [0.45; 2.59] 0.863	1.05 [0.62; 1.76] 0.863	0.02 [-0.19; 0.23] 0.863
Pooled Analysis					
Interaction Test:	p = 0.179				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any ocular AE at the study eye, n (%)	100 (48.8)	94 (46.5)	1.09 [0.73; 1.61] 0.676	1.04 [0.85; 1.27] 0.706	0.02 [-0.08; 0.12] 0.705
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any ocular AE at the study eye, n (%)	28 (34.6)	42 (47.7)	0.59 [0.31; 1.09] 0.093	0.73 [0.50; 1.07] 0.098	-0.13 [-0.27; 0.02] 0.094

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any ocular AE at the study eye, n (%)	38 (46.3)	32 (41.0)	1.25 [0.66; 2.33] 0.493	1.13 [0.79; 1.61] 0.495	0.05 [-0.10; 0.21] 0.491

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-3.9 Any ocular adverse event at the study eye by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.983**					
KESTREL					
Interaction Test:	p = 0.418				
focal					
N'/N	59 / 59	48 / 48			
Any ocular AE at the study eye, n (%)	23 (39.0)	21 (43.8)	0.82 [0.38; 1.78] 0.618	0.89 [0.57; 1.40] 0.617	-0.05 [-0.24; 0.14] 0.618
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular AE at the study eye, n (%)	51 (40.2)	48 (35.8)	1.20 [0.73; 1.98] 0.471	1.12 [0.82; 1.53] 0.471	0.04 [-0.07; 0.16] 0.470
KITE					
Interaction Test:	p = 0.638				
focal					
N'/N	63 / 63	66 / 66			
Any ocular AE at the study eye, n (%)	16 (25.4)	18 (27.3)	0.91 [0.41; 1.99] 0.809	0.93 [0.52; 1.66] 0.809	-0.02 [-0.17; 0.13] 0.809
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular AE at the study eye, n (%)	36 (31.3)	31 (28.4)	1.15 [0.65; 2.03] 0.640	1.10 [0.74; 1.65] 0.640	0.03 [-0.09; 0.15] 0.639
Pooled Analysis					
Interaction Test:	p = 0.379				
focal					
N'/N	122 / 122	114 / 114			
Any ocular AE at the study eye, n (%)	39 (32.0)	39 (34.2)	0.88 [0.51; 1.51] 0.635	0.91 [0.63; 1.30] 0.602	-0.03 [-0.15; 0.09] 0.600

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular AE at the study eye, n (%)	87 (36.0)	79 (32.5)	1.18 [0.81; 1.73] 0.388	1.11 [0.87; 1.42] 0.396	0.04 [-0.05; 0.12] 0.394
Any ocular AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.898**					
KESTREL					
Interaction Test:	p = 0.495				
focal					
N'/N	59 / 59	48 / 48			
Any ocular AE at the study eye, n (%)	26 (44.1)	24 (50.0)	0.79 [0.37; 1.69] 0.541	0.88 [0.59; 1.32] 0.539	-0.06 [-0.25; 0.13] 0.540
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular AE at the study eye, n (%)	65 (51.2)	66 (49.3)	1.08 [0.66; 1.76] 0.756	1.04 [0.82; 1.32] 0.756	0.02 [-0.10; 0.14] 0.756
KITE					
Interaction Test:	p = 0.399				
focal					
N'/N	63 / 63	66 / 66			
Any ocular AE at the study eye, n (%)	22 (34.9)	27 (40.9)	0.78 [0.38; 1.58] 0.484	0.85 [0.55; 1.33] 0.485	-0.06 [-0.23; 0.11] 0.482
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular AE at the study eye, n (%)	50 (43.5)	44 (40.4)	1.14 [0.67; 1.93] 0.637	1.08 [0.79; 1.47] 0.638	0.03 [-0.10; 0.16] 0.637
Pooled Analysis					
Interaction Test:	p = 0.282				
focal					
N'/N	122 / 122	114 / 114			
Any ocular AE at the study eye, n (%)	48 (39.3)	51 (44.7)	0.78 [0.46; 1.32] 0.354	0.87 [0.64; 1.17] 0.355	-0.06 [-0.19; 0.07] 0.352

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular AE at the study eye, n (%)	115 (47.5)	110 (45.3)	1.11 [0.77; 1.59] 0.579	1.05 [0.87; 1.28] 0.584	0.02 [-0.06; 0.11] 0.584

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-3.10 Any ocular adverse event at the study eye by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.983**					
KESTREL					
Interaction Test:	p = 0.589				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any ocular AE at the study eye, n (%)	43 (40.2)	40 (41.7)	0.94 [0.54; 1.65] 0.830	0.96 [0.69; 1.34] 0.830	-0.01 [-0.15; 0.12] 0.830
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any ocular AE at the study eye, n (%)	28 (40.0)	23 (32.4)	1.39 [0.70; 2.77] 0.348	1.23 [0.79; 1.92] 0.350	0.08 [-0.08; 0.23] 0.346
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any ocular AE at the study eye, n (%)	5 (41.7)	10 (50.0)	0.71 [0.17; 3.03] 0.648	0.83 [0.37; 1.85] 0.655	-0.08 [-0.44; 0.27] 0.645
KITE					
Interaction Test:	p = 0.438				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any ocular AE at the study eye, n (%)	26 (30.6)	24 (29.3)	1.06 [0.55; 2.07] 0.852	1.05 [0.66; 1.66] 0.852	0.01 [-0.13; 0.15] 0.852
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any ocular AE at the study eye, n (%)	22 (29.7)	20 (25.3)	1.25 [0.61; 2.54] 0.541	1.17 [0.70; 1.97] 0.542	0.04 [-0.10; 0.19] 0.541
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any ocular AE at the study eye, n (%)	5 (25.0)	8 (42.1)	0.46 [0.12; 1.79] 0.261	0.59 [0.24; 1.50] 0.269	-0.17 [-0.46; 0.12] 0.251

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.294				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any ocular AE at the study eye, n (%)	69 (35.9)	64 (36.0)	0.99 [0.64; 1.52] 0.962	0.99 [0.76; 1.30] 0.966	-0.00 [-0.10; 0.10] 0.966
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any ocular AE at the study eye, n (%)	50 (34.7)	43 (28.7)	1.32 [0.80; 2.17] 0.273	1.21 [0.86; 1.69] 0.273	0.06 [-0.05; 0.17] 0.271
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any ocular AE at the study eye, n (%)	10 (31.3)	18 (46.2)	0.56 [0.21; 1.50] 0.250	0.71 [0.39; 1.30] 0.261	-0.13 [-0.36; 0.09] 0.250
Any ocular AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.898**					
KESTREL					
Interaction Test:	p = 0.720				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any ocular AE at the study eye, n (%)	52 (48.6)	48 (50.0)	0.95 [0.54; 1.64] 0.842	0.97 [0.74; 1.29] 0.842	-0.01 [-0.15; 0.12] 0.842
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any ocular AE at the study eye, n (%)	34 (48.6)	32 (45.1)	1.15 [0.59; 2.23] 0.677	1.08 [0.76; 1.53] 0.677	0.04 [-0.13; 0.20] 0.677
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any ocular AE at the study eye, n (%)	7 (58.3)	14 (70.0)	0.60 [0.13; 2.67] 0.503	0.83 [0.48; 1.46] 0.522	-0.12 [-0.46; 0.23] 0.506

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.892				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any ocular AE at the study eye, n (%)	34 (40.0)	32 (39.0)	1.04 [0.56; 1.94] 0.897	1.03 [0.70; 1.49] 0.897	0.01 [-0.14; 0.16] 0.897
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any ocular AE at the study eye, n (%)	31 (41.9)	33 (41.8)	1.00 [0.53; 1.91] 0.988	1.00 [0.69; 1.46] 0.988	0.00 [-0.16; 0.16] 0.988
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any ocular AE at the study eye, n (%)	8 (40.0)	9 (47.4)	0.74 [0.21; 2.64] 0.643	0.84 [0.41; 1.73] 0.644	-0.07 [-0.38; 0.24] 0.642
Pooled Analysis					
Interaction Test:	p = 0.635				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any ocular AE at the study eye, n (%)	86 (44.8)	80 (44.9)	0.99 [0.65; 1.49] 0.956	0.99 [0.79; 1.24] 0.949	-0.00 [-0.10; 0.10] 0.949
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any ocular AE at the study eye, n (%)	65 (45.1)	65 (43.3)	1.07 [0.67; 1.70] 0.771	1.04 [0.80; 1.34] 0.764	0.02 [-0.10; 0.13] 0.763

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any ocular AE at the study eye, n (%)	15 (46.9)	23 (59.0)	0.64 [0.25; 1.66] 0.359	0.84 [0.54; 1.31] 0.437	-0.09 [-0.32; 0.14] 0.432

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-3.11 Any ocular adverse event at the study eye by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.983**					
KESTREL					
Interaction Test:	p = 0.356				
presence					
N'/N	62 / 62	61 / 61			
Any ocular AE at the study eye, n (%)	22 (35.5)	25 (41.0)	0.79 [0.38; 1.64] 0.531	0.87 [0.55; 1.36] 0.531	-0.05 [-0.23; 0.12] 0.530
absence					
N'/N	127 / 127	126 / 126			
Any ocular AE at the study eye, n (%)	54 (42.5)	48 (38.1)	1.20 [0.73; 1.99] 0.473	1.12 [0.83; 1.51] 0.474	0.04 [-0.08; 0.17] 0.473
KITE					
Interaction Test:	p = 0.348				
presence					
N'/N	56 / 56	67 / 67			
Any ocular AE at the study eye, n (%)	22 (39.3)	21 (31.3)	1.42 [0.67; 2.98] 0.358	1.25 [0.77; 2.03] 0.358	0.08 [-0.09; 0.25] 0.358
absence					
N'/N	123 / 123	114 / 114			
Any ocular AE at the study eye, n (%)	31 (25.2)	31 (27.2)	0.90 [0.51; 1.61] 0.728	0.93 [0.60; 1.42] 0.728	-0.02 [-0.13; 0.09] 0.728
Pooled Analysis					
Interaction Test:	p = 0.948				
presence					
N'/N	118 / 118	128 / 128			
Any ocular AE at the study eye, n (%)	44 (37.3)	46 (35.9)	1.04 [0.61; 1.75] 0.893	1.03 [0.74; 1.43] 0.847	0.01 [-0.11; 0.13] 0.847

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular AE at the study eye, n (%)	85 (34.0)	79 (32.9)	1.06 [0.73; 1.55] 0.767	1.04 [0.81; 1.33] 0.754	0.01 [-0.07; 0.10] 0.754
Any ocular AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.898**					
KESTREL					
Interaction Test:	p = 0.399				
presence					
N'/N	62 / 62	61 / 61			
Any ocular AE at the study eye, n (%)	28 (45.2)	32 (52.5)	0.75 [0.37; 1.52] 0.419	0.86 [0.60; 1.24] 0.420	-0.07 [-0.25; 0.10] 0.417
absence					
N'/N	127 / 127	126 / 126			
Any ocular AE at the study eye, n (%)	65 (51.2)	62 (49.2)	1.08 [0.66; 1.77] 0.753	1.04 [0.81; 1.33] 0.754	0.02 [-0.10; 0.14] 0.753
KITE					
Interaction Test:	p = 0.854				
presence					
N'/N	56 / 56	67 / 67			
Any ocular AE at the study eye, n (%)	26 (46.4)	30 (44.8)	1.07 [0.52; 2.18] 0.855	1.04 [0.70; 1.53] 0.854	0.02 [-0.16; 0.19] 0.855
absence					
N'/N	123 / 123	114 / 114			
Any ocular AE at the study eye, n (%)	47 (38.2)	44 (38.6)	0.98 [0.58; 1.66] 0.951	0.99 [0.72; 1.37] 0.951	-0.00 [-0.13; 0.12] 0.951
Pooled Analysis					
Interaction Test:	p = 0.614				
presence					
N'/N	118 / 118	128 / 128			
Any ocular AE at the study eye, n (%)	54 (45.8)	62 (48.4)	0.88 [0.53; 1.46] 0.623	0.94 [0.72; 1.23] 0.657	-0.03 [-0.15; 0.10] 0.656

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular AE at the study eye, n (%)	112 (44.8)	106 (44.2)	1.03 [0.72; 1.48] 0.857	1.02 [0.84; 1.24] 0.852	0.01 [-0.08; 0.10] 0.852

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-3.12 Any ocular adverse event at the study eye by exposure (week 52) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.983**					
KESTREL					
Interaction Test:	p = 0.420				
Non-exposed					
N'/N	71 / 71	75 / 75			
Any ocular AE at the study eye, n (%)	31 (43.7)	28 (37.3)	1.30 [0.67; 2.52] 0.436	1.17 [0.79; 1.74] 0.437	0.06 [-0.10; 0.22] 0.435
Exposed					
N'/N	118 / 118	112 / 112			
Any ocular AE at the study eye, n (%)	45 (38.1)	45 (40.2)	0.92 [0.54; 1.56] 0.751	0.95 [0.69; 1.31] 0.751	-0.02 [-0.15; 0.11] 0.751
KITE					
Interaction Test:	p = 0.591				
Non-exposed					
N'/N	85 / 85	90 / 90			
Any ocular AE at the study eye, n (%)	25 (29.4)	28 (31.1)	0.92 [0.48; 1.76] 0.807	0.95 [0.60; 1.48] 0.807	-0.02 [-0.15; 0.12] 0.807
Exposed					
N'/N	94 / 94	91 / 91			
Any ocular AE at the study eye, n (%)	28 (29.8)	24 (26.4)	1.18 [0.62; 2.25] 0.606	1.13 [0.71; 1.79] 0.606	0.03 [-0.10; 0.16] 0.605
Pooled Analysis					
Interaction Test:	p = 0.823				
Non-exposed					
N'/N	156 / 156	165 / 165			
Any ocular AE at the study eye, n (%)	56 (35.9)	56 (33.9)	1.09 [0.69; 1.73] 0.711	1.06 [0.79; 1.42] 0.713	0.02 [-0.08; 0.12] 0.713

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	212 / 212	203 / 203			
Any ocular AE at the study eye, n (%)	73 (34.4)	69 (34.0)	1.02 [0.67; 1.53] 0.937	1.01 [0.78; 1.32] 0.933	0.00 [-0.09; 0.09] 0.933

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-3.13 Any ocular adverse event at the study eye by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.898**					
KESTREL					
Interaction Test:	p = 0.131				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any ocular AE at the study eye, n (%)	5 (41.7)	2 (15.4)	3.93 [0.59; 26.10] 0.157	2.71 [0.64; 11.43] 0.175	0.26 [-0.08; 0.60] 0.131
Exposed					
N'/N	177 / 177	174 / 174			
Any ocular AE at the study eye, n (%)	88 (49.7)	92 (52.9)	0.88 [0.58; 1.34] 0.554	0.94 [0.77; 1.15] 0.554	-0.03 [-0.14; 0.07] 0.554
KITE					
Interaction Test:	p = 0.549				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any ocular AE at the study eye, n (%)	6 (35.3)	3 (25.0)	1.64 [0.32; 8.45] 0.557	1.41 [0.44; 4.56] 0.564	0.10 [-0.23; 0.44] 0.546
Exposed					
N'/N	162 / 162	169 / 169			
Any ocular AE at the study eye, n (%)	67 (41.4)	71 (42.0)	0.97 [0.63; 1.51] 0.904	0.98 [0.76; 1.27] 0.904	-0.01 [-0.11; 0.10] 0.904
Pooled Analysis					
Interaction Test:	p = 0.119				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any ocular AE at the study eye, n (%)	11 (37.9)	5 (20.0)	2.55 [0.74; 8.82] 0.138	1.87 [0.76; 4.60] 0.163	0.18 [-0.06; 0.42] 0.145

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any ocular AE at the study eye, n (%)	155 (45.7)	163 (47.5)	0.93 [0.68; 1.25] 0.615	0.96 [0.82; 1.13] 0.610	-0.02 [-0.09; 0.06] 0.610

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-4.1 Any ocular adverse event at the fellow eye (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the fellow eye, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular AE at the fellow eye, n (%)	64 (33.9)	51 (27.3)	1.37 [0.88; 2.12] 0.166	1.24 [0.91; 1.69] 0.168	0.07 [-0.03; 0.16] 0.164
KITE, N'/N	179 / 179	181 / 181			
Any ocular AE at the fellow eye, n (%)	51 (28.5)	54 (29.8)	0.94 [0.59; 1.48] 0.779	0.95 [0.69; 1.32] 0.779	-0.01 [-0.11; 0.08] 0.779
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular AE at the fellow eye, n (%)	115 (31.3)	105 (28.5)	1.14 [0.83; 1.56] 0.432	1.09 [0.88; 1.37] 0.423	0.03 [-0.04; 0.09] 0.422
p_H=0.244					
Any ocular AE at the fellow eye, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular AE at the fellow eye, n (%)	92 (48.7)	71 (38.0)	1.55 [1.03; 2.34] 0.037 *	1.28 [1.01; 1.62] 0.038 *	0.11 [0.01; 0.21] 0.035 *
KITE, N'/N	179 / 179	181 / 181			
Any ocular AE at the fellow eye, n (%)	70 (39.1)	77 (42.5)	0.87 [0.57; 1.32] 0.507	0.92 [0.72; 1.18] 0.508	-0.03 [-0.14; 0.07] 0.507
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular AE at the fellow eye, n (%)	162 (44.0)	148 (40.2)	1.17 [0.87; 1.56] 0.305	1.09 [0.92; 1.30] 0.298	0.04 [-0.03; 0.11] 0.298
p_H=0.053					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-4.2 Any ocular adverse event at the fellow eye by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the fellow eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.244**					
KESTREL					
Interaction Test:	p = 0.969				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular AE at the fellow eye, n (%)	38 (36.5)	28 (30.1)	1.34 [0.74; 2.43] 0.340	1.21 [0.81; 1.81] 0.343	0.06 [-0.07; 0.20] 0.337
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular AE at the fellow eye, n (%)	26 (30.6)	23 (24.5)	1.36 [0.70; 2.63] 0.360	1.25 [0.77; 2.02] 0.360	0.06 [-0.07; 0.19] 0.360
KITE					
Interaction Test:	p = 0.067				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular AE at the fellow eye, n (%)	31 (31.0)	25 (24.5)	1.38 [0.75; 2.57] 0.304	1.26 [0.81; 1.98] 0.305	0.06 [-0.06; 0.19] 0.302
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular AE at the fellow eye, n (%)	20 (25.3)	29 (36.7)	0.58 [0.30; 1.16] 0.123	0.69 [0.43; 1.11] 0.127	-0.11 [-0.26; 0.03] 0.119
Pooled Analysis					
Interaction Test:	p = 0.193				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular AE at the fellow eye, n (%)	69 (33.8)	53 (27.2)	1.37 [0.89; 2.11] 0.148	1.24 [0.92; 1.67] 0.162	0.06 [-0.03; 0.15] 0.159

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular AE at the fellow eye, n (%)	46 (28.0)	52 (30.1)	0.90 [0.56; 1.44] 0.657	0.93 [0.67; 1.30] 0.672	-0.02 [-0.12; 0.08] 0.673
Any ocular AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.053**					
KESTREL					
Interaction Test:	p = 0.922				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular AE at the fellow eye, n (%)	53 (51.0)	38 (40.9)	1.50 [0.86; 2.65] 0.156	1.25 [0.92; 1.70] 0.161	0.10 [-0.04; 0.24] 0.153
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular AE at the fellow eye, n (%)	39 (45.9)	33 (35.1)	1.57 [0.86; 2.86] 0.143	1.31 [0.91; 1.87] 0.144	0.11 [-0.04; 0.25] 0.140
KITE					
Interaction Test:	p = 0.367				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular AE at the fellow eye, n (%)	38 (38.0)	38 (37.3)	1.03 [0.58; 1.82] 0.913	1.02 [0.72; 1.45] 0.913	0.01 [-0.13; 0.14] 0.913
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular AE at the fellow eye, n (%)	32 (40.5)	39 (49.4)	0.70 [0.37; 1.31] 0.264	0.82 [0.58; 1.16] 0.266	-0.09 [-0.24; 0.07] 0.261
Pooled Analysis					
Interaction Test:	p = 0.549				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular AE at the fellow eye, n (%)	91 (44.6)	76 (39.0)	1.27 [0.85; 1.89] 0.245	1.14 [0.90; 1.44] 0.278	0.05 [-0.04; 0.15] 0.276

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular AE at the fellow eye, n (%)	71 (43.3)	72 (41.6)	1.06 [0.69; 1.63] 0.797	1.04 [0.81; 1.33] 0.773	0.02 [-0.09; 0.12] 0.774

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-4.3 Any ocular adverse event at the fellow eye by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the fellow eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.244**					
KESTREL					
Interaction Test:	p = 0.845				
Male					
N'/N	110 / 110	126 / 126			
Any ocular AE at the fellow eye, n (%)	39 (35.5)	35 (27.8)	1.43 [0.82; 2.48] 0.206	1.28 [0.87; 1.86] 0.206	0.08 [-0.04; 0.20] 0.205
Female					
N'/N	79 / 79	61 / 61			
Any ocular AE at the fellow eye, n (%)	25 (31.6)	16 (26.2)	1.30 [0.62; 2.73] 0.486	1.21 [0.71; 2.05] 0.489	0.05 [-0.10; 0.20] 0.481
KITE					
Interaction Test:	p = 0.997				
Male					
N'/N	120 / 120	115 / 115			
Any ocular AE at the fellow eye, n (%)	33 (27.5)	33 (28.7)	0.94 [0.53; 1.67] 0.838	0.96 [0.64; 1.44] 0.838	-0.01 [-0.13; 0.10] 0.838
Female					
N'/N	59 / 59	66 / 66			
Any ocular AE at the fellow eye, n (%)	18 (30.5)	21 (31.8)	0.94 [0.44; 2.01] 0.875	0.96 [0.57; 1.62] 0.875	-0.01 [-0.18; 0.15] 0.875
Pooled Analysis					
Interaction Test:	p = 0.835				
Male					
N'/N	230 / 230	241 / 241			
Any ocular AE at the fellow eye, n (%)	72 (31.3)	68 (28.2)	1.16 [0.78; 1.73] 0.451	1.11 [0.85; 1.47] 0.443	0.03 [-0.05; 0.12] 0.443

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any ocular AE at the fellow eye, n (%)	43 (31.2)	37 (29.1)	1.09 [0.64; 1.84] 0.761	1.08 [0.74; 1.56] 0.696	0.02 [-0.09; 0.13] 0.695
Any ocular AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.053**					
KESTREL					
Interaction Test:	p = 0.599				
Male					
N'/N	110 / 110	126 / 126			
Any ocular AE at the fellow eye, n (%)	54 (49.1)	46 (36.5)	1.68 [1.00; 2.82] 0.052	1.34 [1.00; 1.81] 0.052	0.13 [0.00; 0.25] 0.050 *
Female					
N'/N	79 / 79	61 / 61			
Any ocular AE at the fellow eye, n (%)	38 (48.1)	25 (41.0)	1.33 [0.68; 2.62] 0.402	1.17 [0.80; 1.71] 0.407	0.07 [-0.09; 0.24] 0.399
KITE					
Interaction Test:	p = 0.971				
Male					
N'/N	120 / 120	115 / 115			
Any ocular AE at the fellow eye, n (%)	45 (37.5)	47 (40.9)	0.87 [0.51; 1.47] 0.597	0.92 [0.67; 1.26] 0.597	-0.03 [-0.16; 0.09] 0.597
Female					
N'/N	59 / 59	66 / 66			
Any ocular AE at the fellow eye, n (%)	25 (42.4)	30 (45.5)	0.88 [0.43; 1.79] 0.729	0.93 [0.63; 1.39] 0.730	-0.03 [-0.20; 0.14] 0.729
Pooled Analysis					
Interaction Test:	p = 0.707				
Male					
N'/N	230 / 230	241 / 241			
Any ocular AE at the fellow eye, n (%)	99 (43.0)	93 (38.6)	1.21 [0.84; 1.75] 0.306	1.12 [0.90; 1.39] 0.310	0.05 [-0.04; 0.14] 0.311

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any ocular AE at the fellow eye, n (%)	63 (45.7)	55 (43.3)	1.08 [0.66; 1.76] 0.762	1.05 [0.80; 1.38] 0.712	0.02 [-0.10; 0.14] 0.711

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-4.4 Any ocular adverse event at the fellow eye by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the fellow eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.244**					
KESTREL					
Interaction Test:	p = 0.917				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any ocular AE at the fellow eye, n (%)	25 (33.8)	17 (26.6)	1.41 [0.68; 2.94] 0.359	1.27 [0.76; 2.13] 0.362	0.07 [-0.08; 0.22] 0.354
> 65 letters					
N'/N	115 / 115	123 / 123			
Any ocular AE at the fellow eye, n (%)	39 (33.9)	34 (27.6)	1.34 [0.77; 2.33] 0.295	1.23 [0.84; 1.80] 0.296	0.06 [-0.05; 0.18] 0.294
KITE					
Interaction Test:	p = 0.195				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any ocular AE at the fellow eye, n (%)	15 (23.1)	29 (31.9)	0.64 [0.31; 1.33] 0.231	0.72 [0.42; 1.24] 0.238	-0.09 [-0.23; 0.05] 0.219
> 65 letters					
N'/N	114 / 114	90 / 90			
Any ocular AE at the fellow eye, n (%)	36 (31.6)	25 (27.8)	1.20 [0.65; 2.20] 0.556	1.14 [0.74; 1.75] 0.558	0.04 [-0.09; 0.16] 0.554
Pooled Analysis					
Interaction Test:	p = 0.412				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any ocular AE at the fellow eye, n (%)	40 (28.8)	46 (29.7)	0.96 [0.58; 1.59] 0.874	0.96 [0.66; 1.39] 0.826	-0.01 [-0.12; 0.09] 0.825

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any ocular AE at the fellow eye, n (%)	75 (32.8)	59 (27.7)	1.26 [0.84; 1.90] 0.266	1.19 [0.89; 1.58] 0.243	0.05 [-0.03; 0.14] 0.240
Any ocular AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.053**					
KESTREL					
Interaction Test:	p = 0.420				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any ocular AE at the fellow eye, n (%)	34 (45.9)	26 (40.6)	1.24 [0.63; 2.44] 0.530	1.13 [0.77; 1.66] 0.532	0.05 [-0.11; 0.22] 0.528
> 65 letters					
N'/N	115 / 115	123 / 123			
Any ocular AE at the fellow eye, n (%)	58 (50.4)	45 (36.6)	1.76 [1.05; 2.96] 0.032 *	1.38 [1.03; 1.85] 0.033 *	0.14 [0.01; 0.26] 0.030 *
KITE					
Interaction Test:	p = 0.196				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any ocular AE at the fellow eye, n (%)	21 (32.3)	40 (44.0)	0.61 [0.31; 1.18] 0.143	0.74 [0.48; 1.12] 0.152	-0.12 [-0.27; 0.04] 0.135
> 65 letters					
N'/N	114 / 114	90 / 90			
Any ocular AE at the fellow eye, n (%)	49 (43.0)	37 (41.1)	1.08 [0.62; 1.89] 0.788	1.05 [0.76; 1.45] 0.789	0.02 [-0.12; 0.16] 0.788
Pooled Analysis					
Interaction Test:	p = 0.146				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any ocular AE at the fellow eye, n (%)	55 (39.6)	66 (42.6)	0.89 [0.55; 1.42] 0.614	0.92 [0.69; 1.22] 0.537	-0.04 [-0.15; 0.08] 0.535

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any ocular AE at the fellow eye, n (%)	107 (46.7)	82 (38.5)	1.39 [0.95; 2.03] 0.091	1.22 [0.98; 1.51] 0.077	0.08 [-0.01; 0.18] 0.076

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-4.5 Any ocular adverse event at the fellow eye by region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the fellow eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.244**					
KESTREL					
Interaction Test:	p = 0.126				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE at the fellow eye, n (%)	35 (38.9)	21 (25.3)	1.88 [0.98; 3.60] 0.058	1.54 [0.98; 2.41] 0.062	0.14 [-0.00; 0.27] 0.053
European Region					
N'/N	69 / 69	75 / 75			
Any ocular AE at the fellow eye, n (%)	25 (36.2)	22 (29.3)	1.37 [0.68; 2.75] 0.378	1.24 [0.77; 1.98] 0.379	0.07 [-0.08; 0.22] 0.378
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any ocular AE at the fellow eye, n (%)	4 (13.3)	8 (27.6)	0.40 [0.11; 1.53] 0.182	0.48 [0.16; 1.43] 0.190	-0.14 [-0.35; 0.06] 0.169
KITE					
Interaction Test:	p = 0.385				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE at the fellow eye, n (%)	9 (34.6)	4 (19.0)	2.25 [0.58; 8.73] 0.241	1.82 [0.65; 5.08] 0.255	0.16 [-0.09; 0.40] 0.219
European Region					
N'/N	135 / 135	132 / 132			
Any ocular AE at the fellow eye, n (%)	36 (26.7)	38 (28.8)	0.90 [0.53; 1.54] 0.699	0.93 [0.63; 1.36] 0.699	-0.02 [-0.13; 0.09] 0.699
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any ocular AE at the fellow eye, n (%)	6 (33.3)	12 (42.9)	0.67 [0.19; 2.29] 0.519	0.78 [0.36; 1.70] 0.528	-0.10 [-0.38; 0.19] 0.512

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.099				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE at the fellow eye, n (%)	35 (38.9)	21 (25.3)	1.60 [0.75; 3.41] 0.226	1.54 [0.98; 2.41] 0.057	0.14 [-0.00; 0.27] 0.053
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE at the fellow eye, n (%)	9 (34.6)	4 (19.0)	2.66 [0.65; 10.97] 0.175	1.82 [0.65; 5.08] 0.241	0.16 [-0.09; 0.40] 0.219
European Region					
N'/N	204 / 204	207 / 207			
Any ocular AE at the fellow eye, n (%)	61 (29.9)	60 (29.0)	1.10 [0.71; 1.72] 0.668	1.04 [0.77; 1.40] 0.818	0.01 [-0.08; 0.10] 0.818
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any ocular AE at the fellow eye, n (%)	10 (20.8)	20 (35.1)	0.48 [0.20; 1.16] 0.101	0.64 [0.34; 1.21] 0.164	-0.12 [-0.29; 0.05] 0.154
Any ocular AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.053**					
KESTREL					
Interaction Test:	p = 0.292				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE at the fellow eye, n (%)	46 (51.1)	31 (37.3)	1.75 [0.96; 3.22] 0.070	1.37 [0.97; 1.93] 0.074	0.14 [-0.01; 0.28] 0.066
European Region					
N'/N	69 / 69	75 / 75			
Any ocular AE at the fellow eye, n (%)	37 (53.6)	29 (38.7)	1.83 [0.94; 3.56] 0.073	1.39 [0.97; 1.99] 0.075	0.15 [-0.01; 0.31] 0.069
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any ocular AE at the fellow eye, n (%)	9 (30.0)	11 (37.9)	0.70 [0.24; 2.07] 0.521	0.79 [0.39; 1.62] 0.522	-0.08 [-0.32; 0.16] 0.519

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.295				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE at the fellow eye, n (%)	12 (46.2)	6 (28.6)	2.14 [0.63; 7.26] 0.221	1.62 [0.73; 3.57] 0.236	0.18 [-0.10; 0.45] 0.205
European Region					
N'/N	135 / 135	132 / 132			
Any ocular AE at the fellow eye, n (%)	51 (37.8)	59 (44.7)	0.75 [0.46; 1.22] 0.251	0.85 [0.63; 1.13] 0.252	-0.07 [-0.19; 0.05] 0.250
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any ocular AE at the fellow eye, n (%)	7 (38.9)	12 (42.9)	0.85 [0.25; 2.84] 0.790	0.91 [0.44; 1.86] 0.791	-0.04 [-0.33; 0.25] 0.789
Pooled Analysis					
Interaction Test:	p = 0.272				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE at the fellow eye, n (%)	46 (51.1)	31 (37.3)	1.25 [0.62; 2.53] 0.538	1.37 [0.97; 1.93] 0.070	0.14 [-0.01; 0.28] 0.066
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE at the fellow eye, n (%)	12 (46.2)	6 (28.6)	3.05 [0.85; 10.94] 0.087	1.62 [0.73; 3.57] 0.223	0.18 [-0.10; 0.45] 0.205
European Region					
N'/N	204 / 204	207 / 207			
Any ocular AE at the fellow eye, n (%)	88 (43.1)	88 (42.5)	1.15 [0.76; 1.73] 0.511	1.02 [0.81; 1.27] 0.880	0.01 [-0.09; 0.10] 0.881

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any ocular AE at the fellow eye, n (%)	16 (33.3)	23 (40.4)	0.70 [0.31; 1.56] 0.380	0.84 [0.51; 1.40] 0.515	-0.06 [-0.25; 0.12] 0.510

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-4.6 Any ocular adverse event at the fellow eye by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the fellow eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.244**					
KESTREL					
Interaction Test:	p = 0.049 *				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular AE at the fellow eye, n (%)	3 (25.0)	4 (66.7)	0.17 [0.02; 1.42] 0.101	0.38 [0.12; 1.16] 0.089	-0.42 [-0.87; 0.03] 0.069
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular AE at the fellow eye, n (%)	61 (34.5)	47 (26.0)	1.50 [0.95; 2.36] 0.081	1.33 [0.96; 1.83] 0.082	0.08 [-0.01; 0.18] 0.079
KITE					
Interaction Test:	p = 0.450				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular AE at the fellow eye, n (%)	8 (42.1)	2 (28.6)	1.82 [0.28; 11.87] 0.532	1.47 [0.41; 5.32] 0.554	0.14 [-0.27; 0.54] 0.509
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular AE at the fellow eye, n (%)	43 (26.9)	52 (29.9)	0.86 [0.54; 1.39] 0.543	0.90 [0.64; 1.27] 0.543	-0.03 [-0.13; 0.07] 0.542
Pooled Analysis					
Interaction Test:	p = 0.432				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular AE at the fellow eye, n (%)	11 (35.5)	6 (46.2)	0.67 [0.18; 2.48] 0.544	0.76 [0.34; 1.72] 0.517	-0.11 [-0.44; 0.22] 0.525

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular AE at the fellow eye, n (%)	104 (30.9)	99 (27.9)	1.15 [0.83; 1.59] 0.414	1.11 [0.88; 1.39] 0.395	0.03 [-0.04; 0.10] 0.395
Any ocular AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.053**					
KESTREL					
Interaction Test:	p = 0.078				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular AE at the fellow eye, n (%)	4 (33.3)	4 (66.7)	0.25 [0.03; 2.00] 0.191	0.50 [0.19; 1.33] 0.166	-0.33 [-0.80; 0.13] 0.157
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular AE at the fellow eye, n (%)	88 (49.7)	67 (37.0)	1.68 [1.10; 2.56] 0.016 *	1.34 [1.06; 1.71] 0.016 *	0.13 [0.03; 0.23] 0.015 *
KITE					
Interaction Test:	p = 0.299				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular AE at the fellow eye, n (%)	9 (47.4)	2 (28.6)	2.25 [0.35; 14.61] 0.396	1.66 [0.47; 5.87] 0.433	0.19 [-0.22; 0.59] 0.361
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular AE at the fellow eye, n (%)	61 (38.1)	75 (43.1)	0.81 [0.52; 1.26] 0.355	0.88 [0.68; 1.15] 0.357	-0.05 [-0.16; 0.06] 0.354
Pooled Analysis					
Interaction Test:	p = 0.680				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular AE at the fellow eye, n (%)	13 (41.9)	6 (46.2)	0.89 [0.24; 3.29] 0.861	0.91 [0.42; 1.95] 0.808	-0.04 [-0.37; 0.29] 0.809

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular AE at the fellow eye, n (%)	149 (44.2)	142 (40.0)	1.18 [0.87; 1.60] 0.284	1.10 [0.93; 1.32] 0.267	0.04 [-0.03; 0.12] 0.268

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-4.7 Any ocular adverse event at the fellow eye by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the fellow eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.244**					
KESTREL					
Interaction Test:	p = 0.826				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any ocular AE at the fellow eye, n (%)	23 (30.3)	26 (24.3)	1.35 [0.70; 2.61] 0.370	1.25 [0.77; 2.01] 0.368	0.06 [-0.07; 0.19] 0.374
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any ocular AE at the fellow eye, n (%)	40 (35.7)	25 (31.3)	1.22 [0.66; 2.25] 0.519	1.14 [0.76; 1.72] 0.522	0.04 [-0.09; 0.18] 0.517
KITE					
Interaction Test:	p = 0.070				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any ocular AE at the fellow eye, n (%)	18 (22.0)	31 (32.3)	0.59 [0.30; 1.16] 0.126	0.68 [0.41; 1.12] 0.131	-0.10 [-0.23; 0.03] 0.118
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any ocular AE at the fellow eye, n (%)	33 (34.0)	23 (27.1)	1.39 [0.74; 2.63] 0.311	1.26 [0.81; 1.96] 0.314	0.07 [-0.06; 0.20] 0.307
Pooled Analysis					
Interaction Test:	p = 0.259				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any ocular AE at the fellow eye, n (%)	41 (25.9)	57 (28.1)	0.90 [0.56; 1.44] 0.659	0.92 [0.66; 1.30] 0.647	-0.02 [-0.11; 0.07] 0.647

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any ocular AE at the fellow eye, n (%)	73 (34.9)	48 (29.1)	1.30 [0.84; 2.03] 0.238	1.20 [0.88; 1.62] 0.244	0.06 [-0.04; 0.15] 0.240
Any ocular AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.053**					
KESTREL					
Interaction Test:	p = 0.821				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any ocular AE at the fellow eye, n (%)	34 (44.7)	39 (36.4)	1.41 [0.77; 2.57] 0.260	1.23 [0.86; 1.75] 0.256	0.08 [-0.06; 0.23] 0.260
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any ocular AE at the fellow eye, n (%)	57 (50.9)	32 (40.0)	1.55 [0.87; 2.78] 0.137	1.27 [0.92; 1.76] 0.145	0.11 [-0.03; 0.25] 0.132
KITE					
Interaction Test:	p = 0.069				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any ocular AE at the fellow eye, n (%)	24 (29.3)	41 (42.7)	0.56 [0.30; 1.04] 0.065	0.69 [0.46; 1.03] 0.070	-0.13 [-0.27; 0.01] 0.059
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any ocular AE at the fellow eye, n (%)	46 (47.4)	36 (42.4)	1.23 [0.68; 2.21] 0.493	1.12 [0.81; 1.55] 0.495	0.05 [-0.09; 0.20] 0.492
Pooled Analysis					
Interaction Test:	p = 0.155				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any ocular AE at the fellow eye, n (%)	58 (36.7)	80 (39.4)	0.90 [0.58; 1.38] 0.614	0.94 [0.72; 1.22] 0.622	-0.03 [-0.13; 0.08] 0.623

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any ocular AE at the fellow eye, n (%)	103 (49.3)	68 (41.2)	1.38 [0.91; 2.09] 0.126	1.19 [0.95; 1.50] 0.123	0.08 [-0.02; 0.18] 0.121

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-4.8 Any ocular adverse event at the fellow eye by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the fellow eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.244**					
KESTREL					
Interaction Test:	p = 0.252				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any ocular AE at the fellow eye, n (%)	46 (38.3)	34 (30.9)	1.39 [0.80; 2.40] 0.238	1.24 [0.87; 1.78] 0.241	0.07 [-0.05; 0.20] 0.235
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any ocular AE at the fellow eye, n (%)	5 (16.7)	10 (25.6)	0.58 [0.17; 1.92] 0.373	0.65 [0.25; 1.70] 0.380	-0.09 [-0.28; 0.10] 0.358
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any ocular AE at the fellow eye, n (%)	13 (33.3)	7 (18.4)	2.21 [0.77; 6.37] 0.140	1.81 [0.81; 4.04] 0.148	0.15 [-0.04; 0.34] 0.129
KITE					
Interaction Test:	p = 0.857				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any ocular AE at the fellow eye, n (%)	22 (25.9)	25 (27.2)	0.94 [0.48; 1.83] 0.846	0.95 [0.58; 1.56] 0.846	-0.01 [-0.14; 0.12] 0.846
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any ocular AE at the fellow eye, n (%)	14 (27.5)	16 (32.7)	0.78 [0.33; 1.84] 0.571	0.84 [0.46; 1.53] 0.571	-0.05 [-0.23; 0.13] 0.570
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any ocular AE at the fellow eye, n (%)	15 (34.9)	13 (32.5)	1.11 [0.45; 2.77] 0.818	1.07 [0.59; 1.97] 0.819	0.02 [-0.18; 0.23] 0.818

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.360				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any ocular AE at the fellow eye, n (%)	68 (33.2)	59 (29.2)	1.18 [0.77; 1.80] 0.446	1.12 [0.84; 1.50] 0.429	0.04 [-0.05; 0.13] 0.427
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any ocular AE at the fellow eye, n (%)	19 (23.5)	26 (29.5)	0.76 [0.38; 1.51] 0.430	0.77 [0.46; 1.29] 0.325	-0.07 [-0.20; 0.06] 0.318
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any ocular AE at the fellow eye, n (%)	28 (34.1)	20 (25.6)	1.52 [0.77; 3.01] 0.232	1.33 [0.82; 2.15] 0.247	0.08 [-0.06; 0.23] 0.242
Any ocular AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.053**					
KESTREL					
Interaction Test:	p = 0.374				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any ocular AE at the fellow eye, n (%)	65 (54.2)	43 (39.1)	1.84 [1.09; 3.11] 0.023 *	1.39 [1.04; 1.84] 0.025 *	0.15 [0.02; 0.28] 0.021 *
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any ocular AE at the fellow eye, n (%)	11 (36.7)	16 (41.0)	0.83 [0.31; 2.22] 0.713	0.89 [0.49; 1.63] 0.715	-0.04 [-0.28; 0.19] 0.712
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any ocular AE at the fellow eye, n (%)	16 (41.0)	12 (31.6)	1.51 [0.59; 3.84] 0.390	1.30 [0.71; 2.37] 0.393	0.09 [-0.12; 0.31] 0.386

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.926				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any ocular AE at the fellow eye, n (%)	32 (37.6)	36 (39.1)	0.94 [0.51; 1.72] 0.839	0.96 [0.66; 1.40] 0.839	-0.01 [-0.16; 0.13] 0.839
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any ocular AE at the fellow eye, n (%)	20 (39.2)	22 (44.9)	0.79 [0.36; 1.75] 0.565	0.87 [0.55; 1.39] 0.565	-0.06 [-0.25; 0.14] 0.564
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any ocular AE at the fellow eye, n (%)	18 (41.9)	19 (47.5)	0.80 [0.33; 1.89] 0.606	0.88 [0.55; 1.42] 0.606	-0.06 [-0.27; 0.16] 0.605
Pooled Analysis					
Interaction Test:	p = 0.479				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any ocular AE at the fellow eye, n (%)	97 (47.3)	79 (39.1)	1.35 [0.91; 2.01] 0.134	1.20 [0.96; 1.51] 0.109	0.08 [-0.02; 0.17] 0.108
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any ocular AE at the fellow eye, n (%)	31 (38.3)	38 (43.2)	0.86 [0.47; 1.61] 0.645	0.88 [0.61; 1.27] 0.500	-0.05 [-0.20; 0.10] 0.496

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any ocular AE at the fellow eye, n (%)	34 (41.5)	31 (39.7)	1.09 [0.58; 2.05] 0.791	1.04 [0.72; 1.51] 0.835	0.02 [-0.14; 0.17] 0.834

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-4.9 Any ocular adverse event at the fellow eye by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the fellow eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.244**					
KESTREL					
Interaction Test:	p = 0.680				
focal					
N'/N	59 / 59	48 / 48			
Any ocular AE at the fellow eye, n (%)	20 (33.9)	11 (22.9)	1.72 [0.73; 4.08] 0.215	1.48 [0.79; 2.78] 0.223	0.11 [-0.06; 0.28] 0.204
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular AE at the fellow eye, n (%)	43 (33.9)	36 (26.9)	1.39 [0.82; 2.37] 0.220	1.26 [0.87; 1.83] 0.221	0.07 [-0.04; 0.18] 0.219
KITE					
Interaction Test:	p = 0.724				
focal					
N'/N	63 / 63	66 / 66			
Any ocular AE at the fellow eye, n (%)	17 (27.0)	20 (30.3)	0.85 [0.40; 1.83] 0.677	0.89 [0.52; 1.54] 0.677	-0.03 [-0.19; 0.12] 0.677
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular AE at the fellow eye, n (%)	34 (29.6)	32 (29.4)	1.01 [0.57; 1.79] 0.973	1.01 [0.67; 1.51] 0.973	0.00 [-0.12; 0.12] 0.973
Pooled Analysis					
Interaction Test:	p = 0.986				
focal					
N'/N	122 / 122	114 / 114			
Any ocular AE at the fellow eye, n (%)	37 (30.3)	31 (27.2)	1.19 [0.68; 2.11] 0.542	1.12 [0.74; 1.68] 0.598	0.03 [-0.08; 0.15] 0.596

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular AE at the fellow eye, n (%)	77 (31.8)	68 (28.0)	1.19 [0.80; 1.75] 0.391	1.14 [0.87; 1.49] 0.354	0.04 [-0.04; 0.12] 0.354
Any ocular AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.053**					
KESTREL					
Interaction Test:	p = 0.510				
focal					
N'/N	59 / 59	48 / 48			
Any ocular AE at the fellow eye, n (%)	29 (49.2)	15 (31.3)	2.13 [0.96; 4.71] 0.063	1.57 [0.96; 2.58] 0.072	0.18 [-0.00; 0.36] 0.055
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular AE at the fellow eye, n (%)	62 (48.8)	51 (38.1)	1.55 [0.95; 2.54] 0.080	1.28 [0.97; 1.70] 0.081	0.11 [-0.01; 0.23] 0.078
KITE					
Interaction Test:	p = 0.773				
focal					
N'/N	63 / 63	66 / 66			
Any ocular AE at the fellow eye, n (%)	23 (36.5)	27 (40.9)	0.83 [0.41; 1.69] 0.608	0.89 [0.58; 1.38] 0.609	-0.04 [-0.21; 0.12] 0.608
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular AE at the fellow eye, n (%)	47 (40.9)	46 (42.2)	0.95 [0.56; 1.61] 0.840	0.97 [0.71; 1.32] 0.840	-0.01 [-0.14; 0.12] 0.840
Pooled Analysis					
Interaction Test:	p = 0.807				
focal					
N'/N	122 / 122	114 / 114			
Any ocular AE at the fellow eye, n (%)	52 (42.6)	42 (36.8)	1.31 [0.78; 2.23] 0.309	1.15 [0.84; 1.60] 0.378	0.06 [-0.07; 0.18] 0.377

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular AE at the fellow eye, n (%)	109 (45.0)	97 (39.9)	1.21 [0.84; 1.74] 0.295	1.13 [0.92; 1.39] 0.250	0.05 [-0.04; 0.14] 0.249

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-4.10 Any ocular adverse event at the fellow eye by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the fellow eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.244**					
KESTREL					
Interaction Test:	p = 0.547				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any ocular AE at the fellow eye, n (%)	34 (31.8)	26 (27.1)	1.25 [0.68; 2.30] 0.465	1.17 [0.76; 1.80] 0.466	0.05 [-0.08; 0.17] 0.463
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any ocular AE at the fellow eye, n (%)	25 (35.7)	16 (22.5)	1.91 [0.91; 4.00] 0.087	1.58 [0.93; 2.70] 0.091	0.13 [-0.02; 0.28] 0.082
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any ocular AE at the fellow eye, n (%)	5 (41.7)	9 (45.0)	0.87 [0.21; 3.71] 0.854	0.93 [0.41; 2.12] 0.855	-0.03 [-0.39; 0.32] 0.854
KITE					
Interaction Test:	p = 0.925				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any ocular AE at the fellow eye, n (%)	25 (29.4)	25 (30.5)	0.95 [0.49; 1.84] 0.879	0.96 [0.61; 1.53] 0.879	-0.01 [-0.15; 0.13] 0.879
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any ocular AE at the fellow eye, n (%)	22 (29.7)	24 (30.4)	0.97 [0.49; 1.94] 0.930	0.98 [0.60; 1.59] 0.930	-0.01 [-0.15; 0.14] 0.930
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any ocular AE at the fellow eye, n (%)	4 (20.0)	5 (26.3)	0.70 [0.16; 3.13] 0.641	0.76 [0.24; 2.41] 0.641	-0.06 [-0.33; 0.20] 0.640

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.535				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any ocular AE at the fellow eye, n (%)	59 (30.7)	51 (28.7)	1.08 [0.69; 1.70] 0.722	1.07 [0.78; 1.47] 0.662	0.02 [-0.07; 0.11] 0.661
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any ocular AE at the fellow eye, n (%)	47 (32.6)	40 (26.7)	1.35 [0.81; 2.23] 0.248	1.22 [0.86; 1.75] 0.263	0.06 [-0.04; 0.16] 0.262
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any ocular AE at the fellow eye, n (%)	9 (28.1)	14 (35.9)	0.72 [0.26; 1.99] 0.527	0.85 [0.43; 1.68] 0.652	-0.05 [-0.26; 0.16] 0.647
Any ocular AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.053**					
KESTREL					
Interaction Test:	p = 0.872				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any ocular AE at the fellow eye, n (%)	50 (46.7)	36 (37.5)	1.46 [0.83; 2.56] 0.185	1.25 [0.90; 1.73] 0.189	0.09 [-0.04; 0.23] 0.181
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any ocular AE at the fellow eye, n (%)	34 (48.6)	24 (33.8)	1.85 [0.94; 3.65] 0.076	1.44 [0.96; 2.15] 0.079	0.15 [-0.01; 0.31] 0.072
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any ocular AE at the fellow eye, n (%)	8 (66.7)	11 (55.0)	1.64 [0.37; 7.25] 0.517	1.21 [0.69; 2.13] 0.503	0.12 [-0.23; 0.46] 0.507

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.806				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any ocular AE at the fellow eye, n (%)	34 (40.0)	34 (41.5)	0.94 [0.51; 1.75] 0.847	0.96 [0.67; 1.39] 0.847	-0.01 [-0.16; 0.13] 0.847
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any ocular AE at the fellow eye, n (%)	31 (41.9)	35 (44.3)	0.91 [0.48; 1.72] 0.763	0.95 [0.66; 1.36] 0.764	-0.02 [-0.18; 0.13] 0.763
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any ocular AE at the fellow eye, n (%)	5 (25.0)	7 (36.8)	0.57 [0.14; 2.26] 0.425	0.68 [0.26; 1.77] 0.429	-0.12 [-0.41; 0.17] 0.421
Pooled Analysis					
Interaction Test:	p = 0.728				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any ocular AE at the fellow eye, n (%)	84 (43.8)	70 (39.3)	1.17 [0.77; 1.77] 0.460	1.11 [0.87; 1.42] 0.393	0.04 [-0.06; 0.14] 0.391
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any ocular AE at the fellow eye, n (%)	65 (45.1)	59 (39.3)	1.29 [0.81; 2.05] 0.286	1.15 [0.88; 1.50] 0.313	0.06 [-0.05; 0.17] 0.312

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any ocular AE at the fellow eye, n (%)	13 (40.6)	18 (46.2)	0.84 [0.32; 2.17] 0.717	0.96 [0.58; 1.60] 0.889	-0.02 [-0.24; 0.21] 0.888

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-4.11 Any ocular adverse event at the fellow eye by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the fellow eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.244**					
KESTREL					
Interaction Test:	p = 0.263				
presence					
N'/N	62 / 62	61 / 61			
Any ocular AE at the fellow eye, n (%)	22 (35.5)	22 (36.1)	0.97 [0.47; 2.04] 0.946	0.98 [0.61; 1.58] 0.946	-0.01 [-0.18; 0.16] 0.946
absence					
N'/N	127 / 127	126 / 126			
Any ocular AE at the fellow eye, n (%)	42 (33.1)	29 (23.0)	1.65 [0.95; 2.88] 0.076	1.44 [0.96; 2.15] 0.079	0.10 [-0.01; 0.21] 0.073
KITE					
Interaction Test:	p = 0.584				
presence					
N'/N	56 / 56	67 / 67			
Any ocular AE at the fellow eye, n (%)	19 (33.9)	21 (31.3)	1.12 [0.53; 2.40] 0.761	1.08 [0.65; 1.80] 0.760	0.03 [-0.14; 0.19] 0.761
absence					
N'/N	123 / 123	114 / 114			
Any ocular AE at the fellow eye, n (%)	32 (26.0)	33 (28.9)	0.86 [0.49; 1.53] 0.613	0.90 [0.59; 1.36] 0.613	-0.03 [-0.14; 0.08] 0.614
Pooled Analysis					
Interaction Test:	p = 0.688				
presence					
N'/N	118 / 118	128 / 128			
Any ocular AE at the fellow eye, n (%)	41 (34.7)	43 (33.6)	1.05 [0.62; 1.78] 0.855	1.03 [0.73; 1.46] 0.870	0.01 [-0.11; 0.13] 0.870

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular AE at the fellow eye, n (%)	74 (29.6)	62 (25.8)	1.20 [0.81; 1.79] 0.362	1.15 [0.86; 1.53] 0.351	0.04 [-0.04; 0.12] 0.351
Any ocular AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.053**					
KESTREL					
Interaction Test:	p = 0.351				
presence					
N'/N	62 / 62	61 / 61			
Any ocular AE at the fellow eye, n (%)	31 (50.0)	28 (45.9)	1.18 [0.58; 2.39] 0.649	1.09 [0.75; 1.58] 0.650	0.04 [-0.14; 0.22] 0.649
absence					
N'/N	127 / 127	126 / 126			
Any ocular AE at the fellow eye, n (%)	61 (48.0)	43 (34.1)	1.78 [1.07; 2.96] 0.025 *	1.41 [1.04; 1.90] 0.027 *	0.14 [0.02; 0.26] 0.023 *
KITE					
Interaction Test:	p = 0.836				
presence					
N'/N	56 / 56	67 / 67			
Any ocular AE at the fellow eye, n (%)	25 (44.6)	31 (46.3)	0.94 [0.46; 1.91] 0.857	0.96 [0.65; 1.42] 0.857	-0.02 [-0.19; 0.16] 0.857
absence					
N'/N	123 / 123	114 / 114			
Any ocular AE at the fellow eye, n (%)	45 (36.6)	46 (40.4)	0.85 [0.50; 1.44] 0.552	0.91 [0.66; 1.25] 0.551	-0.04 [-0.16; 0.09] 0.551
Pooled Analysis					
Interaction Test:	p = 0.603				
presence					
N'/N	118 / 118	128 / 128			
Any ocular AE at the fellow eye, n (%)	56 (47.5)	59 (46.1)	1.06 [0.64; 1.75] 0.833	1.03 [0.79; 1.34] 0.845	0.01 [-0.11; 0.14] 0.845

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular AE at the fellow eye, n (%)	106 (42.4)	89 (37.1)	1.24 [0.86; 1.79] 0.239	1.14 [0.92; 1.43] 0.226	0.05 [-0.03; 0.14] 0.226

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-4.12 Any ocular adverse event at the fellow eye by exposure (week 52) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the fellow eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.244**					
KESTREL					
Interaction Test:	p = 0.297				
Non-exposed					
N'/N	71 / 71	75 / 75			
Any ocular AE at the fellow eye, n (%)	21 (29.6)	22 (29.3)	1.01 [0.50; 2.06] 0.974	1.01 [0.61; 1.67] 0.974	0.00 [-0.15; 0.15] 0.974
Exposed					
N'/N	118 / 118	112 / 112			
Any ocular AE at the fellow eye, n (%)	43 (36.4)	29 (25.9)	1.64 [0.93; 2.89] 0.086	1.41 [0.95; 2.09] 0.089	0.11 [-0.01; 0.22] 0.082
KITE					
Interaction Test:	p = 0.939				
Non-exposed					
N'/N	85 / 85	90 / 90			
Any ocular AE at the fellow eye, n (%)	25 (29.4)	28 (31.1)	0.92 [0.48; 1.76] 0.807	0.95 [0.60; 1.48] 0.807	-0.02 [-0.15; 0.12] 0.807
Exposed					
N'/N	94 / 94	91 / 91			
Any ocular AE at the fellow eye, n (%)	26 (27.7)	26 (28.6)	0.96 [0.50; 1.81] 0.890	0.97 [0.61; 1.53] 0.890	-0.01 [-0.14; 0.12] 0.890
Pooled Analysis					
Interaction Test:	p = 0.417				
Non-exposed					
N'/N	156 / 156	165 / 165			
Any ocular AE at the fellow eye, n (%)	46 (29.5)	50 (30.3)	0.98 [0.61; 1.58] 0.929	0.97 [0.70; 1.36] 0.874	-0.01 [-0.11; 0.09] 0.873

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	212 / 212	203 / 203			
Any ocular AE at the fellow eye, n (%)	69 (32.5)	55 (27.1)	1.28 [0.83; 1.95] 0.260	1.20 [0.89; 1.62] 0.227	0.05 [-0.03; 0.14] 0.226

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-4.13 Any ocular adverse event at the fellow eye by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.053**					
KESTREL					
Interaction Test:	p = 0.716				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any ocular AE at the fellow eye, n (%)	3 (25.0)	3 (23.1)	1.11 [0.18; 6.97] 0.910	1.08 [0.27; 4.37] 0.910	0.02 [-0.32; 0.35] 0.911
Exposed					
N'/N	177 / 177	174 / 174			
Any ocular AE at the fellow eye, n (%)	89 (50.3)	68 (39.1)	1.58 [1.03; 2.41] 0.035 *	1.29 [1.02; 1.63] 0.037 *	0.11 [0.01; 0.22] 0.034 *
KITE					
Interaction Test:	p = 0.672				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any ocular AE at the fellow eye, n (%)	5 (29.4)	3 (25.0)	1.25 [0.23; 6.65] 0.794	1.18 [0.35; 4.01] 0.795	0.04 [-0.28; 0.37] 0.791
Exposed					
N'/N	162 / 162	169 / 169			
Any ocular AE at the fellow eye, n (%)	65 (40.1)	74 (43.8)	0.86 [0.56; 1.33] 0.500	0.92 [0.71; 1.18] 0.500	-0.04 [-0.14; 0.07] 0.499
Pooled Analysis					
Interaction Test:	p = 0.930				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any ocular AE at the fellow eye, n (%)	8 (27.6)	6 (24.0)	1.24 [0.36; 4.25] 0.730	1.13 [0.45; 2.85] 0.791	0.03 [-0.20; 0.27] 0.786

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any ocular AE at the fellow eye, n (%)	154 (45.4)	142 (41.4)	1.17 [0.87; 1.59] 0.305	1.10 [0.92; 1.30] 0.294	0.04 [-0.03; 0.11] 0.294

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-5.1 Any non-ocular adverse event (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any non-ocular AE, n (%)	129 (68.3)	122 (65.2)	1.15 [0.75; 1.76] 0.535	1.05 [0.91; 1.21] 0.535	0.03 [-0.07; 0.13] 0.535
KITE, N'/N	179 / 179	181 / 181			
Any non-ocular AE, n (%)	108 (60.3)	127 (70.2)	0.65 [0.42; 1.00] 0.051	0.86 [0.74; 1.00] 0.052	-0.10 [-0.20; -0.00] 0.049 *
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any non-ocular AE, n (%)	237 (64.4)	249 (67.7)	0.87 [0.64; 1.18] 0.356	0.95 [0.86; 1.06] 0.350	-0.03 [-0.10; 0.04] 0.350
p_H=0.068					
Any non-ocular AE, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any non-ocular AE, n (%)	147 (77.8)	143 (76.5)	1.08 [0.67; 1.74] 0.763	1.02 [0.91; 1.14] 0.763	0.01 [-0.07; 0.10] 0.763
KITE, N'/N	179 / 179	181 / 181			
Any non-ocular AE, n (%)	136 (76.0)	141 (77.9)	0.90 [0.55; 1.47] 0.665	0.98 [0.87; 1.09] 0.665	-0.02 [-0.11; 0.07] 0.665
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any non-ocular AE, n (%)	283 (76.9)	284 (77.2)	0.98 [0.70; 1.39] 0.930	1.00 [0.92; 1.08] 0.930	-0.00 [-0.06; 0.06] 0.930
p_H=0.603					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-5.2 Any non-ocular adverse event by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.068**					
KESTREL					
Interaction Test:	p = 0.422				
< 65 years					
N'/N	104 / 104	93 / 93			
Any non-ocular AE, n (%)	72 (69.2)	58 (62.4)	1.36 [0.75; 2.45] 0.311	1.11 [0.91; 1.36] 0.314	0.07 [-0.06; 0.20] 0.310
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any non-ocular AE, n (%)	57 (67.1)	64 (68.1)	0.95 [0.51; 1.79] 0.884	0.98 [0.80; 1.21] 0.884	-0.01 [-0.15; 0.13] 0.884
KITE					
Interaction Test:	p = 0.666				
< 65 years					
N'/N	100 / 100	102 / 102			
Any non-ocular AE, n (%)	64 (64.0)	73 (71.6)	0.71 [0.39; 1.28] 0.251	0.89 [0.74; 1.08] 0.252	-0.08 [-0.20; 0.05] 0.248
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any non-ocular AE, n (%)	44 (55.7)	54 (68.4)	0.58 [0.30; 1.11] 0.102	0.81 [0.64; 1.04] 0.105	-0.13 [-0.28; 0.02] 0.098
Pooled Analysis					
Interaction Test:	p = 0.359				
< 65 years					
N'/N	204 / 204	195 / 195			
Any non-ocular AE, n (%)	136 (66.7)	131 (67.2)	0.99 [0.65; 1.50] 0.953	0.99 [0.86; 1.14] 0.924	-0.00 [-0.10; 0.09] 0.924
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any non-ocular AE, n (%)	101 (61.6)	118 (68.2)	0.74 [0.47; 1.16] 0.191	0.90 [0.77; 1.06] 0.213	-0.06 [-0.17; 0.04] 0.212

	Treatment Groups		Comparison		
Any non-ocular adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL					
Interaction Test:	p = 0.568				
< 65 years					
N'/N	104 / 104	93 / 93			
Any non-ocular AE, n (%)	85 (81.7)	73 (78.5)	1.23 [0.61; 2.47] 0.570	1.04 [0.91; 1.20] 0.571	0.03 [-0.08; 0.14] 0.570
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any non-ocular AE, n (%)	62 (72.9)	70 (74.5)	0.92 [0.47; 1.80] 0.817	0.98 [0.82; 1.17] 0.817	-0.02 [-0.14; 0.11] 0.817
KITE					
Interaction Test:	p = 0.921				
< 65 years					
N'/N	100 / 100	102 / 102			
Any non-ocular AE, n (%)	78 (78.0)	81 (79.4)	0.92 [0.47; 1.80] 0.806	0.98 [0.85; 1.13] 0.806	-0.01 [-0.13; 0.10] 0.806
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any non-ocular AE, n (%)	58 (73.4)	60 (75.9)	0.87 [0.43; 1.79] 0.714	0.97 [0.81; 1.16] 0.715	-0.03 [-0.16; 0.11] 0.714
Pooled Analysis					
Interaction Test:	p = 0.638				
< 65 years					
N'/N	204 / 204	195 / 195			
Any non-ocular AE, n (%)	163 (79.9)	154 (79.0)	1.06 [0.65; 1.73] 0.810	1.01 [0.91; 1.12] 0.828	0.01 [-0.07; 0.09] 0.828

	Treatment Groups		Comparison		
Any non-ocular adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any non-ocular AE, n (%)	120 (73.2)	130 (75.1)	0.90 [0.55; 1.47] 0.671	0.97 [0.86; 1.10] 0.676	-0.02 [-0.11; 0.07] 0.675

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-5.3 Any non-ocular adverse event by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.068**					
KESTREL					
Interaction Test:	p = 0.889				
Male					
N'/N	110 / 110	126 / 126			
Any non-ocular AE, n (%)	71 (64.5)	79 (62.7)	1.08 [0.64; 1.84] 0.769	1.03 [0.85; 1.25] 0.768	0.02 [-0.10; 0.14] 0.768
Female					
N'/N	79 / 79	61 / 61			
Any non-ocular AE, n (%)	58 (73.4)	43 (70.5)	1.16 [0.55; 2.43] 0.702	1.04 [0.84; 1.28] 0.704	0.03 [-0.12; 0.18] 0.703
KITE					
Interaction Test:	p = 0.330				
Male					
N'/N	120 / 120	115 / 115			
Any non-ocular AE, n (%)	76 (63.3)	80 (69.6)	0.76 [0.44; 1.30] 0.313	0.91 [0.76; 1.09] 0.312	-0.06 [-0.18; 0.06] 0.311
Female					
N'/N	59 / 59	66 / 66			
Any non-ocular AE, n (%)	32 (54.2)	47 (71.2)	0.48 [0.23; 1.00] 0.051	0.76 [0.58; 1.01] 0.057	-0.17 [-0.34; -0.00] 0.047 *
Pooled Analysis					
Interaction Test:	p = 0.557				
Male					
N'/N	230 / 230	241 / 241			
Any non-ocular AE, n (%)	147 (63.9)	159 (66.0)	0.92 [0.63; 1.35] 0.679	0.97 [0.85; 1.10] 0.619	-0.02 [-0.11; 0.06] 0.618
Female					
N'/N	138 / 138	127 / 127			
Any non-ocular AE, n (%)	90 (65.2)	90 (70.9)	0.76 [0.45; 1.28] 0.303	0.91 [0.77; 1.08] 0.257	-0.07 [-0.18; 0.05] 0.257

	Treatment Groups		Comparison		
Any non-ocular adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL					
Interaction Test:	p = 0.601				
Male					
N'/N	110 / 110	126 / 126			
Any non-ocular AE, n (%)	82 (74.5)	95 (75.4)	0.96 [0.53; 1.72] 0.880	0.99 [0.85; 1.15] 0.880	-0.01 [-0.12; 0.10] 0.880
Female					
N'/N	79 / 79	61 / 61			
Any non-ocular AE, n (%)	65 (82.3)	48 (78.7)	1.26 [0.54; 2.92] 0.594	1.05 [0.89; 1.23] 0.598	0.04 [-0.10; 0.17] 0.596
KITE					
Interaction Test:	p = 0.529				
Male					
N'/N	120 / 120	115 / 115			
Any non-ocular AE, n (%)	93 (77.5)	89 (77.4)	1.01 [0.55; 1.86] 0.984	1.00 [0.87; 1.15] 0.984	0.00 [-0.11; 0.11] 0.984
Female					
N'/N	59 / 59	66 / 66			
Any non-ocular AE, n (%)	43 (72.9)	52 (78.8)	0.72 [0.32; 1.65] 0.441	0.93 [0.76; 1.13] 0.444	-0.06 [-0.21; 0.09] 0.441
Pooled Analysis					
Interaction Test:	p = 0.958				
Male					
N'/N	230 / 230	241 / 241			
Any non-ocular AE, n (%)	175 (76.1)	184 (76.3)	0.99 [0.65; 1.51] 0.955	1.00 [0.90; 1.10] 0.925	-0.00 [-0.08; 0.07] 0.925

	Treatment Groups		Comparison		
Any non-ocular adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any non-ocular AE, n (%)	108 (78.3)	100 (78.7)	0.97 [0.54; 1.74] 0.916	0.99 [0.87; 1.12] 0.856	-0.01 [-0.11; 0.09] 0.856

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-5.4 Any non-ocular adverse event by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.068**					
KESTREL					
Interaction Test:	p = 0.869				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any non-ocular AE, n (%)	49 (66.2)	41 (64.1)	1.10 [0.54; 2.22] 0.791	1.03 [0.81; 1.32] 0.792	0.02 [-0.14; 0.18] 0.791
> 65 letters					
N'/N	115 / 115	123 / 123			
Any non-ocular AE, n (%)	80 (69.6)	81 (65.9)	1.19 [0.69; 2.04] 0.541	1.06 [0.89; 1.26] 0.540	0.04 [-0.08; 0.16] 0.540
KITE					
Interaction Test:	p = 0.340				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any non-ocular AE, n (%)	34 (52.3)	63 (69.2)	0.49 [0.25; 0.94] 0.033 *	0.76 [0.58; 0.99] 0.042 *	-0.17 [-0.32; -0.02] 0.031 *
> 65 letters					
N'/N	114 / 114	90 / 90			
Any non-ocular AE, n (%)	74 (64.9)	64 (71.1)	0.75 [0.41; 1.36] 0.348	0.91 [0.76; 1.10] 0.343	-0.06 [-0.19; 0.07] 0.343
Pooled Analysis					
Interaction Test:	p = 0.426				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any non-ocular AE, n (%)	83 (59.7)	104 (67.1)	0.74 [0.46; 1.19] 0.215	0.88 [0.74; 1.06] 0.166	-0.08 [-0.19; 0.03] 0.167
> 65 letters					
N'/N	229 / 229	213 / 213			
Any non-ocular AE, n (%)	154 (67.2)	145 (68.1)	0.95 [0.64; 1.42] 0.815	0.99 [0.87; 1.12] 0.853	-0.01 [-0.10; 0.08] 0.852

	Treatment Groups		Comparison		
Any non-ocular adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL					
Interaction Test:	p = 0.886				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any non-ocular AE, n (%)	55 (74.3)	47 (73.4)	1.05 [0.49; 2.24] 0.906	1.01 [0.83; 1.24] 0.906	0.01 [-0.14; 0.16] 0.906
> 65 letters					
N'/N	115 / 115	123 / 123			
Any non-ocular AE, n (%)	92 (80.0)	96 (78.0)	1.12 [0.60; 2.10] 0.712	1.03 [0.90; 1.17] 0.712	0.02 [-0.08; 0.12] 0.712
KITE					
Interaction Test:	p = 0.164				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any non-ocular AE, n (%)	43 (66.2)	70 (76.9)	0.59 [0.29; 1.19] 0.140	0.86 [0.70; 1.06] 0.154	-0.11 [-0.25; 0.04] 0.143
> 65 letters					
N'/N	114 / 114	90 / 90			
Any non-ocular AE, n (%)	93 (81.6)	71 (78.9)	1.19 [0.59; 2.37] 0.631	1.03 [0.90; 1.19] 0.634	0.03 [-0.08; 0.14] 0.633
Pooled Analysis					
Interaction Test:	p = 0.279				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any non-ocular AE, n (%)	98 (70.5)	117 (75.5)	0.78 [0.47; 1.31] 0.354	0.93 [0.81; 1.07] 0.317	-0.05 [-0.16; 0.05] 0.319

	Treatment Groups		Comparison		
Any non-ocular adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any non-ocular AE, n (%)	185 (80.8)	167 (78.4)	1.15 [0.72; 1.83] 0.554	1.03 [0.94; 1.13] 0.552	0.02 [-0.05; 0.10] 0.552

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-5.5 Any non-ocular adverse event by region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.068**					
KESTREL					
Interaction Test:	p = 0.047 *				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any non-ocular AE, n (%)	64 (71.1)	60 (72.3)	0.94 [0.49; 1.83] 0.864	0.98 [0.82; 1.19] 0.863	-0.01 [-0.15; 0.12] 0.864
European Region					
N'/N	69 / 69	75 / 75			
Any non-ocular AE, n (%)	42 (60.9)	49 (65.3)	0.83 [0.42; 1.63] 0.579	0.93 [0.72; 1.20] 0.580	-0.04 [-0.20; 0.11] 0.579
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any non-ocular AE, n (%)	23 (76.7)	13 (44.8)	4.04 [1.32; 12.38] 0.014 *	1.71 [1.09; 2.68] 0.019 *	0.32 [0.08; 0.55] 0.008 *
KITE					
Interaction Test:	p = 0.696				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any non-ocular AE, n (%)	14 (53.8)	11 (52.4)	1.06 [0.34; 3.36] 0.920	1.03 [0.60; 1.77] 0.920	0.01 [-0.27; 0.30] 0.920
European Region					
N'/N	135 / 135	132 / 132			
Any non-ocular AE, n (%)	81 (60.0)	93 (70.5)	0.63 [0.38; 1.05] 0.074	0.85 [0.71; 1.02] 0.075	-0.10 [-0.22; 0.01] 0.071
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any non-ocular AE, n (%)	13 (72.2)	23 (82.1)	0.57 [0.14; 2.32] 0.429	0.88 [0.63; 1.23] 0.451	-0.10 [-0.35; 0.15] 0.438

	Treatment Groups		Comparison		
Any non-ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.255				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any non-ocular AE, n (%)	64 (71.1)	60 (72.3)	0.69 [0.32; 1.48] 0.342	0.98 [0.82; 1.19] 0.864	-0.01 [-0.15; 0.12] 0.864
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any non-ocular AE, n (%)	14 (53.8)	11 (52.4)	1.46 [0.43; 4.94] 0.539	1.03 [0.60; 1.77] 0.921	0.01 [-0.27; 0.30] 0.920
European Region					
N'/N	204 / 204	207 / 207			
Any non-ocular AE, n (%)	123 (60.3)	142 (68.6)	0.75 [0.49; 1.15] 0.191	0.88 [0.76; 1.01] 0.077	-0.08 [-0.18; 0.01] 0.076
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any non-ocular AE, n (%)	36 (75.0)	36 (63.2)	1.72 [0.73; 4.03] 0.212	1.23 [0.93; 1.62] 0.123	0.14 [-0.04; 0.32] 0.124
Any non-ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL					
Interaction Test:	p = 0.290				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any non-ocular AE, n (%)	74 (82.2)	69 (83.1)	0.94 [0.43; 2.07] 0.874	0.99 [0.86; 1.13] 0.874	-0.01 [-0.12; 0.10] 0.874
European Region					
N'/N	69 / 69	75 / 75			
Any non-ocular AE, n (%)	49 (71.0)	56 (74.7)	0.83 [0.40; 1.73] 0.622	0.95 [0.78; 1.16] 0.624	-0.04 [-0.18; 0.11] 0.623
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any non-ocular AE, n (%)	24 (80.0)	18 (62.1)	2.44 [0.76; 7.86] 0.133	1.29 [0.92; 1.80] 0.139	0.18 [-0.05; 0.41] 0.122

	Treatment Groups		Comparison		
Any non-ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.469				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any non-ocular AE, n (%)	17 (65.4)	12 (57.1)	1.42 [0.43; 4.62] 0.564	1.14 [0.72; 1.82] 0.569	0.08 [-0.20; 0.36] 0.564
European Region					
N'/N	135 / 135	132 / 132			
Any non-ocular AE, n (%)	106 (78.5)	105 (79.5)	0.94 [0.52; 1.69] 0.837	0.99 [0.87; 1.12] 0.837	-0.01 [-0.11; 0.09] 0.837
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any non-ocular AE, n (%)	13 (72.2)	24 (85.7)	0.43 [0.10; 1.90] 0.267	0.84 [0.61; 1.16] 0.300	-0.13 [-0.38; 0.11] 0.279
Pooled Analysis					
Interaction Test:	p = 0.789				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any non-ocular AE, n (%)	74 (82.2)	69 (83.1)	0.82 [0.34; 2.01] 0.672	0.99 [0.86; 1.13] 0.875	-0.01 [-0.12; 0.10] 0.874
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any non-ocular AE, n (%)	17 (65.4)	12 (57.1)	1.62 [0.46; 5.70] 0.452	1.14 [0.72; 1.82] 0.568	0.08 [-0.20; 0.36] 0.564
European Region					
N'/N	204 / 204	207 / 207			
Any non-ocular AE, n (%)	155 (76.0)	161 (77.8)	0.92 [0.58; 1.48] 0.735	0.98 [0.88; 1.08] 0.640	-0.02 [-0.10; 0.06] 0.639

	Treatment Groups		Comparison		
Any non-ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any non-ocular AE, n (%)	37 (77.1)	42 (73.7)	1.22 [0.50; 3.01] 0.663	1.06 [0.84; 1.34] 0.596	0.05 [-0.12; 0.22] 0.601

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-5.6 Any non-ocular adverse event by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.068**					
KESTREL					
Interaction Test:	p = 0.395				
Type 1					
N'/N	12 / 12	6 / 6			
Any non-ocular AE, n (%)	8 (66.7)	5 (83.3)	0.40 [0.03; 4.68] 0.465	0.80 [0.47; 1.37] 0.415	-0.17 [-0.57; 0.23] 0.414
Type 2					
N'/N	177 / 177	181 / 181			
Any non-ocular AE, n (%)	121 (68.4)	117 (64.6)	1.18 [0.76; 1.83] 0.456	1.06 [0.91; 1.23] 0.456	0.04 [-0.06; 0.13] 0.455
KITE					
Interaction Test:	p = 0.636				
Type 1					
N'/N	19 / 19	7 / 7			
Any non-ocular AE, n (%)	13 (68.4)	6 (85.7)	0.36 [0.04; 3.70] 0.391	0.80 [0.52; 1.23] 0.304	-0.17 [-0.51; 0.16] 0.309
Type 2					
N'/N	160 / 160	174 / 174			
Any non-ocular AE, n (%)	95 (59.4)	121 (69.5)	0.64 [0.41; 1.01] 0.053	0.85 [0.73; 1.00] 0.055	-0.10 [-0.20; 0.00] 0.051
Pooled Analysis					
Interaction Test:	p = 0.377				
Type 1					
N'/N	31 / 31	13 / 13			
Any non-ocular AE, n (%)	21 (67.7)	11 (84.6)	0.40 [0.07; 2.18] 0.292	0.80 [0.57; 1.12] 0.260	-0.17 [-0.43; 0.09] 0.193

	Treatment Groups		Comparison		
Any non-ocular adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any non-ocular AE, n (%)	216 (64.1)	238 (67.0)	0.87 [0.64; 1.20] 0.405	0.96 [0.86; 1.07] 0.411	-0.03 [-0.10; 0.04] 0.411
Any non-ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any non-ocular AE, n (%)	10 (83.3)	6 (100.0)	N.E.	0.83 [0.65; 1.07] 0.158	-0.17 [-0.38; 0.04] 0.121
Type 2					
N'/N	177 / 177	181 / 181			
Any non-ocular AE, n (%)	137 (77.4)	137 (75.7)	1.10 [0.67; 1.79] 0.703	1.02 [0.91; 1.15] 0.703	0.02 [-0.07; 0.10] 0.702
KITE					
Interaction Test:	p = 0.984				
Type 1					
N'/N	19 / 19	7 / 7			
Any non-ocular AE, n (%)	16 (84.2)	6 (85.7)	0.89 [0.08; 10.30] 0.925	0.98 [0.69; 1.41] 0.923	-0.02 [-0.32; 0.29] 0.923
Type 2					
N'/N	160 / 160	174 / 174			
Any non-ocular AE, n (%)	120 (75.0)	135 (77.6)	0.87 [0.52; 1.44] 0.579	0.97 [0.86; 1.09] 0.580	-0.03 [-0.12; 0.07] 0.579
Pooled Analysis					
Interaction Test:	p = 0.495				
Type 1					
N'/N	31 / 31	13 / 13			
Any non-ocular AE, n (%)	26 (83.9)	12 (92.3)	0.44 [0.05; 4.21] 0.478	0.93 [0.72; 1.19] 0.583	-0.08 [-0.28; 0.12] 0.418

	Treatment Groups		Comparison		
Any non-ocular adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any non-ocular AE, n (%)	257 (76.3)	272 (76.6)	0.98 [0.69; 1.39] 0.906	1.00 [0.92; 1.08] 0.911	-0.00 [-0.07; 0.06] 0.911

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL: logit(proportion) = treatment [by diabetes type].

Table 12-5.7 Any non-ocular adverse event by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.068**					
KESTREL					
Interaction Test:	p = 0.377				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any non-ocular AE, n (%)	49 (64.5)	71 (66.4)	0.92 [0.50; 1.71] 0.792	0.97 [0.78; 1.20] 0.793	-0.02 [-0.16; 0.12] 0.792
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any non-ocular AE, n (%)	79 (70.5)	51 (63.8)	1.36 [0.74; 2.51] 0.322	1.11 [0.90; 1.36] 0.331	0.07 [-0.07; 0.20] 0.325
KITE					
Interaction Test:	p = 0.624				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any non-ocular AE, n (%)	48 (58.5)	64 (66.7)	0.71 [0.38; 1.30] 0.264	0.88 [0.70; 1.11] 0.269	-0.08 [-0.22; 0.06] 0.263
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any non-ocular AE, n (%)	60 (61.9)	63 (74.1)	0.57 [0.30; 1.07] 0.079	0.83 [0.68; 1.02] 0.077	-0.12 [-0.26; 0.01] 0.073
Pooled Analysis					
Interaction Test:	p = 0.761				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any non-ocular AE, n (%)	97 (61.4)	135 (66.5)	0.81 [0.52; 1.25] 0.332	0.92 [0.79; 1.08] 0.327	-0.05 [-0.15; 0.05] 0.327
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any non-ocular AE, n (%)	139 (66.5)	114 (69.1)	0.89 [0.57; 1.38] 0.594	0.96 [0.83; 1.11] 0.595	-0.03 [-0.12; 0.07] 0.596

	Treatment Groups		Comparison		
Any non-ocular adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL					
Interaction Test:	p = 0.194				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any non-ocular AE, n (%)	56 (73.7)	84 (78.5)	0.77 [0.39; 1.53] 0.449	0.94 [0.79; 1.11] 0.457	-0.05 [-0.17; 0.08] 0.453
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any non-ocular AE, n (%)	90 (80.4)	59 (73.8)	1.46 [0.74; 2.88] 0.280	1.09 [0.93; 1.28] 0.292	0.07 [-0.06; 0.19] 0.286
KITE					
Interaction Test:	p = 0.172				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any non-ocular AE, n (%)	66 (80.5)	73 (76.0)	1.30 [0.63; 2.67] 0.475	1.06 [0.91; 1.24] 0.472	0.04 [-0.08; 0.17] 0.472
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any non-ocular AE, n (%)	70 (72.2)	68 (80.0)	0.65 [0.32; 1.30] 0.220	0.90 [0.77; 1.06] 0.215	-0.08 [-0.20; 0.04] 0.213
Pooled Analysis					
Interaction Test:	p = 0.959				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any non-ocular AE, n (%)	122 (77.2)	157 (77.3)	0.99 [0.61; 1.63] 0.983	1.00 [0.89; 1.12] 0.965	-0.00 [-0.09; 0.09] 0.965

	Treatment Groups		Comparison		
Any non-ocular adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any non-ocular AE, n (%)	160 (76.6)	127 (77.0)	0.98 [0.60; 1.58] 0.924	0.99 [0.89; 1.11] 0.909	-0.01 [-0.09; 0.08] 0.909

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-5.8 Any non-ocular adverse event by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.068**					
KESTREL					
Interaction Test:	p = 0.427				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any non-ocular AE, n (%)	86 (71.7)	74 (67.3)	1.23 [0.70; 2.16] 0.470	1.07 [0.90; 1.27] 0.471	0.04 [-0.08; 0.16] 0.470
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any non-ocular AE, n (%)	16 (53.3)	25 (64.1)	0.64 [0.24; 1.69] 0.368	0.83 [0.55; 1.25] 0.378	-0.11 [-0.34; 0.13] 0.366
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any non-ocular AE, n (%)	27 (69.2)	23 (60.5)	1.47 [0.57; 3.76] 0.424	1.14 [0.82; 1.59] 0.427	0.09 [-0.13; 0.30] 0.422
KITE					
Interaction Test:	p = 0.437				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any non-ocular AE, n (%)	49 (57.6)	68 (73.9)	0.48 [0.25; 0.91] 0.023 *	0.78 [0.63; 0.97] 0.026 *	-0.16 [-0.30; -0.02] 0.021 *
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any non-ocular AE, n (%)	30 (58.8)	31 (63.3)	0.83 [0.37; 1.86] 0.649	0.93 [0.68; 1.27] 0.649	-0.04 [-0.24; 0.15] 0.648
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any non-ocular AE, n (%)	29 (67.4)	28 (70.0)	0.89 [0.35; 2.25] 0.802	0.96 [0.72; 1.29] 0.802	-0.03 [-0.23; 0.17] 0.802

	Treatment Groups		Comparison		
Any non-ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.603				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any non-ocular AE, n (%)	135 (65.9)	142 (70.3)	0.79 [0.52; 1.20] 0.270	0.93 [0.82; 1.07] 0.322	-0.05 [-0.14; 0.05] 0.323
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any non-ocular AE, n (%)	46 (56.8)	56 (63.6)	0.80 [0.43; 1.49] 0.476	0.89 [0.69; 1.14] 0.357	-0.07 [-0.22; 0.08] 0.354
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any non-ocular AE, n (%)	56 (68.3)	51 (65.4)	1.16 [0.60; 2.25] 0.657	1.04 [0.84; 1.30] 0.702	0.03 [-0.12; 0.17] 0.701
Any non-ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL					
Interaction Test:	p = 0.313				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any non-ocular AE, n (%)	100 (83.3)	88 (80.0)	1.25 [0.64; 2.44] 0.514	1.04 [0.92; 1.18] 0.515	0.03 [-0.07; 0.13] 0.514
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any non-ocular AE, n (%)	18 (60.0)	29 (74.4)	0.52 [0.19; 1.44] 0.207	0.81 [0.57; 1.14] 0.223	-0.14 [-0.37; 0.08] 0.206
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any non-ocular AE, n (%)	29 (74.4)	26 (68.4)	1.34 [0.50; 3.61] 0.565	1.09 [0.82; 1.44] 0.566	0.06 [-0.14; 0.26] 0.564

	Treatment Groups		Comparison		
Any non-ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.387				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any non-ocular AE, n (%)	64 (75.3)	76 (82.6)	0.64 [0.31; 1.33] 0.234	0.91 [0.78; 1.06] 0.237	-0.07 [-0.19; 0.05] 0.232
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any non-ocular AE, n (%)	39 (76.5)	34 (69.4)	1.43 [0.59; 3.48] 0.426	1.10 [0.87; 1.40] 0.428	0.07 [-0.10; 0.24] 0.424
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any non-ocular AE, n (%)	33 (76.7)	31 (77.5)	0.96 [0.34; 2.67] 0.935	0.99 [0.78; 1.25] 0.935	-0.01 [-0.19; 0.17] 0.935
Pooled Analysis					
Interaction Test:	p = 0.880				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any non-ocular AE, n (%)	164 (80.0)	164 (81.2)	0.92 [0.56; 1.51] 0.741	0.98 [0.89; 1.08] 0.741	-0.01 [-0.09; 0.06] 0.742
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any non-ocular AE, n (%)	57 (70.4)	63 (71.6)	0.95 [0.49; 1.86] 0.888	0.98 [0.80; 1.19] 0.822	-0.02 [-0.15; 0.12] 0.823

	Treatment Groups		Comparison		
Any non-ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any non-ocular AE, n (%)	62 (75.6)	57 (73.1)	1.15 [0.56; 2.33] 0.708	1.03 [0.86; 1.24] 0.722	0.02 [-0.11; 0.16] 0.721

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-5.9 Any non-ocular adverse event by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.068**					
KESTREL					
Interaction Test:	p = 0.592				
focal					
N'/N	59 / 59	48 / 48			
Any non-ocular AE, n (%)	35 (59.3)	29 (60.4)	0.96 [0.44; 2.08] 0.909	0.98 [0.72; 1.34] 0.908	-0.01 [-0.20; 0.18] 0.909
diffuse					
N'/N	127 / 127	134 / 134			
Any non-ocular AE, n (%)	91 (71.7)	90 (67.2)	1.24 [0.73; 2.10] 0.432	1.07 [0.91; 1.25] 0.431	0.04 [-0.07; 0.16] 0.431
KITE					
Interaction Test:	p = 0.357				
focal					
N'/N	63 / 63	66 / 66			
Any non-ocular AE, n (%)	37 (58.7)	49 (74.2)	0.49 [0.23; 1.04] 0.064	0.79 [0.62; 1.02] 0.067	-0.16 [-0.32; 0.01] 0.059
diffuse					
N'/N	115 / 115	109 / 109			
Any non-ocular AE, n (%)	71 (61.7)	74 (67.9)	0.76 [0.44; 1.32] 0.336	0.91 [0.75; 1.10] 0.336	-0.06 [-0.19; 0.06] 0.334
Pooled Analysis					
Interaction Test:	p = 0.307				
focal					
N'/N	122 / 122	114 / 114			
Any non-ocular AE, n (%)	72 (59.0)	78 (68.4)	0.68 [0.40; 1.17] 0.164	0.87 [0.71; 1.05] 0.152	-0.09 [-0.21; 0.03] 0.150

	Treatment Groups		Comparison		
Any non-ocular adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any non-ocular AE, n (%)	162 (66.9)	164 (67.5)	0.96 [0.66; 1.41] 0.849	0.99 [0.88; 1.12] 0.921	-0.00 [-0.09; 0.08] 0.921
Any non-ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL					
Interaction Test:	p = 0.597				
focal					
N'/N	59 / 59	48 / 48			
Any non-ocular AE, n (%)	41 (69.5)	34 (70.8)	0.94 [0.41; 2.16] 0.880	0.98 [0.77; 1.26] 0.880	-0.01 [-0.19; 0.16] 0.880
diffuse					
N'/N	127 / 127	134 / 134			
Any non-ocular AE, n (%)	103 (81.1)	104 (77.6)	1.24 [0.68; 2.26] 0.487	1.04 [0.92; 1.18] 0.486	0.03 [-0.06; 0.13] 0.485
KITE					
Interaction Test:	p = 0.452				
focal					
N'/N	63 / 63	66 / 66			
Any non-ocular AE, n (%)	50 (79.4)	51 (77.3)	1.13 [0.49; 2.62] 0.773	1.03 [0.86; 1.23] 0.773	0.02 [-0.12; 0.16] 0.773
diffuse					
N'/N	115 / 115	109 / 109			
Any non-ocular AE, n (%)	85 (73.9)	86 (78.9)	0.76 [0.41; 1.41] 0.381	0.94 [0.81; 1.08] 0.380	-0.05 [-0.16; 0.06] 0.378
Pooled Analysis					
Interaction Test:	p = 0.881				
focal					
N'/N	122 / 122	114 / 114			
Any non-ocular AE, n (%)	91 (74.6)	85 (74.6)	1.02 [0.57; 1.83] 0.954	1.01 [0.87; 1.17] 0.924	0.01 [-0.11; 0.12] 0.923

	Treatment Groups		Comparison		
Any non-ocular adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any non-ocular AE, n (%)	188 (77.7)	190 (78.2)	0.96 [0.63; 1.48] 0.860	0.99 [0.90; 1.09] 0.910	-0.00 [-0.08; 0.07] 0.910

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-5.10 Any non-ocular adverse event by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.068**					
KESTREL					
Interaction Test:	p = 0.192				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any non-ocular AE, n (%)	74 (69.2)	60 (62.5)	1.35 [0.75; 2.41] 0.318	1.11 [0.91; 1.35] 0.321	0.07 [-0.06; 0.20] 0.317
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any non-ocular AE, n (%)	50 (71.4)	48 (67.6)	1.20 [0.58; 2.46] 0.622	1.06 [0.85; 1.31] 0.622	0.04 [-0.11; 0.19] 0.622
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any non-ocular AE, n (%)	5 (41.7)	14 (70.0)	0.31 [0.07; 1.36] 0.120	0.60 [0.29; 1.23] 0.163	-0.28 [-0.63; 0.06] 0.106
KITE					
Interaction Test:	p = 0.324				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any non-ocular AE, n (%)	55 (64.7)	55 (67.1)	0.90 [0.47; 1.71] 0.747	0.96 [0.78; 1.20] 0.747	-0.02 [-0.17; 0.12] 0.747
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any non-ocular AE, n (%)	43 (58.1)	60 (75.9)	0.44 [0.22; 0.88] 0.020 *	0.77 [0.61; 0.96] 0.022 *	-0.18 [-0.33; -0.03] 0.017 *
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any non-ocular AE, n (%)	10 (50.0)	11 (57.9)	0.73 [0.21; 2.57] 0.621	0.86 [0.48; 1.55] 0.622	-0.08 [-0.39; 0.23] 0.620

	Treatment Groups		Comparison		
Any non-ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.239				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any non-ocular AE, n (%)	129 (67.2)	115 (64.6)	1.10 [0.72; 1.70] 0.659	1.04 [0.90; 1.21] 0.602	0.03 [-0.07; 0.12] 0.602
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any non-ocular AE, n (%)	93 (64.6)	108 (72.0)	0.72 [0.44; 1.18] 0.194	0.90 [0.77; 1.05] 0.171	-0.07 [-0.18; 0.03] 0.172
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any non-ocular AE, n (%)	15 (46.9)	25 (64.1)	0.51 [0.20; 1.34] 0.173	0.73 [0.47; 1.16] 0.165	-0.17 [-0.40; 0.07] 0.158
Any non-ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL					
Interaction Test:	p = 0.331				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any non-ocular AE, n (%)	84 (78.5)	71 (74.0)	1.29 [0.67; 2.46] 0.447	1.06 [0.91; 1.24] 0.450	0.05 [-0.07; 0.16] 0.448
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any non-ocular AE, n (%)	56 (80.0)	56 (78.9)	1.07 [0.47; 2.43] 0.869	1.01 [0.86; 1.20] 0.869	0.01 [-0.12; 0.14] 0.869
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any non-ocular AE, n (%)	7 (58.3)	16 (80.0)	0.35 [0.07; 1.71] 0.195	0.73 [0.43; 1.23] 0.239	-0.22 [-0.55; 0.11] 0.197

	Treatment Groups		Comparison		
Any non-ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.578				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any non-ocular AE, n (%)	66 (77.6)	61 (74.4)	1.20 [0.59; 2.44] 0.622	1.04 [0.88; 1.24] 0.623	0.03 [-0.10; 0.16] 0.622
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any non-ocular AE, n (%)	57 (77.0)	65 (82.3)	0.72 [0.33; 1.59] 0.420	0.94 [0.80; 1.10] 0.422	-0.05 [-0.18; 0.08] 0.420
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any non-ocular AE, n (%)	13 (65.0)	14 (73.7)	0.66 [0.17; 2.62] 0.558	0.88 [0.58; 1.34] 0.558	-0.09 [-0.37; 0.20] 0.554
Pooled Analysis					
Interaction Test:	p = 0.267				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any non-ocular AE, n (%)	150 (78.1)	132 (74.2)	1.24 [0.77; 2.00] 0.381	1.05 [0.94; 1.18] 0.372	0.04 [-0.05; 0.13] 0.372
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any non-ocular AE, n (%)	113 (78.5)	121 (80.7)	0.88 [0.50; 1.55] 0.650	0.97 [0.87; 1.09] 0.642	-0.02 [-0.11; 0.07] 0.642

	Treatment Groups		Comparison		
Any non-ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any non-ocular AE, n (%)	20 (62.5)	30 (76.9)	0.50 [0.18; 1.42] 0.195	0.81 [0.58; 1.13] 0.199	-0.14 [-0.36; 0.07] 0.196

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-5.11 Any non-ocular adverse event by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.068**					
KESTREL					
Interaction Test:	p = 0.559				
presence					
N'/N	62 / 62	61 / 61			
Any non-ocular AE, n (%)	42 (67.7)	42 (68.9)	0.95 [0.44; 2.03] 0.895	0.98 [0.77; 1.25] 0.895	-0.01 [-0.18; 0.15] 0.895
absence					
N'/N	127 / 127	126 / 126			
Any non-ocular AE, n (%)	87 (68.5)	80 (63.5)	1.25 [0.74; 2.11] 0.400	1.08 [0.90; 1.29] 0.401	0.05 [-0.07; 0.17] 0.399
KITE					
Interaction Test:	p = 0.939				
presence					
N'/N	56 / 56	67 / 67			
Any non-ocular AE, n (%)	31 (55.4)	44 (65.7)	0.65 [0.31; 1.34] 0.244	0.84 [0.63; 1.13] 0.252	-0.10 [-0.28; 0.07] 0.242
absence					
N'/N	123 / 123	114 / 114			
Any non-ocular AE, n (%)	77 (62.6)	83 (72.8)	0.63 [0.36; 1.08] 0.095	0.86 [0.72; 1.03] 0.094	-0.10 [-0.22; 0.02] 0.091
Pooled Analysis					
Interaction Test:	p = 0.706				
presence					
N'/N	118 / 118	128 / 128			
Any non-ocular AE, n (%)	73 (61.9)	86 (67.2)	0.80 [0.47; 1.34] 0.392	0.92 [0.76; 1.10] 0.352	-0.06 [-0.18; 0.06] 0.350

	Treatment Groups		Comparison		
Any non-ocular adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any non-ocular AE, n (%)	164 (65.6)	163 (67.9)	0.90 [0.62; 1.31] 0.587	0.97 [0.85; 1.09] 0.583	-0.02 [-0.11; 0.06] 0.583
Any non-ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL					
Interaction Test:	p = 0.885				
presence					
N'/N	62 / 62	61 / 61			
Any non-ocular AE, n (%)	49 (79.0)	48 (78.7)	1.02 [0.43; 2.43] 0.963	1.00 [0.84; 1.21] 0.963	0.00 [-0.14; 0.15] 0.963
absence					
N'/N	127 / 127	126 / 126			
Any non-ocular AE, n (%)	98 (77.2)	95 (75.4)	1.10 [0.62; 1.97] 0.741	1.02 [0.89; 1.17] 0.741	0.02 [-0.09; 0.12] 0.741
KITE					
Interaction Test:	p = 0.376				
presence					
N'/N	56 / 56	67 / 67			
Any non-ocular AE, n (%)	39 (69.6)	52 (77.6)	0.66 [0.29; 1.49] 0.317	0.90 [0.72; 1.11] 0.324	-0.08 [-0.24; 0.08] 0.318
absence					
N'/N	123 / 123	114 / 114			
Any non-ocular AE, n (%)	97 (78.9)	89 (78.1)	1.05 [0.56; 1.95] 0.882	1.01 [0.88; 1.15] 0.882	0.01 [-0.10; 0.11] 0.882
Pooled Analysis					
Interaction Test:	p = 0.464				
presence					
N'/N	118 / 118	128 / 128			
Any non-ocular AE, n (%)	88 (74.6)	100 (78.1)	0.82 [0.46; 1.48] 0.516	0.95 [0.83; 1.09] 0.485	-0.04 [-0.14; 0.07] 0.485

	Treatment Groups		Comparison		
Any non-ocular adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any non-ocular AE, n (%)	195 (78.0)	184 (76.7)	1.08 [0.71; 1.65] 0.727	1.02 [0.92; 1.12] 0.732	0.01 [-0.06; 0.09] 0.732

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-5.12 Any non-ocular adverse event by exposure (week 52) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.068**					
KESTREL					
Interaction Test:	p = 0.901				
Non-exposed					
N'/N	71 / 71	75 / 75			
Any non-ocular AE, n (%)	50 (70.4)	50 (66.7)	1.19 [0.59; 2.40] 0.626	1.06 [0.85; 1.32] 0.625	0.04 [-0.11; 0.19] 0.625
Exposed					
N'/N	118 / 118	112 / 112			
Any non-ocular AE, n (%)	79 (66.9)	72 (64.3)	1.13 [0.65; 1.94] 0.671	1.04 [0.86; 1.26] 0.671	0.03 [-0.10; 0.15] 0.671
KITE					
Interaction Test:	p = 0.415				
Non-exposed					
N'/N	85 / 85	90 / 90			
Any non-ocular AE, n (%)	55 (64.7)	63 (70.0)	0.79 [0.42; 1.48] 0.456	0.92 [0.75; 1.14] 0.457	-0.05 [-0.19; 0.09] 0.455
Exposed					
N'/N	94 / 94	91 / 91			
Any non-ocular AE, n (%)	53 (56.4)	64 (70.3)	0.55 [0.30; 1.00] 0.050	0.80 [0.64; 1.00] 0.051	-0.14 [-0.28; -0.00] 0.047 *
Pooled Analysis					
Interaction Test:	p = 0.500				
Non-exposed					
N'/N	156 / 156	165 / 165			
Any non-ocular AE, n (%)	105 (67.3)	113 (68.5)	0.98 [0.61; 1.58] 0.942	0.98 [0.85; 1.14] 0.822	-0.01 [-0.11; 0.09] 0.821

	Treatment Groups		Comparison		
Any non-ocular adverse event by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	212 / 212	203 / 203			
Any non-ocular AE, n (%)	132 (62.3)	136 (67.0)	0.79 [0.53; 1.19] 0.263	0.93 [0.81; 1.07] 0.314	-0.05 [-0.14; 0.04] 0.313

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 12-5.13 Any non-ocular adverse event by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.603**					
KESTREL					
Interaction Test:	p = 0.552				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any non-ocular AE, n (%)	8 (66.7)	7 (53.8)	1.71 [0.34; 8.67] 0.516	1.24 [0.65; 2.35] 0.515	0.13 [-0.25; 0.51] 0.509
Exposed					
N'/N	177 / 177	174 / 174			
Any non-ocular AE, n (%)	139 (78.5)	136 (78.2)	1.02 [0.61; 1.70] 0.933	1.00 [0.90; 1.12] 0.933	0.00 [-0.08; 0.09] 0.933
KITE					
Interaction Test:	p = 0.402				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any non-ocular AE, n (%)	12 (70.6)	7 (58.3)	1.71 [0.36; 8.08] 0.496	1.21 [0.69; 2.14] 0.511	0.12 [-0.23; 0.48] 0.496
Exposed					
N'/N	162 / 162	169 / 169			
Any non-ocular AE, n (%)	124 (76.5)	134 (79.3)	0.85 [0.51; 1.43] 0.547	0.97 [0.86; 1.08] 0.548	-0.03 [-0.12; 0.06] 0.547
Pooled Analysis					
Interaction Test:	p = 0.291				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any non-ocular AE, n (%)	20 (69.0)	14 (56.0)	1.76 [0.58; 5.37] 0.321	1.22 [0.80; 1.87] 0.353	0.13 [-0.13; 0.38] 0.343

	Treatment Groups		Comparison		
Any non-ocular adverse event by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any non-ocular AE, n (%)	263 (77.6)	270 (78.7)	0.93 [0.65; 1.34] 0.717	0.99 [0.91; 1.07] 0.719	-0.01 [-0.07; 0.05] 0.718

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

13 Safety analysis: Any serious adverse event

Table 13-1.1 Any serious adverse event (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious adverse event (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any SAE, n (%)	37 (19.6)	43 (23.0)	0.82 [0.50; 1.34] 0.419	0.85 [0.58; 1.26] 0.419	-0.03 [-0.12; 0.05] 0.418
KITE, N'/N	179 / 179	181 / 181			
Any SAE, n (%)	34 (19.0)	40 (22.1)	0.83 [0.50; 1.38] 0.466	0.86 [0.57; 1.29] 0.467	-0.03 [-0.11; 0.05] 0.466
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any SAE, n (%)	71 (19.3)	83 (22.6)	0.82 [0.57; 1.17] 0.277	0.86 [0.65; 1.13] 0.277	-0.03 [-0.09; 0.03] 0.276
p_H=0.970					
Any SAE, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any SAE, n (%)	59 (31.2)	63 (33.7)	0.89 [0.58; 1.38] 0.609	0.93 [0.69; 1.24] 0.609	-0.02 [-0.12; 0.07] 0.608
KITE, N'/N	179 / 179	181 / 181			
Any SAE, n (%)	53 (29.6)	60 (33.1)	0.85 [0.54; 1.32] 0.469	0.89 [0.66; 1.21] 0.470	-0.04 [-0.13; 0.06] 0.469

	Treatment Groups		Comparison		
Any serious adverse event (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any SAE, n (%)	112 (30.4)	123 (33.4)	0.87 [0.64; 1.19] 0.383	0.91 [0.74; 1.12] 0.384	-0.03 [-0.10; 0.04] 0.383
p_H=0.870					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-1.2 Any serious adverse event by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.970**					
KESTREL					
Interaction Test:	p = 0.350				
< 65 years					
N'/N	104 / 104	93 / 93			
Any SAE, n (%)	19 (18.3)	16 (17.2)	1.08 [0.52; 2.24] 0.845	1.06 [0.58; 1.94] 0.845	0.01 [-0.10; 0.12] 0.845
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any SAE, n (%)	18 (21.2)	27 (28.7)	0.67 [0.34; 1.32] 0.247	0.74 [0.44; 1.24] 0.250	-0.08 [-0.20; 0.05] 0.241
KITE					
Interaction Test:	p = 0.718				
< 65 years					
N'/N	100 / 100	102 / 102			
Any SAE, n (%)	19 (19.0)	24 (23.5)	0.76 [0.39; 1.50] 0.432	0.81 [0.47; 1.38] 0.433	-0.05 [-0.16; 0.07] 0.431
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any SAE, n (%)	15 (19.0)	16 (20.3)	0.92 [0.42; 2.02] 0.841	0.94 [0.50; 1.76] 0.841	-0.01 [-0.14; 0.11] 0.841
Pooled Analysis					
Interaction Test:	p = 0.680				
< 65 years					
N'/N	204 / 204	195 / 195			
Any SAE, n (%)	38 (18.6)	40 (20.5)	0.89 [0.54; 1.45] 0.632	0.91 [0.61; 1.36] 0.656	-0.02 [-0.10; 0.06] 0.656
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any SAE, n (%)	33 (20.1)	43 (24.9)	0.76 [0.46; 1.28] 0.301	0.81 [0.55; 1.22] 0.313	-0.05 [-0.13; 0.04] 0.310

	Treatment Groups		Comparison		
Any serious adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.870**					
KESTREL					
Interaction Test:	p = 0.202				
< 65 years					
N'/N	104 / 104	93 / 93			
Any SAE, n (%)	33 (31.7)	26 (28.0)	1.20 [0.65; 2.21] 0.564	1.13 [0.74; 1.75] 0.565	0.04 [-0.09; 0.17] 0.563
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any SAE, n (%)	26 (30.6)	37 (39.4)	0.68 [0.37; 1.26] 0.221	0.78 [0.52; 1.17] 0.224	-0.09 [-0.23; 0.05] 0.216
KITE					
Interaction Test:	p = 0.109				
< 65 years					
N'/N	100 / 100	102 / 102			
Any SAE, n (%)	23 (23.0)	34 (33.3)	0.60 [0.32; 1.11] 0.104	0.69 [0.44; 1.08] 0.107	-0.10 [-0.23; 0.02] 0.100
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any SAE, n (%)	30 (38.0)	26 (32.9)	1.25 [0.65; 2.40] 0.506	1.15 [0.76; 1.76] 0.507	0.05 [-0.10; 0.20] 0.505
Pooled Analysis					
Interaction Test:	p = 0.847				
< 65 years					
N'/N	204 / 204	195 / 195			
Any SAE, n (%)	56 (27.5)	60 (30.8)	0.85 [0.55; 1.31] 0.465	0.89 [0.65; 1.21] 0.459	-0.03 [-0.12; 0.06] 0.459

	Treatment Groups		Comparison		
Any serious adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any SAE, n (%)	56 (34.1)	63 (36.4)	0.90 [0.58; 1.42] 0.661	0.94 [0.70; 1.25] 0.663	-0.02 [-0.13; 0.08] 0.662

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-1.3 Any serious adverse event by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.970**					
KESTREL					
Interaction Test:	p = 0.669				
Male					
N'/N	110 / 110	126 / 126			
Any SAE, n (%)	23 (20.9)	32 (25.4)	0.78 [0.42; 1.43] 0.416	0.82 [0.51; 1.32] 0.418	-0.04 [-0.15; 0.06] 0.413
Female					
N'/N	79 / 79	61 / 61			
Any SAE, n (%)	14 (17.7)	11 (18.0)	0.98 [0.41; 2.34] 0.962	0.98 [0.48; 2.01] 0.962	-0.00 [-0.13; 0.12] 0.962
KITE					
Interaction Test:	p = 0.475				
Male					
N'/N	120 / 120	115 / 115			
Any SAE, n (%)	24 (20.0)	24 (20.9)	0.95 [0.50; 1.79] 0.869	0.96 [0.58; 1.59] 0.869	-0.01 [-0.11; 0.09] 0.869
Female					
N'/N	59 / 59	66 / 66			
Any SAE, n (%)	10 (16.9)	16 (24.2)	0.64 [0.26; 1.54] 0.318	0.70 [0.34; 1.42] 0.322	-0.07 [-0.21; 0.07] 0.310
Pooled Analysis					
Interaction Test:	p = 0.812				
Male					
N'/N	230 / 230	241 / 241			
Any SAE, n (%)	47 (20.4)	56 (23.2)	0.85 [0.55; 1.32] 0.469	0.88 [0.63; 1.25] 0.483	-0.03 [-0.10; 0.05] 0.481
Female					
N'/N	138 / 138	127 / 127			
Any SAE, n (%)	24 (17.4)	27 (21.3)	0.78 [0.42; 1.43] 0.417	0.83 [0.50; 1.37] 0.458	-0.04 [-0.13; 0.06] 0.456

	Treatment Groups		Comparison		
Any serious adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.870**					
KESTREL					
Interaction Test:	p = 0.826				
Male					
N'/N	110 / 110	126 / 126			
Any SAE, n (%)	37 (33.6)	44 (34.9)	0.94 [0.55; 1.62] 0.836	0.96 [0.68; 1.37] 0.836	-0.01 [-0.13; 0.11] 0.836
Female					
N'/N	79 / 79	61 / 61			
Any SAE, n (%)	22 (27.8)	19 (31.1)	0.85 [0.41; 1.77] 0.671	0.89 [0.53; 1.50] 0.670	-0.03 [-0.19; 0.12] 0.672
KITE					
Interaction Test:	p = 0.711				
Male					
N'/N	120 / 120	115 / 115			
Any SAE, n (%)	36 (30.0)	37 (32.2)	0.90 [0.52; 1.57] 0.719	0.93 [0.64; 1.36] 0.719	-0.02 [-0.14; 0.10] 0.719
Female					
N'/N	59 / 59	66 / 66			
Any SAE, n (%)	17 (28.8)	23 (34.8)	0.76 [0.35; 1.61] 0.471	0.83 [0.49; 1.39] 0.473	-0.06 [-0.22; 0.10] 0.468
Pooled Analysis					
Interaction Test:	p = 0.649				
Male					
N'/N	230 / 230	241 / 241			
Any SAE, n (%)	73 (31.7)	81 (33.6)	0.92 [0.63; 1.35] 0.676	0.95 [0.73; 1.23] 0.690	-0.02 [-0.10; 0.07] 0.689

	Treatment Groups		Comparison		
Any serious adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any SAE, n (%)	39 (28.3)	42 (33.1)	0.79 [0.47; 1.34] 0.383	0.86 [0.60; 1.24] 0.420	-0.05 [-0.16; 0.07] 0.419

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-1.4 Any serious adverse event by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.970**					
KESTREL					
Interaction Test:	p = 0.398				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any SAE, n (%)	16 (21.6)	13 (20.3)	1.08 [0.48; 2.46] 0.851	1.06 [0.56; 2.04] 0.851	0.01 [-0.12; 0.15] 0.850
> 65 letters					
N'/N	115 / 115	123 / 123			
Any SAE, n (%)	21 (18.3)	30 (24.4)	0.69 [0.37; 1.30] 0.251	0.75 [0.46; 1.23] 0.253	-0.06 [-0.16; 0.04] 0.246
KITE					
Interaction Test:	p = 0.057				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any SAE, n (%)	9 (13.8)	24 (26.4)	0.45 [0.19; 1.04] 0.063	0.53 [0.26; 1.05] 0.070	-0.13 [-0.25; -0.00] 0.047 *
> 65 letters					
N'/N	114 / 114	90 / 90			
Any SAE, n (%)	25 (21.9)	16 (17.8)	1.30 [0.65; 2.61] 0.463	1.23 [0.70; 2.17] 0.465	0.04 [-0.07; 0.15] 0.458
Pooled Analysis					
Interaction Test:	p = 0.457				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any SAE, n (%)	25 (18.0)	37 (23.9)	0.69 [0.39; 1.23] 0.210	0.75 [0.47; 1.19] 0.216	-0.06 [-0.15; 0.03] 0.209
> 65 letters					
N'/N	229 / 229	213 / 213			
Any SAE, n (%)	46 (20.1)	46 (21.6)	0.92 [0.58; 1.46] 0.715	0.93 [0.65; 1.35] 0.715	-0.01 [-0.09; 0.06] 0.714

	Treatment Groups		Comparison		
Any serious adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.870**					
KESTREL					
Interaction Test:	p = 0.423				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any SAE, n (%)	24 (32.4)	19 (29.7)	1.14 [0.55; 2.35] 0.729	1.09 [0.66; 1.80] 0.729	0.03 [-0.13; 0.18] 0.728
> 65 letters					
N'/N	115 / 115	123 / 123			
Any SAE, n (%)	35 (30.4)	44 (35.8)	0.79 [0.46; 1.35] 0.383	0.85 [0.59; 1.22] 0.384	-0.05 [-0.17; 0.07] 0.381
KITE					
Interaction Test:	p = 0.066				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any SAE, n (%)	16 (24.6)	35 (38.5)	0.52 [0.26; 1.06] 0.071	0.64 [0.39; 1.05] 0.079	-0.14 [-0.28; 0.01] 0.061
> 65 letters					
N'/N	114 / 114	90 / 90			
Any SAE, n (%)	37 (32.5)	25 (27.8)	1.25 [0.68; 2.29] 0.471	1.17 [0.76; 1.79] 0.473	0.05 [-0.08; 0.17] 0.468
Pooled Analysis					
Interaction Test:	p = 0.452				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any SAE, n (%)	40 (28.8)	54 (34.8)	0.75 [0.46; 1.23] 0.258	0.83 [0.58; 1.17] 0.279	-0.06 [-0.17; 0.05] 0.275

	Treatment Groups		Comparison		
Any serious adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any SAE, n (%)	72 (31.4)	69 (32.4)	0.96 [0.64; 1.43] 0.843	0.98 [0.74; 1.29] 0.867	-0.01 [-0.09; 0.08] 0.867

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-1.5 Any serious adverse event by region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.970**					
KESTREL					
Interaction Test:	p = 0.934				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any SAE, n (%)	19 (21.1)	22 (26.5)	0.74 [0.37; 1.50] 0.405	0.80 [0.47; 1.36] 0.406	-0.05 [-0.18; 0.07] 0.405
European Region					
N'/N	69 / 69	75 / 75			
Any SAE, n (%)	12 (17.4)	15 (20.0)	0.84 [0.36; 1.95] 0.689	0.87 [0.44; 1.73] 0.689	-0.03 [-0.15; 0.10] 0.688
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any SAE, n (%)	6 (20.0)	6 (20.7)	0.96 [0.27; 3.41] 0.948	0.97 [0.35; 2.65] 0.948	-0.01 [-0.21; 0.20] 0.948
KITE					
Interaction Test:	p = 0.057				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any SAE, n (%)	6 (23.1)	2 (9.5)	2.85 [0.51; 15.90] 0.232	2.42 [0.54; 10.79] 0.245	0.14 [-0.07; 0.34] 0.195
European Region					
N'/N	135 / 135	132 / 132			
Any SAE, n (%)	21 (15.6)	32 (24.2)	0.58 [0.31; 1.06] 0.077	0.64 [0.39; 1.05] 0.079	-0.09 [-0.18; 0.01] 0.074
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any SAE, n (%)	7 (38.9)	6 (21.4)	2.33 [0.63; 8.64] 0.204	1.81 [0.73; 4.53] 0.202	0.17 [-0.10; 0.45] 0.208

	Treatment Groups		Comparison		
Any serious adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.228				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any SAE, n (%)	19 (21.1)	22 (26.5)	0.73 [0.32; 1.67] 0.450	0.80 [0.47; 1.36] 0.406	-0.05 [-0.18; 0.07] 0.405
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any SAE, n (%)	6 (23.1)	2 (9.5)	2.92 [0.49; 17.32] 0.239	2.42 [0.54; 10.79] 0.224	0.14 [-0.07; 0.34] 0.195
European Region					
N'/N	204 / 204	207 / 207			
Any SAE, n (%)	33 (16.2)	47 (22.7)	0.66 [0.39; 1.11] 0.119	0.71 [0.48; 1.06] 0.094	-0.07 [-0.14; 0.01] 0.092
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any SAE, n (%)	13 (27.1)	12 (21.1)	1.42 [0.58; 3.51] 0.446	1.34 [0.68; 2.61] 0.403	0.07 [-0.10; 0.24] 0.406
Any SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.870**					
KESTREL					
Interaction Test:	p = 0.986				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any SAE, n (%)	32 (35.6)	32 (38.6)	0.88 [0.47; 1.63] 0.683	0.92 [0.63; 1.36] 0.683	-0.03 [-0.17; 0.11] 0.683
European Region					
N'/N	69 / 69	75 / 75			
Any SAE, n (%)	18 (26.1)	22 (29.3)	0.85 [0.41; 1.77] 0.664	0.89 [0.52; 1.51] 0.665	-0.03 [-0.18; 0.11] 0.663
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any SAE, n (%)	9 (30.0)	9 (31.0)	0.95 [0.31; 2.89] 0.931	0.97 [0.45; 2.09] 0.931	-0.01 [-0.25; 0.22] 0.931

	Treatment Groups		Comparison		
Any serious adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.646				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any SAE, n (%)	7 (26.9)	4 (19.0)	1.57 [0.39; 6.30] 0.528	1.41 [0.48; 4.19] 0.532	0.08 [-0.16; 0.32] 0.519
European Region					
N'/N	135 / 135	132 / 132			
Any SAE, n (%)	39 (28.9)	45 (34.1)	0.79 [0.47; 1.32] 0.360	0.85 [0.59; 1.21] 0.361	-0.05 [-0.16; 0.06] 0.360
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any SAE, n (%)	7 (38.9)	11 (39.3)	0.98 [0.29; 3.31] 0.979	0.99 [0.47; 2.07] 0.979	-0.00 [-0.29; 0.28] 0.979
Pooled Analysis					
Interaction Test:	p = 0.831				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any SAE, n (%)	32 (35.6)	32 (38.6)	0.85 [0.41; 1.77] 0.673	0.92 [0.63; 1.36] 0.684	-0.03 [-0.17; 0.11] 0.683
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any SAE, n (%)	7 (26.9)	4 (19.0)	1.61 [0.38; 6.87] 0.518	1.41 [0.48; 4.19] 0.531	0.08 [-0.16; 0.32] 0.519
European Region					
N'/N	204 / 204	207 / 207			
Any SAE, n (%)	57 (27.9)	67 (32.4)	0.81 [0.52; 1.27] 0.366	0.86 [0.64; 1.16] 0.319	-0.05 [-0.13; 0.04] 0.318

	Treatment Groups		Comparison		
Any serious adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any SAE, n (%)	16 (33.3)	20 (35.1)	0.95 [0.42; 2.14] 0.896	0.98 [0.57; 1.67] 0.935	-0.01 [-0.19; 0.17] 0.935

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-1.6 Any serious adverse event by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.970**					
KESTREL					
Interaction Test:	p = 0.532				
Type 1					
N'/N	12 / 12	6 / 6			
Any SAE, n (%)	2 (16.7)	2 (33.3)	0.40 [0.04; 3.90] 0.430	0.50 [0.09; 2.73] 0.423	-0.17 [-0.60; 0.27] 0.450
Type 2					
N'/N	177 / 177	181 / 181			
Any SAE, n (%)	35 (19.8)	41 (22.7)	0.84 [0.51; 1.40] 0.506	0.87 [0.58; 1.30] 0.506	-0.03 [-0.11; 0.06] 0.505
KITE					
Interaction Test:	p = 0.879				
Type 1					
N'/N	19 / 19	7 / 7			
Any SAE, n (%)	2 (10.5)	1 (14.3)	0.71 [0.05; 9.27] 0.791	0.74 [0.08; 6.91] 0.789	-0.04 [-0.33; 0.26] 0.802
Type 2					
N'/N	160 / 160	174 / 174			
Any SAE, n (%)	32 (20.0)	39 (22.4)	0.87 [0.51; 1.46] 0.590	0.89 [0.59; 1.35] 0.591	-0.02 [-0.11; 0.06] 0.589
Pooled Analysis					
Interaction Test:	p = 0.530				
Type 1					
N'/N	31 / 31	13 / 13			
Any SAE, n (%)	4 (12.9)	3 (23.1)	0.49 [0.09; 2.61] 0.406	0.58 [0.15; 2.25] 0.447	-0.09 [-0.35; 0.16] 0.469

	Treatment Groups		Comparison		
Any serious adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any SAE, n (%)	67 (19.9)	80 (22.5)	0.85 [0.59; 1.23] 0.394	0.88 [0.66; 1.18] 0.394	-0.03 [-0.09; 0.03] 0.393
Any SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.870**					
KESTREL					
Interaction Test:	p = 0.567				
Type 1					
N'/N	12 / 12	6 / 6			
Any SAE, n (%)	4 (33.3)	3 (50.0)	0.50 [0.07; 3.70] 0.497	0.67 [0.22; 2.07] 0.483	-0.17 [-0.65; 0.31] 0.497
Type 2					
N'/N	177 / 177	181 / 181			
Any SAE, n (%)	55 (31.1)	60 (33.1)	0.91 [0.58; 1.42] 0.674	0.94 [0.69; 1.27] 0.674	-0.02 [-0.12; 0.08] 0.674
KITE					
Interaction Test:	p = 0.851				
Type 1					
N'/N	19 / 19	7 / 7			
Any SAE, n (%)	3 (15.8)	1 (14.3)	1.12 [0.10; 13.03] 0.925	1.11 [0.14; 8.94] 0.925	0.02 [-0.29; 0.32] 0.923
Type 2					
N'/N	160 / 160	174 / 174			
Any SAE, n (%)	50 (31.3)	59 (33.9)	0.89 [0.56; 1.40] 0.605	0.92 [0.68; 1.26] 0.605	-0.03 [-0.13; 0.07] 0.604
Pooled Analysis					
Interaction Test:	p = 0.686				
Type 1					
N'/N	31 / 31	13 / 13			
Any SAE, n (%)	7 (22.6)	4 (30.8)	0.66 [0.16; 2.81] 0.575	0.78 [0.28; 2.16] 0.651	-0.06 [-0.34; 0.22] 0.651

	Treatment Groups		Comparison		
Any serious adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any SAE, n (%)	105 (31.2)	119 (33.5)	0.90 [0.65; 1.23] 0.503	0.93 [0.75; 1.15] 0.508	-0.02 [-0.09; 0.05] 0.508

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-1.7 Any serious adverse event by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.970**					
KESTREL					
Interaction Test:	p = 0.223				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any SAE, n (%)	15 (19.7)	20 (18.7)	1.07 [0.51; 2.25] 0.859	1.06 [0.58; 1.93] 0.859	0.01 [-0.11; 0.13] 0.860
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any SAE, n (%)	21 (18.8)	23 (28.8)	0.57 [0.29; 1.13] 0.106	0.65 [0.39; 1.09] 0.105	-0.10 [-0.22; 0.02] 0.110
KITE					
Interaction Test:	p = 0.135				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any SAE, n (%)	19 (23.2)	19 (19.8)	1.22 [0.60; 2.51] 0.584	1.17 [0.67; 2.06] 0.583	0.03 [-0.09; 0.16] 0.585
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any SAE, n (%)	15 (15.5)	21 (24.7)	0.56 [0.27; 1.17] 0.121	0.63 [0.35; 1.14] 0.123	-0.09 [-0.21; 0.02] 0.120
Pooled Analysis					
Interaction Test:	p = 0.054				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any SAE, n (%)	34 (21.5)	39 (19.2)	1.16 [0.69; 1.94] 0.583	1.11 [0.74; 1.68] 0.605	0.02 [-0.06; 0.11] 0.606
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any SAE, n (%)	36 (17.2)	44 (26.7)	0.57 [0.35; 0.94] 0.027 *	0.64 [0.43; 0.95] 0.025 *	-0.10 [-0.18; -0.01] 0.026 *

	Treatment Groups		Comparison		
Any serious adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.870**					
KESTREL					
Interaction Test:	p = 0.227				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any SAE, n (%)	23 (30.3)	30 (28.0)	1.11 [0.58; 2.13] 0.744	1.08 [0.68; 1.70] 0.743	0.02 [-0.11; 0.16] 0.744
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any SAE, n (%)	35 (31.3)	33 (41.3)	0.65 [0.36; 1.18] 0.154	0.76 [0.52; 1.11] 0.151	-0.10 [-0.24; 0.04] 0.155
KITE					
Interaction Test:	p = 0.410				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any SAE, n (%)	27 (32.9)	31 (32.3)	1.03 [0.55; 1.93] 0.928	1.02 [0.67; 1.56] 0.928	0.01 [-0.13; 0.14] 0.928
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any SAE, n (%)	26 (26.8)	29 (34.1)	0.71 [0.37; 1.33] 0.285	0.79 [0.50; 1.22] 0.285	-0.07 [-0.21; 0.06] 0.284
Pooled Analysis					
Interaction Test:	p = 0.151				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any SAE, n (%)	50 (31.6)	61 (30.0)	1.08 [0.69; 1.69] 0.737	1.05 [0.77; 1.43] 0.771	0.01 [-0.08; 0.11] 0.770

	Treatment Groups		Comparison		
Any serious adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any SAE, n (%)	61 (29.2)	62 (37.6)	0.68 [0.44; 1.05] 0.085	0.77 [0.58; 1.03] 0.077	-0.09 [-0.18; 0.01] 0.077

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-1.8 Any serious adverse event by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.970**					
KESTREL					
Interaction Test:	p = 0.430				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any SAE, n (%)	20 (16.7)	26 (23.6)	0.65 [0.34; 1.24] 0.189	0.71 [0.42; 1.19] 0.190	-0.07 [-0.17; 0.03] 0.188
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any SAE, n (%)	5 (16.7)	8 (20.5)	0.78 [0.23; 2.67] 0.686	0.81 [0.30; 2.23] 0.687	-0.04 [-0.22; 0.15] 0.682
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any SAE, n (%)	12 (30.8)	9 (23.7)	1.43 [0.52; 3.94] 0.486	1.30 [0.62; 2.72] 0.488	0.07 [-0.13; 0.27] 0.483
KITE					
Interaction Test:	p = 0.538				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any SAE, n (%)	18 (21.2)	18 (19.6)	1.10 [0.53; 2.30] 0.790	1.08 [0.60; 1.94] 0.790	0.02 [-0.10; 0.13] 0.790
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any SAE, n (%)	8 (15.7)	12 (24.5)	0.57 [0.21; 1.55] 0.275	0.64 [0.29; 1.43] 0.278	-0.09 [-0.24; 0.07] 0.270
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any SAE, n (%)	8 (18.6)	10 (25.0)	0.69 [0.24; 1.96] 0.481	0.74 [0.33; 1.70] 0.482	-0.06 [-0.24; 0.11] 0.480

	Treatment Groups		Comparison		
Any serious adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.728				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any SAE, n (%)	38 (18.5)	44 (21.8)	0.82 [0.50; 1.33] 0.417	0.85 [0.58; 1.25] 0.417	-0.03 [-0.11; 0.05] 0.417
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any SAE, n (%)	13 (16.0)	20 (22.7)	0.65 [0.30; 1.42] 0.279	0.70 [0.37; 1.32] 0.269	-0.07 [-0.19; 0.05] 0.263
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any SAE, n (%)	20 (24.4)	19 (24.4)	1.00 [0.49; 2.06] 0.997	1.00 [0.58; 1.73] 0.989	0.00 [-0.13; 0.13] 0.989
Any SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.870**					
KESTREL					
Interaction Test:	p = 0.604				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any SAE, n (%)	36 (30.0)	39 (35.5)	0.78 [0.45; 1.36] 0.378	0.85 [0.58; 1.23] 0.379	-0.05 [-0.18; 0.07] 0.378
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any SAE, n (%)	8 (26.7)	12 (30.8)	0.82 [0.28; 2.35] 0.710	0.87 [0.41; 1.85] 0.711	-0.04 [-0.26; 0.17] 0.708
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any SAE, n (%)	15 (38.5)	12 (31.6)	1.35 [0.53; 3.47] 0.527	1.22 [0.66; 2.25] 0.529	0.07 [-0.14; 0.28] 0.526

	Treatment Groups		Comparison		
Any serious adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.135				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any SAE, n (%)	29 (34.1)	26 (28.3)	1.31 [0.69; 2.49] 0.401	1.21 [0.78; 1.87] 0.401	0.06 [-0.08; 0.20] 0.400
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any SAE, n (%)	13 (25.5)	21 (42.9)	0.46 [0.20; 1.06] 0.069	0.59 [0.34; 1.05] 0.074	-0.17 [-0.36; 0.01] 0.063
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any SAE, n (%)	11 (25.6)	13 (32.5)	0.71 [0.28; 1.85] 0.488	0.79 [0.40; 1.55] 0.489	-0.07 [-0.26; 0.13] 0.487
Pooled Analysis					
Interaction Test:	p = 0.407				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any SAE, n (%)	65 (31.7)	65 (32.2)	0.98 [0.64; 1.48] 0.912	0.98 [0.74; 1.30] 0.908	-0.01 [-0.10; 0.09] 0.908
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any SAE, n (%)	21 (25.9)	33 (37.5)	0.59 [0.30; 1.13] 0.113	0.68 [0.43; 1.08] 0.097	-0.12 [-0.26; 0.02] 0.092

	Treatment Groups		Comparison		
Any serious adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any SAE, n (%)	26 (31.7)	25 (32.1)	0.98 [0.51; 1.92] 0.964	0.99 [0.63; 1.56] 0.971	-0.00 [-0.15; 0.14] 0.971

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-1.9 Any serious adverse event by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.970**					
KESTREL					
Interaction Test:	p = 0.632				
focal					
N'/N	59 / 59	48 / 48			
Any SAE, n (%)	7 (11.9)	8 (16.7)	0.67 [0.23; 2.01] 0.479	0.71 [0.28; 1.82] 0.479	-0.05 [-0.18; 0.09] 0.482
diffuse					
N'/N	127 / 127	134 / 134			
Any SAE, n (%)	30 (23.6)	34 (25.4)	0.91 [0.52; 1.60] 0.742	0.93 [0.61; 1.43] 0.743	-0.02 [-0.12; 0.09] 0.742
KITE					
Interaction Test:	p = 0.939				
focal					
N'/N	63 / 63	66 / 66			
Any SAE, n (%)	12 (19.0)	14 (21.2)	0.87 [0.37; 2.07] 0.759	0.90 [0.45; 1.79] 0.760	-0.02 [-0.16; 0.12] 0.759
diffuse					
N'/N	115 / 115	109 / 109			
Any SAE, n (%)	22 (19.1)	24 (22.0)	0.84 [0.44; 1.60] 0.593	0.87 [0.52; 1.46] 0.593	-0.03 [-0.13; 0.08] 0.593
Pooled Analysis					
Interaction Test:	p = 0.753				
focal					
N'/N	122 / 122	114 / 114			
Any SAE, n (%)	19 (15.6)	22 (19.3)	0.77 [0.39; 1.51] 0.446	0.82 [0.47; 1.44] 0.498	-0.03 [-0.13; 0.06] 0.498
diffuse					
N'/N	242 / 242	243 / 243			
Any SAE, n (%)	52 (21.5)	58 (23.9)	0.87 [0.57; 1.34] 0.537	0.90 [0.65; 1.26] 0.550	-0.02 [-0.10; 0.05] 0.549

	Treatment Groups		Comparison		
Any serious adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.870**					
KESTREL					
Interaction Test:	p = 0.382				
focal					
N'/N	59 / 59	48 / 48			
Any SAE, n (%)	16 (27.1)	17 (35.4)	0.68 [0.30; 1.55] 0.356	0.77 [0.43; 1.35] 0.356	-0.08 [-0.26; 0.09] 0.357
diffuse					
N'/N	127 / 127	134 / 134			
Any SAE, n (%)	43 (33.9)	44 (32.8)	1.05 [0.63; 1.75] 0.861	1.03 [0.73; 1.45] 0.861	0.01 [-0.10; 0.12] 0.861
KITE					
Interaction Test:	p = 0.667				
focal					
N'/N	63 / 63	66 / 66			
Any SAE, n (%)	21 (33.3)	22 (33.3)	1.00 [0.48; 2.08] 1.000	1.00 [0.61; 1.63] 1.000	-0.00 [-0.16; 0.16] 1.000
diffuse					
N'/N	115 / 115	109 / 109			
Any SAE, n (%)	32 (27.8)	35 (32.1)	0.82 [0.46; 1.45] 0.484	0.87 [0.58; 1.29] 0.484	-0.04 [-0.16; 0.08] 0.484
Pooled Analysis					
Interaction Test:	p = 0.746				
focal					
N'/N	122 / 122	114 / 114			
Any SAE, n (%)	37 (30.3)	39 (34.2)	0.83 [0.48; 1.44] 0.519	0.89 [0.62; 1.29] 0.541	-0.04 [-0.16; 0.08] 0.540

	Treatment Groups		Comparison		
Any serious adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any SAE, n (%)	75 (31.0)	79 (32.5)	0.93 [0.64; 1.37] 0.722	0.96 [0.74; 1.24] 0.736	-0.01 [-0.10; 0.07] 0.736

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-1.10 Any serious adverse event by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.970**					
KESTREL					
Interaction Test:	p = 0.937				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any SAE, n (%)	20 (18.7)	21 (21.9)	0.82 [0.41; 1.63] 0.573	0.85 [0.49; 1.48] 0.573	-0.03 [-0.14; 0.08] 0.574
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any SAE, n (%)	15 (21.4)	17 (23.9)	0.87 [0.39; 1.91] 0.722	0.89 [0.49; 1.65] 0.722	-0.03 [-0.16; 0.11] 0.721
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any SAE, n (%)	2 (16.7)	5 (25.0)	0.60 [0.10; 3.72] 0.583	0.67 [0.15; 2.92] 0.590	-0.08 [-0.37; 0.20] 0.565
KITE					
Interaction Test:	p = 0.806				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any SAE, n (%)	17 (20.0)	19 (23.2)	0.83 [0.40; 1.74] 0.619	0.86 [0.48; 1.54] 0.619	-0.03 [-0.16; 0.09] 0.618
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any SAE, n (%)	13 (17.6)	18 (22.8)	0.72 [0.33; 1.60] 0.423	0.77 [0.41; 1.46] 0.425	-0.05 [-0.18; 0.07] 0.420
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any SAE, n (%)	4 (20.0)	3 (15.8)	1.33 [0.26; 6.94] 0.733	1.27 [0.33; 4.93] 0.733	0.04 [-0.20; 0.28] 0.731

	Treatment Groups		Comparison		
Any serious adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.981				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any SAE, n (%)	37 (19.3)	40 (22.5)	0.82 [0.50; 1.36] 0.449	0.86 [0.58; 1.28] 0.453	-0.03 [-0.11; 0.05] 0.453
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any SAE, n (%)	28 (19.4)	35 (23.3)	0.79 [0.45; 1.39] 0.416	0.83 [0.54; 1.29] 0.414	-0.04 [-0.13; 0.05] 0.411
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any SAE, n (%)	6 (18.8)	8 (20.5)	0.90 [0.28; 2.93] 0.860	0.94 [0.35; 2.51] 0.898	-0.01 [-0.20; 0.17] 0.896
Any SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.870**					
KESTREL					
Interaction Test:	p = 0.965				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any SAE, n (%)	34 (31.8)	32 (33.3)	0.93 [0.52; 1.68] 0.813	0.95 [0.64; 1.42] 0.813	-0.02 [-0.14; 0.11] 0.813
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any SAE, n (%)	21 (30.0)	23 (32.4)	0.89 [0.44; 1.82] 0.759	0.93 [0.57; 1.51] 0.759	-0.02 [-0.18; 0.13] 0.759
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any SAE, n (%)	4 (33.3)	8 (40.0)	0.75 [0.17; 3.35] 0.706	0.83 [0.32; 2.18] 0.711	-0.07 [-0.41; 0.28] 0.703

	Treatment Groups		Comparison		
Any serious adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.425				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any SAE, n (%)	28 (32.9)	25 (30.5)	1.12 [0.58; 2.15] 0.734	1.08 [0.69; 1.69] 0.734	0.02 [-0.12; 0.17] 0.733
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any SAE, n (%)	19 (25.7)	29 (36.7)	0.60 [0.30; 1.19] 0.143	0.70 [0.43; 1.13] 0.148	-0.11 [-0.26; 0.04] 0.138
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any SAE, n (%)	6 (30.0)	6 (31.6)	0.93 [0.24; 3.62] 0.915	0.95 [0.37; 2.44] 0.915	-0.02 [-0.31; 0.27] 0.915
Pooled Analysis					
Interaction Test:	p = 0.614				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any SAE, n (%)	62 (32.3)	57 (32.0)	1.01 [0.65; 1.56] 0.965	1.01 [0.75; 1.36] 0.958	0.00 [-0.09; 0.10] 0.958
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any SAE, n (%)	40 (27.8)	52 (34.7)	0.73 [0.44; 1.19] 0.205	0.80 [0.57; 1.13] 0.205	-0.07 [-0.17; 0.04] 0.202

	Treatment Groups		Comparison		
Any serious adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any SAE, n (%)	10 (31.3)	14 (35.9)	0.82 [0.30; 2.21] 0.694	0.89 [0.46; 1.75] 0.742	-0.04 [-0.26; 0.18] 0.738

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-1.11 Any serious adverse event by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.970**					
KESTREL					
Interaction Test:	p = 0.443				
presence					
N'/N	62 / 62	61 / 61			
Any SAE, n (%)	13 (21.0)	12 (19.7)	1.08 [0.45; 2.61] 0.858	1.07 [0.53; 2.15] 0.858	0.01 [-0.13; 0.16] 0.858
absence					
N'/N	127 / 127	126 / 126			
Any SAE, n (%)	24 (18.9)	31 (24.6)	0.71 [0.39; 1.30] 0.272	0.77 [0.48; 1.23] 0.274	-0.06 [-0.16; 0.04] 0.270
KITE					
Interaction Test:	p = 0.853				
presence					
N'/N	56 / 56	67 / 67			
Any SAE, n (%)	11 (19.6)	16 (23.9)	0.78 [0.33; 1.85] 0.572	0.82 [0.42; 1.62] 0.574	-0.04 [-0.19; 0.10] 0.569
absence					
N'/N	123 / 123	114 / 114			
Any SAE, n (%)	23 (18.7)	24 (21.1)	0.86 [0.46; 1.63] 0.650	0.89 [0.53; 1.48] 0.650	-0.02 [-0.13; 0.08] 0.650
Pooled Analysis					
Interaction Test:	p = 0.687				
presence					
N'/N	118 / 118	128 / 128			
Any SAE, n (%)	24 (20.3)	28 (21.9)	0.91 [0.49; 1.68] 0.763	0.93 [0.57; 1.52] 0.780	-0.01 [-0.12; 0.09] 0.779

	Treatment Groups		Comparison		
Any serious adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any SAE, n (%)	47 (18.8)	55 (22.9)	0.78 [0.50; 1.21] 0.264	0.82 [0.58; 1.16] 0.266	-0.04 [-0.11; 0.03] 0.266
Any SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.870**					
KESTREL					
Interaction Test:	p = 0.454				
presence					
N'/N	62 / 62	61 / 61			
Any SAE, n (%)	19 (30.6)	17 (27.9)	1.14 [0.53; 2.49] 0.735	1.10 [0.63; 1.91] 0.735	0.03 [-0.13; 0.19] 0.735
absence					
N'/N	127 / 127	126 / 126			
Any SAE, n (%)	40 (31.5)	46 (36.5)	0.80 [0.47; 1.35] 0.400	0.86 [0.61; 1.22] 0.401	-0.05 [-0.17; 0.07] 0.399
KITE					
Interaction Test:	p = 0.773				
presence					
N'/N	56 / 56	67 / 67			
Any SAE, n (%)	17 (30.4)	24 (35.8)	0.78 [0.37; 1.67] 0.522	0.85 [0.51; 1.41] 0.525	-0.05 [-0.22; 0.11] 0.520
absence					
N'/N	123 / 123	114 / 114			
Any SAE, n (%)	36 (29.3)	36 (31.6)	0.90 [0.52; 1.56] 0.699	0.93 [0.63; 1.36] 0.699	-0.02 [-0.14; 0.09] 0.699
Pooled Analysis					
Interaction Test:	p = 0.768				
presence					
N'/N	118 / 118	128 / 128			
Any SAE, n (%)	36 (30.5)	41 (32.0)	0.93 [0.54; 1.60] 0.791	0.96 [0.66; 1.39] 0.823	-0.01 [-0.13; 0.10] 0.823

	Treatment Groups		Comparison		
Any serious adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any SAE, n (%)	76 (30.4)	82 (34.2)	0.84 [0.58; 1.23] 0.373	0.89 [0.69; 1.15] 0.381	-0.04 [-0.12; 0.05] 0.380

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-1.12 Any serious adverse event by exposure (week 52) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious adverse event by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.970**					
KESTREL					
Interaction Test:	p = 0.143				
Non-exposed					
N'/N	71 / 71	75 / 75			
Any SAE, n (%)	20 (28.2)	18 (24.0)	1.24 [0.59; 2.60] 0.566	1.17 [0.68; 2.03] 0.567	0.04 [-0.10; 0.18] 0.566
Exposed					
N'/N	118 / 118	112 / 112			
Any SAE, n (%)	17 (14.4)	25 (22.3)	0.59 [0.30; 1.16] 0.123	0.65 [0.37; 1.13] 0.125	-0.08 [-0.18; 0.02] 0.120
KITE					
Interaction Test:	p = 0.060				
Non-exposed					
N'/N	85 / 85	90 / 90			
Any SAE, n (%)	23 (27.1)	20 (22.2)	1.30 [0.65; 2.59] 0.458	1.22 [0.72; 2.05] 0.459	0.05 [-0.08; 0.18] 0.458
Exposed					
N'/N	94 / 94	91 / 91			
Any SAE, n (%)	11 (11.7)	20 (22.0)	0.47 [0.21; 1.05] 0.065	0.53 [0.27; 1.05] 0.068	-0.10 [-0.21; 0.00] 0.060
Pooled Analysis					
Interaction Test:	p = 0.018 *				
Non-exposed					
N'/N	156 / 156	165 / 165			
Any SAE, n (%)	43 (27.6)	38 (23.0)	1.28 [0.77; 2.12] 0.345	1.20 [0.82; 1.75] 0.351	0.05 [-0.05; 0.14] 0.350

	Treatment Groups		Comparison		
Any serious adverse event by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	212 / 212	203 / 203			
Any SAE, n (%)	28 (13.2)	45 (22.2)	0.53 [0.32; 0.89] 0.017 *	0.60 [0.39; 0.92] 0.017 *	-0.09 [-0.16; -0.02] 0.016 *

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-1.13 Any serious adverse event by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious adverse event by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.870**					
KESTREL					
Interaction Test:	p = 0.926				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any SAE, n (%)	5 (41.7)	6 (46.2)	0.83 [0.17; 4.06] 0.821	0.90 [0.37; 2.20] 0.822	-0.04 [-0.43; 0.34] 0.821
Exposed					
N'/N	177 / 177	174 / 174			
Any SAE, n (%)	54 (30.5)	57 (32.8)	0.90 [0.57; 1.41] 0.650	0.93 [0.68; 1.27] 0.650	-0.02 [-0.12; 0.07] 0.650
KITE					
Interaction Test:	p = 0.751				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any SAE, n (%)	10 (58.8)	7 (58.3)	1.02 [0.23; 4.57] 0.979	1.01 [0.54; 1.88] 0.979	0.00 [-0.36; 0.37] 0.979
Exposed					
N'/N	162 / 162	169 / 169			
Any SAE, n (%)	43 (26.5)	53 (31.4)	0.79 [0.49; 1.27] 0.335	0.85 [0.60; 1.19] 0.336	-0.05 [-0.15; 0.05] 0.333
Pooled Analysis					
Interaction Test:	p = 0.772				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any SAE, n (%)	15 (51.7)	13 (52.0)	1.00 [0.34; 2.92] 1.000	0.96 [0.58; 1.62] 0.894	-0.02 [-0.28; 0.25] 0.892

	Treatment Groups		Comparison		
Any serious adverse event by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any SAE, n (%)	97 (28.6)	110 (32.1)	0.85 [0.61; 1.18] 0.321	0.89 [0.71; 1.12] 0.321	-0.03 [-0.10; 0.03] 0.320

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-2.1 Any serious ocular adverse event (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular SAE, n (%)	2 (1.1)	7 (3.7)	0.28 [0.06; 1.34] 0.110	0.28 [0.06; 1.34] 0.112	-0.03 [-0.06; 0.00] 0.088
KITE, N'/N	179 / 179	181 / 181			
Any ocular SAE, n (%)	5 (2.8)	3 (1.7)	1.70 [0.40; 7.24] 0.470	1.69 [0.41; 6.95] 0.470	0.01 [-0.02; 0.04] 0.465
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular SAE, n (%)	7 (1.9)	10 (2.7)	0.67 [0.23; 1.97] 0.469	0.70 [0.27; 1.82] 0.462	-0.01 [-0.03; 0.01] 0.462
p_H=0.096					
Any ocular SAE, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular SAE, n (%)	9 (4.8)	10 (5.3)	0.89 [0.35; 2.23] 0.796	0.89 [0.37; 2.14] 0.796	-0.01 [-0.05; 0.04] 0.795
KITE, N'/N	179 / 179	181 / 181			
Any ocular SAE, n (%)	6 (3.4)	4 (2.2)	1.53 [0.43; 5.53] 0.513	1.52 [0.44; 5.28] 0.513	0.01 [-0.02; 0.05] 0.510
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular SAE, n (%)	15 (4.1)	14 (3.8)	1.16 [0.53; 2.54] 0.713	1.07 [0.52; 2.18] 0.856	0.00 [-0.03; 0.03] 0.856
p_H=0.495					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-2.2 Any serious ocular adverse event by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.096**					
KESTREL					
Interaction Test:	N.E.				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular SAE, n (%)	0 (0.0)	3 (3.2)	N.E.	0.13 [0.01; 2.44] 0.172	-0.03 [-0.07; 0.00] 0.078
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular SAE, n (%)	2 (2.4)	4 (4.3)	0.54 [0.10; 3.04] 0.486	0.55 [0.10; 2.94] 0.487	-0.02 [-0.07; 0.03] 0.473
KITE					
Interaction Test:	N.E.				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular SAE, n (%)	1 (1.0)	0 (0.0)	N.E.	3.06 [0.13; 74.22] 0.492	0.01 [-0.01; 0.03] 0.315
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular SAE, n (%)	4 (5.1)	3 (3.8)	1.35 [0.29; 6.24] 0.700	1.33 [0.31; 5.76] 0.700	0.01 [-0.05; 0.08] 0.699
Pooled Analysis					
Interaction Test:	p = 0.390				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular SAE, n (%)	1 (0.5)	3 (1.5)	0.29 [0.03; 2.96] 0.298	0.47 [0.09; 2.48] 0.365	-0.01 [-0.03; 0.01] 0.292
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular SAE, n (%)	6 (3.7)	7 (4.0)	0.89 [0.27; 2.95] 0.845	0.90 [0.31; 2.63] 0.844	-0.00 [-0.05; 0.04] 0.843

	Treatment Groups		Comparison		
Any serious ocular adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.495**					
KESTREL					
Interaction Test:	p = 0.955				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular SAE, n (%)	3 (2.9)	3 (3.2)	0.89 [0.18; 4.53] 0.889	0.89 [0.18; 4.32] 0.889	-0.00 [-0.05; 0.04] 0.890
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular SAE, n (%)	6 (7.1)	7 (7.4)	0.94 [0.30; 2.93] 0.920	0.95 [0.33; 2.71] 0.920	-0.00 [-0.08; 0.07] 0.920
KITE					
Interaction Test:	p = 0.747				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular SAE, n (%)	1 (1.0)	1 (1.0)	1.02 [0.06; 16.54] 0.989	1.02 [0.06; 16.08] 0.989	0.00 [-0.03; 0.03] 0.989
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular SAE, n (%)	5 (6.3)	3 (3.8)	1.71 [0.39; 7.42] 0.473	1.67 [0.41; 6.74] 0.474	0.03 [-0.04; 0.09] 0.467
Pooled Analysis					
Interaction Test:	p = 0.767				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular SAE, n (%)	4 (2.0)	4 (2.1)	1.00 [0.24; 4.11] 0.996	0.92 [0.24; 3.63] 0.910	-0.00 [-0.03; 0.03] 0.910

	Treatment Groups		Comparison		
Any serious ocular adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular SAE, n (%)	11 (6.7)	10 (5.8)	1.28 [0.51; 3.23] 0.599	1.17 [0.51; 2.69] 0.710	0.01 [-0.04; 0.06] 0.709

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE: logit(proportion) = treatment [by age].

Table 13-2.3 Any serious ocular adverse event by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.096**					
KESTREL					
Interaction Test:	N.E.				
Male					
N'/N	110 / 110	126 / 126			
Any ocular SAE, n (%)	2 (1.8)	5 (4.0)	0.45 [0.09; 2.36] 0.343	0.46 [0.09; 2.31] 0.345	-0.02 [-0.06; 0.02] 0.319
Female					
N'/N	79 / 79	61 / 61			
Any ocular SAE, n (%)	0 (0.0)	2 (3.3)	N.E.	0.16 [0.01; 3.17] 0.226	-0.03 [-0.08; 0.01] 0.150
KITE					
Interaction Test:	p = 0.769				
Male					
N'/N	120 / 120	115 / 115			
Any ocular SAE, n (%)	3 (2.5)	2 (1.7)	1.45 [0.24; 8.83] 0.688	1.44 [0.24; 8.45] 0.688	0.01 [-0.03; 0.04] 0.685
Female					
N'/N	59 / 59	66 / 66			
Any ocular SAE, n (%)	2 (3.4)	1 (1.5)	2.28 [0.20; 25.82] 0.505	2.24 [0.21; 24.04] 0.506	0.02 [-0.04; 0.07] 0.502
Pooled Analysis					
Interaction Test:	p = 0.893				
Male					
N'/N	230 / 230	241 / 241			
Any ocular SAE, n (%)	5 (2.2)	7 (2.9)	0.71 [0.20; 2.50] 0.593	0.76 [0.24; 2.39] 0.633	-0.01 [-0.04; 0.02] 0.630

	Treatment Groups		Comparison		
Any serious ocular adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any ocular SAE, n (%)	2 (1.4)	3 (2.4)	0.61 [0.10; 3.86] 0.601	0.68 [0.15; 3.13] 0.616	-0.01 [-0.04; 0.03] 0.636
Any ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.495**					
KESTREL					
Interaction Test:	p = 0.806				
Male					
N'/N	110 / 110	126 / 126			
Any ocular SAE, n (%)	5 (4.5)	7 (5.6)	0.81 [0.25; 2.63] 0.725	0.82 [0.27; 2.50] 0.725	-0.01 [-0.07; 0.05] 0.723
Female					
N'/N	79 / 79	61 / 61			
Any ocular SAE, n (%)	4 (5.1)	3 (4.9)	1.03 [0.22; 4.79] 0.969	1.03 [0.24; 4.43] 0.969	0.00 [-0.07; 0.07] 0.969
KITE					
Interaction Test:	p = 0.898				
Male					
N'/N	120 / 120	115 / 115			
Any ocular SAE, n (%)	3 (2.5)	2 (1.7)	1.45 [0.24; 8.83] 0.688	1.44 [0.24; 8.45] 0.688	0.01 [-0.03; 0.04] 0.685
Female					
N'/N	59 / 59	66 / 66			
Any ocular SAE, n (%)	3 (5.1)	2 (3.0)	1.71 [0.28; 10.63] 0.562	1.68 [0.29; 9.70] 0.563	0.02 [-0.05; 0.09] 0.563
Pooled Analysis					
Interaction Test:	p = 0.728				
Male					
N'/N	230 / 230	241 / 241			
Any ocular SAE, n (%)	8 (3.5)	9 (3.7)	1.03 [0.38; 2.81] 0.954	0.97 [0.38; 2.47] 0.942	-0.00 [-0.03; 0.03] 0.942

	Treatment Groups		Comparison		
Any serious ocular adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any ocular SAE, n (%)	7 (5.1)	5 (3.9)	1.35 [0.41; 4.50] 0.624	1.26 [0.41; 3.84] 0.683	0.01 [-0.04; 0.06] 0.682

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL: logit(proportion) = treatment [by gender].

Table 13-2.4 Any serious ocular adverse event by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.096**					
KESTREL					
Interaction Test:	N.E.				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any ocular SAE, n (%)	2 (2.7)	5 (7.8)	0.33 [0.06; 1.75] 0.192	0.35 [0.07; 1.72] 0.195	-0.05 [-0.13; 0.02] 0.184
> 65 letters					
N'/N	115 / 115	123 / 123			
Any ocular SAE, n (%)	0 (0.0)	2 (1.6)	N.E.	0.21 [0.01; 4.41] 0.318	-0.02 [-0.04; 0.01] 0.154
KITE					
Interaction Test:	p = 0.434				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any ocular SAE, n (%)	4 (6.2)	2 (2.2)	2.92 [0.52; 16.43] 0.225	2.80 [0.53; 14.83] 0.226	0.04 [-0.03; 0.11] 0.238
> 65 letters					
N'/N	114 / 114	90 / 90			
Any ocular SAE, n (%)	1 (0.9)	1 (1.1)	0.79 [0.05; 12.77] 0.867	0.79 [0.05; 12.45] 0.867	-0.00 [-0.03; 0.03] 0.868
Pooled Analysis					
Interaction Test:	p = 0.439				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any ocular SAE, n (%)	6 (4.3)	7 (4.5)	0.88 [0.27; 2.89] 0.833	0.93 [0.34; 2.56] 0.885	-0.00 [-0.05; 0.05] 0.888

	Treatment Groups		Comparison		
Any serious ocular adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any ocular SAE, n (%)	1 (0.4)	3 (1.4)	0.32 [0.03; 3.36] 0.344	0.40 [0.06; 2.80] 0.336	-0.01 [-0.03; 0.01] 0.276
Any ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.495**					
KESTREL					
Interaction Test:	p = 0.656				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any ocular SAE, n (%)	5 (6.8)	6 (9.4)	0.70 [0.20; 2.41] 0.573	0.72 [0.23; 2.25] 0.573	-0.03 [-0.12; 0.07] 0.575
> 65 letters					
N'/N	115 / 115	123 / 123			
Any ocular SAE, n (%)	4 (3.5)	4 (3.3)	1.07 [0.26; 4.39] 0.923	1.07 [0.27; 4.18] 0.923	0.00 [-0.04; 0.05] 0.923
KITE					
Interaction Test:	p = 0.481				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any ocular SAE, n (%)	5 (7.7)	3 (3.3)	2.44 [0.56; 10.62] 0.233	2.33 [0.58; 9.42] 0.234	0.04 [-0.03; 0.12] 0.247
> 65 letters					
N'/N	114 / 114	90 / 90			
Any ocular SAE, n (%)	1 (0.9)	1 (1.1)	0.79 [0.05; 12.77] 0.867	0.79 [0.05; 12.45] 0.867	-0.00 [-0.03; 0.03] 0.868
Pooled Analysis					
Interaction Test:	p = 0.886				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any ocular SAE, n (%)	10 (7.2)	9 (5.8)	1.27 [0.49; 3.29] 0.629	1.17 [0.50; 2.73] 0.714	0.01 [-0.05; 0.07] 0.719

	Treatment Groups		Comparison		
Any serious ocular adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any ocular SAE, n (%)	5 (2.2)	5 (2.3)	1.13 [0.31; 4.15] 0.857	1.01 [0.30; 3.41] 0.991	0.00 [-0.03; 0.03] 0.991

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL: logit(proportion) = treatment [by BCVA].

Table 13-2.5 Any serious ocular adverse event by region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.495**					
KESTREL					
Interaction Test:	N.E.				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular SAE, n (%)	7 (7.8)	6 (7.2)	1.08 [0.35; 3.36] 0.891	1.08 [0.38; 3.07] 0.891	0.01 [-0.07; 0.08] 0.891
European Region					
N'/N	69 / 69	75 / 75			
Any ocular SAE, n (%)	2 (2.9)	2 (2.7)	1.09 [0.15; 7.95] 0.933	1.09 [0.16; 7.51] 0.933	0.00 [-0.05; 0.06] 0.933
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any ocular SAE, n (%)	0 (0.0)	2 (6.9)	N.E.	0.19 [0.01; 3.87] 0.282	-0.07 [-0.16; 0.02] 0.143
KITE					
Interaction Test:	N.E.				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular SAE, n (%)	2 (7.7)	2 (9.5)	0.79 [0.10; 6.15] 0.823	0.81 [0.12; 5.26] 0.823	-0.02 [-0.18; 0.14] 0.825
European Region					
N'/N	135 / 135	132 / 132			
Any ocular SAE, n (%)	4 (3.0)	2 (1.5)	1.98 [0.36; 11.02] 0.433	1.96 [0.36; 10.50] 0.434	0.01 [-0.02; 0.05] 0.423
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any ocular SAE, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any serious ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	N.E.				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular SAE, n (%)	7 (7.8)	6 (7.2)	N.E.	1.08 [0.38; 3.07] 0.891	0.01 [-0.07; 0.08] 0.891
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular SAE, n (%)	2 (7.7)	2 (9.5)	N.E.	0.81 [0.12; 5.26] 0.825	-0.02 [-0.18; 0.14] 0.825
European Region					
N'/N	204 / 204	207 / 207			
Any ocular SAE, n (%)	6 (2.9)	4 (1.9)	1.46 [0.39; 5.45] 0.572	1.53 [0.44; 5.38] 0.502	0.01 [-0.02; 0.04] 0.501
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any ocular SAE, n (%)	0 (0.0)	2 (3.5)	N.E.	0.19 [0.01; 3.87] 0.229	-0.04 [-0.09; 0.01] 0.128

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by region].
Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by region].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 13-2.6 Any serious ocular adverse event by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.096**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular SAE, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular SAE, n (%)	2 (1.1)	7 (3.9)	0.28 [0.06; 1.39] 0.120	0.29 [0.06; 1.39] 0.122	-0.03 [-0.06; 0.00] 0.095
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular SAE, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular SAE, n (%)	5 (3.1)	3 (1.7)	1.84 [0.43; 7.82] 0.410	1.81 [0.44; 7.46] 0.410	0.01 [-0.02; 0.05] 0.408
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular SAE, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular SAE, n (%)	7 (2.1)	10 (2.8)	0.71 [0.24; 2.08] 0.532	0.74 [0.29; 1.91] 0.529	-0.01 [-0.03; 0.02] 0.529
Any ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.495**					

	Treatment Groups		Comparison		
Any serious ocular adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular SAE, n (%)	0 (0.0)	1 (16.7)	N.E.	0.18 [0.01; 3.85] 0.272	-0.17 [-0.46; 0.13] 0.273
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular SAE, n (%)	9 (5.1)	9 (5.0)	1.02 [0.40; 2.64] 0.961	1.02 [0.42; 2.52] 0.961	0.00 [-0.04; 0.05] 0.961
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular SAE, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular SAE, n (%)	6 (3.8)	4 (2.3)	1.66 [0.46; 5.98] 0.441	1.63 [0.47; 5.68] 0.442	0.01 [-0.02; 0.05] 0.441
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular SAE, n (%)	0 (0.0)	1 (7.7)	N.E.	0.18 [0.01; 3.85] 0.223	-0.07 [-0.22; 0.07] 0.313

	Treatment Groups		Comparison		
Any serious ocular adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular SAE, n (%)	15 (4.5)	13 (3.7)	1.30 [0.59; 2.86] 0.522	1.21 [0.58; 2.49] 0.613	0.01 [-0.02; 0.04] 0.614

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE, Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by diabetes type].
Week 52 / Pooled Analysis, Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 13-2.7 Any serious ocular adverse event by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.096**					
KESTREL					
Interaction Test:	N.E.				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any ocular SAE, n (%)	2 (2.6)	1 (0.9)	2.86 [0.26; 32.18] 0.394	2.82 [0.26; 30.50] 0.394	0.02 [-0.02; 0.06] 0.410
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any ocular SAE, n (%)	0 (0.0)	6 (7.5)	N.E.	0.06 [0.00; 0.96] 0.047 *	-0.08 [-0.13; -0.02] 0.011 *
KITE					
Interaction Test:	N.E.				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any ocular SAE, n (%)	4 (4.9)	0 (0.0)	N.E.	10.52 [0.57; 192.50] 0.113	0.05 [0.00; 0.10] 0.040 *
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any ocular SAE, n (%)	1 (1.0)	3 (3.5)	0.28 [0.03; 2.79] 0.281	0.29 [0.03; 2.76] 0.282	-0.02 [-0.07; 0.02] 0.267
Pooled Analysis					
Interaction Test:	p = 0.003 *				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any ocular SAE, n (%)	6 (3.8)	1 (0.5)	7.99 [0.90; 71.02] 0.062	5.57 [0.92; 33.51] 0.034 *	0.03 [0.00; 0.06] 0.039 *

	Treatment Groups		Comparison		
Any serious ocular adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any ocular SAE, n (%)	1 (0.5)	9 (5.5)	0.08 [0.01; 0.69] 0.021 *	0.13 [0.02; 0.67] 0.004 *	-0.05 [-0.09; -0.01] 0.007 *
Any ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.495**					
KESTREL					
Interaction Test:	p = 0.045 *				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any ocular SAE, n (%)	4 (5.3)	2 (1.9)	2.92 [0.52; 16.35] 0.224	2.82 [0.53; 14.98] 0.225	0.03 [-0.02; 0.09] 0.238
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any ocular SAE, n (%)	4 (3.6)	8 (10.0)	0.33 [0.10; 1.15] 0.082	0.36 [0.11; 1.15] 0.083	-0.06 [-0.14; 0.01] 0.089
KITE					
Interaction Test:	N.E.				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any ocular SAE, n (%)	5 (6.1)	0 (0.0)	N.E.	12.86 [0.72; 229.05] 0.082	0.06 [0.01; 0.11] 0.021 *
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any ocular SAE, n (%)	1 (1.0)	4 (4.7)	0.21 [0.02; 1.93] 0.168	0.22 [0.02; 1.92] 0.171	-0.04 [-0.09; 0.01] 0.144
Pooled Analysis					
Interaction Test:	p = 0.002 *				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any ocular SAE, n (%)	9 (5.7)	2 (1.0)	6.95 [1.44; 33.58] 0.016 *	5.00 [1.23; 20.35] 0.012 *	0.05 [0.01; 0.09] 0.016 *

	Treatment Groups		Comparison		
Any serious ocular adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any ocular SAE, n (%)	5 (2.4)	12 (7.3)	0.33 [0.11; 1.00] 0.049 *	0.31 [0.11; 0.88] 0.019 *	-0.05 [-0.10; -0.01] 0.026 *

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE, Week 100 / KITE: logit(proportion) = treatment [by HbA1c].

Table 13-2.8 Any serious ocular adverse event by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.495**					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any ocular SAE, n (%)	7 (5.8)	6 (5.5)	1.07 [0.35; 3.30] 0.901	1.07 [0.37; 3.08] 0.901	0.00 [-0.06; 0.06] 0.901
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any ocular SAE, n (%)	2 (6.7)	3 (7.7)	0.86 [0.13; 5.48] 0.871	0.87 [0.15; 4.86] 0.871	-0.01 [-0.13; 0.11] 0.869
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any ocular SAE, n (%)	0 (0.0)	1 (2.6)	N.E.	0.33 [0.01; 7.74] 0.487	-0.03 [-0.08; 0.02] 0.311
KITE					
Interaction Test:	p = 0.902				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any ocular SAE, n (%)	2 (2.4)	1 (1.1)	2.19 [0.20; 24.63] 0.525	2.16 [0.20; 23.44] 0.525	0.01 [-0.03; 0.05] 0.520
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any ocular SAE, n (%)	3 (5.9)	2 (4.1)	1.47 [0.23; 9.19] 0.681	1.44 [0.25; 8.26] 0.682	0.02 [-0.07; 0.10] 0.678
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any ocular SAE, n (%)	1 (2.3)	1 (2.5)	0.93 [0.06; 15.36] 0.959	0.93 [0.06; 14.38] 0.959	-0.00 [-0.07; 0.06] 0.959

	Treatment Groups		Comparison		
Any serious ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.753				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any ocular SAE, n (%)	9 (4.4)	7 (3.5)	1.39 [0.48; 4.03] 0.542	1.22 [0.47; 3.17] 0.691	0.01 [-0.03; 0.05] 0.690
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any ocular SAE, n (%)	5 (6.2)	5 (5.7)	1.18 [0.32; 4.31] 0.803	1.12 [0.33; 3.78] 0.857	0.01 [-0.06; 0.08] 0.856
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any ocular SAE, n (%)	1 (1.2)	2 (2.6)	0.51 [0.04; 5.79] 0.585	0.57 [0.08; 4.25] 0.581	-0.01 [-0.06; 0.03] 0.529

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL: logit(proportion) = treatment [by duration of DME].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 13-2.9 Any serious ocular adverse event by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.096**					
KESTREL					
Interaction Test:	N.E.				
focal					
N'/N	59 / 59	48 / 48			
Any ocular SAE, n (%)	0 (0.0)	1 (2.1)	N.E.	0.27 [0.01; 6.53] 0.422	-0.02 [-0.06; 0.02] 0.312
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular SAE, n (%)	2 (1.6)	6 (4.5)	0.34 [0.07; 1.72] 0.193	0.35 [0.07; 1.71] 0.195	-0.03 [-0.07; 0.01] 0.167
KITE					
Interaction Test:	N.E.				
focal					
N'/N	63 / 63	66 / 66			
Any ocular SAE, n (%)	3 (4.8)	2 (3.0)	1.60 [0.26; 9.91] 0.613	1.57 [0.27; 9.09] 0.614	0.02 [-0.05; 0.08] 0.612
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular SAE, n (%)	2 (1.7)	0 (0.0)	N.E.	4.74 [0.23; 97.66] 0.313	0.02 [-0.01; 0.04] 0.154
Pooled Analysis					
Interaction Test:	p = 0.885				
focal					
N'/N	122 / 122	114 / 114			
Any ocular SAE, n (%)	3 (2.5)	3 (2.6)	0.88 [0.16; 4.83] 0.883	0.98 [0.23; 4.08] 0.974	0.00 [-0.04; 0.04] 0.996

	Treatment Groups		Comparison		
Any serious ocular adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular SAE, n (%)	4 (1.7)	6 (2.5)	0.76 [0.18; 3.09] 0.696	0.71 [0.21; 2.36] 0.569	-0.01 [-0.03; 0.02] 0.554
Any ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.495**					
KESTREL					
Interaction Test:	p = 0.910				
focal					
N'/N	59 / 59	48 / 48			
Any ocular SAE, n (%)	2 (3.4)	2 (4.2)	0.81 [0.11; 5.95] 0.833	0.81 [0.12; 5.56] 0.833	-0.01 [-0.08; 0.07] 0.835
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular SAE, n (%)	7 (5.5)	8 (6.0)	0.92 [0.32; 2.61] 0.874	0.92 [0.34; 2.47] 0.874	-0.00 [-0.06; 0.05] 0.874
KITE					
Interaction Test:	p = 0.933				
focal					
N'/N	63 / 63	66 / 66			
Any ocular SAE, n (%)	4 (6.3)	2 (3.0)	2.17 [0.38; 12.28] 0.381	2.10 [0.40; 11.04] 0.383	0.03 [-0.04; 0.11] 0.373
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular SAE, n (%)	2 (1.7)	1 (0.9)	1.91 [0.17; 21.39] 0.599	1.90 [0.17; 20.61] 0.599	0.01 [-0.02; 0.04] 0.590
Pooled Analysis					
Interaction Test:	p = 0.790				
focal					
N'/N	122 / 122	114 / 114			
Any ocular SAE, n (%)	6 (4.9)	4 (3.5)	1.50 [0.40; 5.62] 0.547	1.42 [0.42; 4.82] 0.577	0.01 [-0.04; 0.07] 0.576

	Treatment Groups		Comparison		
Any serious ocular adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular SAE, n (%)	9 (3.7)	9 (3.7)	1.21 [0.43; 3.35] 0.719	1.04 [0.42; 2.56] 0.938	0.00 [-0.03; 0.03] 0.938

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE: logit(proportion) = treatment [by DME type].

Table 13-2.10 Any serious ocular adverse event by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.495**					
KESTREL					
Interaction Test:	p = 0.765				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any ocular SAE, n (%)	5 (4.7)	5 (5.2)	0.89 [0.25; 3.18] 0.860	0.90 [0.27; 3.00] 0.860	-0.01 [-0.07; 0.05] 0.861
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any ocular SAE, n (%)	3 (4.3)	2 (2.8)	1.54 [0.25; 9.54] 0.640	1.52 [0.26; 8.83] 0.640	0.01 [-0.05; 0.08] 0.637
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any ocular SAE, n (%)	1 (8.3)	3 (15.0)	0.52 [0.05; 5.60] 0.586	0.56 [0.06; 4.76] 0.592	-0.07 [-0.29; 0.15] 0.555
KITE					
Interaction Test:	N.E.				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any ocular SAE, n (%)	3 (3.5)	2 (2.4)	1.46 [0.24; 8.99] 0.681	1.45 [0.25; 8.44] 0.681	0.01 [-0.04; 0.06] 0.678
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any ocular SAE, n (%)	1 (1.4)	2 (2.5)	0.53 [0.05; 5.94] 0.605	0.53 [0.05; 5.76] 0.605	-0.01 [-0.06; 0.03] 0.595
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any ocular SAE, n (%)	2 (10.0)	0 (0.0)	N.E.	4.76 [0.24; 93.19] 0.304	0.10 [-0.03; 0.23] 0.136

	Treatment Groups		Comparison		
Any serious ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.972				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any ocular SAE, n (%)	8 (4.2)	7 (3.9)	1.14 [0.39; 3.37] 0.808	1.05 [0.39; 2.83] 0.923	0.00 [-0.04; 0.04] 0.922
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any ocular SAE, n (%)	4 (2.8)	4 (2.7)	1.10 [0.26; 4.55] 0.900	1.03 [0.26; 4.07] 0.962	0.00 [-0.04; 0.04] 0.962
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any ocular SAE, n (%)	3 (9.4)	3 (7.7)	1.41 [0.26; 7.67] 0.693	1.34 [0.29; 6.20] 0.711	0.03 [-0.10; 0.16] 0.675

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KITE: logit(proportion) = treatment [by CSFT].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 13-2.11 Any serious ocular adverse event by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.096**					
KESTREL					
Interaction Test:	N.E.				
presence					
N'/N	62 / 62	61 / 61			
Any ocular SAE, n (%)	0 (0.0)	3 (4.9)	N.E.	0.14 [0.01; 2.67] 0.191	-0.05 [-0.10; 0.01] 0.076
absence					
N'/N	127 / 127	126 / 126			
Any ocular SAE, n (%)	2 (1.6)	4 (3.2)	0.49 [0.09; 2.71] 0.412	0.50 [0.09; 2.66] 0.413	-0.02 [-0.05; 0.02] 0.403
KITE					
Interaction Test:	p = 0.366				
presence					
N'/N	56 / 56	67 / 67			
Any ocular SAE, n (%)	3 (5.4)	1 (1.5)	3.74 [0.38; 36.96] 0.260	3.59 [0.38; 33.55] 0.262	0.04 [-0.03; 0.10] 0.249
absence					
N'/N	123 / 123	114 / 114			
Any ocular SAE, n (%)	2 (1.6)	2 (1.8)	0.93 [0.13; 6.68] 0.939	0.93 [0.13; 6.47] 0.939	-0.00 [-0.03; 0.03] 0.939
Pooled Analysis					
Interaction Test:	p = 0.827				
presence					
N'/N	118 / 118	128 / 128			
Any ocular SAE, n (%)	3 (2.5)	4 (3.1)	0.77 [0.16; 3.74] 0.749	0.85 [0.22; 3.24] 0.809	-0.01 [-0.05; 0.04] 0.802

	Treatment Groups		Comparison		
Any serious ocular adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular SAE, n (%)	4 (1.6)	6 (2.5)	0.62 [0.16; 2.42] 0.491	0.64 [0.18; 2.26] 0.488	-0.01 [-0.03; 0.02] 0.488
Any ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.495**					
KESTREL					
Interaction Test:	p = 0.394				
presence					
N'/N	62 / 62	61 / 61			
Any ocular SAE, n (%)	2 (3.2)	4 (6.6)	0.48 [0.08; 2.69] 0.401	0.49 [0.09; 2.59] 0.402	-0.03 [-0.11; 0.04] 0.391
absence					
N'/N	127 / 127	126 / 126			
Any ocular SAE, n (%)	7 (5.5)	6 (4.8)	1.17 [0.38; 3.57] 0.787	1.16 [0.40; 3.35] 0.787	0.01 [-0.05; 0.06] 0.787
KITE					
Interaction Test:	p = 0.330				
presence					
N'/N	56 / 56	67 / 67			
Any ocular SAE, n (%)	3 (5.4)	1 (1.5)	3.74 [0.38; 36.97] 0.260	3.59 [0.38; 33.55] 0.262	0.04 [-0.03; 0.10] 0.249
absence					
N'/N	123 / 123	114 / 114			
Any ocular SAE, n (%)	3 (2.4)	3 (2.6)	0.93 [0.18; 4.68] 0.925	0.93 [0.19; 4.50] 0.925	-0.00 [-0.04; 0.04] 0.925
Pooled Analysis					
Interaction Test:	p = 0.969				
presence					
N'/N	118 / 118	128 / 128			
Any ocular SAE, n (%)	5 (4.2)	5 (3.9)	1.14 [0.31; 4.13] 0.844	1.06 [0.32; 3.50] 0.921	0.00 [-0.05; 0.05] 0.922

	Treatment Groups		Comparison		
Any serious ocular adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular SAE, n (%)	10 (4.0)	9 (3.8)	1.17 [0.45; 3.06] 0.743	1.08 [0.45; 2.60] 0.866	0.00 [-0.03; 0.04] 0.866

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL: logit(proportion) = treatment [by status of SRF].

Table 13-2.12 Any serious ocular adverse event by exposure (week 52) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.096**					
KESTREL					
Interaction Test:	p = 0.527				
Non-exposed					
N'/N	71 / 71	75 / 75			
Any ocular SAE, n (%)	1 (1.4)	2 (2.7)	0.52 [0.05; 5.88] 0.598	0.53 [0.05; 5.70] 0.599	-0.01 [-0.06; 0.03] 0.589
Exposed					
N'/N	118 / 118	112 / 112			
Any ocular SAE, n (%)	1 (0.8)	5 (4.5)	0.18 [0.02; 1.59] 0.124	0.19 [0.02; 1.60] 0.127	-0.04 [-0.08; 0.01] 0.089
KITE					
Interaction Test:	N.E.				
Non-exposed					
N'/N	85 / 85	90 / 90			
Any ocular SAE, n (%)	4 (4.7)	3 (3.3)	1.43 [0.31; 6.59] 0.645	1.41 [0.33; 6.12] 0.645	0.01 [-0.04; 0.07] 0.645
Exposed					
N'/N	94 / 94	91 / 91			
Any ocular SAE, n (%)	1 (1.1)	0 (0.0)	N.E.	2.91 [0.12; 70.41] 0.512	0.01 [-0.01; 0.03] 0.315
Pooled Analysis					
Interaction Test:	p = 0.413				
Non-exposed					
N'/N	156 / 156	165 / 165			
Any ocular SAE, n (%)	5 (3.2)	5 (3.0)	0.96 [0.25; 3.68] 0.957	1.06 [0.31; 3.58] 0.928	0.00 [-0.04; 0.04] 0.928

	Treatment Groups		Comparison		
Any serious ocular adverse event by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	212 / 212	203 / 203			
Any ocular SAE, n (%)	2 (0.9)	5 (2.5)	0.40 [0.07; 2.22] 0.296	0.43 [0.10; 1.91] 0.255	-0.02 [-0.04; 0.01] 0.231

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KITE: logit(proportion) = treatment [by exposure (week 52)].

Table 13-2.13 Any serious ocular adverse event by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.495**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any ocular SAE, n (%)	0 (0.0)	1 (7.7)	N.E.	0.36 [0.02; 8.05] 0.519	-0.08 [-0.22; 0.07] 0.298
Exposed					
N'/N	177 / 177	174 / 174			
Any ocular SAE, n (%)	9 (5.1)	9 (5.2)	0.98 [0.38; 2.54] 0.970	0.98 [0.40; 2.42] 0.970	-0.00 [-0.05; 0.05] 0.970
KITE					
Interaction Test:	p = 0.975				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any ocular SAE, n (%)	2 (11.8)	1 (8.3)	1.47 [0.12; 18.30] 0.766	1.41 [0.14; 13.86] 0.767	0.03 [-0.18; 0.25] 0.759
Exposed					
N'/N	162 / 162	169 / 169			
Any ocular SAE, n (%)	4 (2.5)	3 (1.8)	1.40 [0.31; 6.36] 0.662	1.39 [0.32; 6.12] 0.662	0.01 [-0.02; 0.04] 0.662
Pooled Analysis					
Interaction Test:	p = 0.852				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any ocular SAE, n (%)	2 (6.9)	2 (8.0)	0.96 [0.12; 7.49] 0.966	0.83 [0.14; 4.77] 0.837	-0.02 [-0.16; 0.12] 0.799

	Treatment Groups		Comparison		
Any serious ocular adverse event by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any ocular SAE, n (%)	13 (3.8)	12 (3.5)	1.18 [0.51; 2.73] 0.701	1.08 [0.50; 2.33] 0.839	0.00 [-0.03; 0.03] 0.839

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL: logit(proportion) = treatment [by exposure (week 100)].

Table 13-3.1 Any serious ocular adverse event at the study eye (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the study eye, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular SAE at the study eye, n (%)	2 (1.1)	4 (2.1)	0.49 [0.09; 2.70] 0.413	0.49 [0.09; 2.67] 0.413	-0.01 [-0.04; 0.01] 0.403
KITE, N'/N	179 / 179	181 / 181			
Any ocular SAE at the study eye, n (%)	4 (2.2)	3 (1.7)	1.36 [0.30; 6.15] 0.693	1.35 [0.31; 5.94] 0.693	0.01 [-0.02; 0.03] 0.692
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular SAE at the study eye, n (%) p_H=0.381	6 (1.6)	7 (1.9)	0.81 [0.26; 2.53] 0.712	0.86 [0.29; 2.53] 0.781	-0.00 [-0.02; 0.02] 0.781
Any ocular SAE at the study eye, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular SAE at the study eye, n (%)	7 (3.7)	5 (2.7)	1.40 [0.44; 4.49] 0.572	1.39 [0.45; 4.29] 0.572	0.01 [-0.03; 0.05] 0.570
KITE, N'/N	179 / 179	181 / 181			
Any ocular SAE at the study eye, n (%)	5 (2.8)	3 (1.7)	1.70 [0.40; 7.24] 0.470	1.69 [0.41; 6.95] 0.470	0.01 [-0.02; 0.04] 0.465

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular SAE at the study eye, n (%) p_H=0.835	12 (3.3)	8 (2.2)	1.54 [0.61; 3.89] 0.359	1.50 [0.62; 3.62] 0.367	0.01 [-0.01; 0.03] 0.366

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-3.2 Any serious ocular adverse event at the study eye by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.381**					
KESTREL					
Interaction Test:	N.E.				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular SAE at the study eye, n (%)	0 (0.0)	2 (2.2)	N.E.	0.18 [0.01; 3.68] 0.265	-0.02 [-0.05; 0.01] 0.153
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular SAE at the study eye, n (%)	2 (2.4)	2 (2.1)	1.11 [0.15; 8.05] 0.919	1.11 [0.16; 7.68] 0.919	0.00 [-0.04; 0.05] 0.919
KITE					
Interaction Test:	N.E.				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular SAE at the study eye, n (%)	1 (1.0)	0 (0.0)	N.E.	3.06 [0.13; 74.22] 0.492	0.01 [-0.01; 0.03] 0.315
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular SAE at the study eye, n (%)	3 (3.8)	3 (3.8)	1.00 [0.20; 5.11] 1.000	1.00 [0.21; 4.80] 1.000	0.00 [-0.06; 0.06] 1.000
Pooled Analysis					
Interaction Test:	p = 0.554				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular SAE at the study eye, n (%)	1 (0.5)	2 (1.0)	0.44 [0.04; 5.01] 0.509	0.63 [0.11; 3.64] 0.606	-0.01 [-0.02; 0.01] 0.534

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular SAE at the study eye, n (%)	5 (3.0)	5 (2.9)	1.00 [0.27; 3.67] 0.998	1.04 [0.31; 3.52] 0.949	0.00 [-0.04; 0.04] 0.948
Any ocular SAE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.835**					
KESTREL					
Interaction Test:	p = 0.932				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular SAE at the study eye, n (%)	3 (2.9)	2 (2.2)	1.35 [0.22; 8.27] 0.745	1.34 [0.23; 7.85] 0.745	0.01 [-0.04; 0.05] 0.742
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular SAE at the study eye, n (%)	4 (4.7)	3 (3.2)	1.50 [0.33; 6.89] 0.604	1.47 [0.34; 6.40] 0.604	0.02 [-0.04; 0.07] 0.605
KITE					
Interaction Test:	N.E.				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular SAE at the study eye, n (%)	1 (1.0)	0 (0.0)	N.E.	3.06 [0.13; 74.22] 0.492	0.01 [-0.01; 0.03] 0.315
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular SAE at the study eye, n (%)	4 (5.1)	3 (3.8)	1.35 [0.29; 6.24] 0.700	1.33 [0.31; 5.76] 0.700	0.01 [-0.05; 0.08] 0.699
Pooled Analysis					
Interaction Test:	p = 0.788				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular SAE at the study eye, n (%)	4 (2.0)	2 (1.0)	1.93 [0.35; 10.69] 0.454	1.67 [0.36; 7.65] 0.507	0.01 [-0.01; 0.03] 0.472

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular SAE at the study eye, n (%)	8 (4.9)	6 (3.5)	1.46 [0.49; 4.38] 0.501	1.40 [0.50; 3.95] 0.522	0.01 [-0.03; 0.06] 0.522

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE, Week 100 / KITE: logit(proportion) = treatment [by age].

Table 13-3.3 Any serious ocular adverse event at the study eye by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.835**					
KESTREL					
Interaction Test:	p = 0.159				
Male					
N'/N	110 / 110	126 / 126			
Any ocular SAE at the study eye, n (%)	5 (4.5)	2 (1.6)	2.95 [0.56; 15.53] 0.201	2.86 [0.57; 14.47] 0.203	0.03 [-0.02; 0.07] 0.194
Female					
N'/N	79 / 79	61 / 61			
Any ocular SAE at the study eye, n (%)	2 (2.5)	3 (4.9)	0.50 [0.08; 3.10] 0.459	0.51 [0.09; 2.99] 0.459	-0.02 [-0.09; 0.04] 0.468
KITE					
Interaction Test:	p = 0.403				
Male					
N'/N	120 / 120	115 / 115			
Any ocular SAE at the study eye, n (%)	2 (1.7)	2 (1.7)	0.96 [0.13; 6.91] 0.966	0.96 [0.14; 6.69] 0.966	-0.00 [-0.03; 0.03] 0.966
Female					
N'/N	59 / 59	66 / 66			
Any ocular SAE at the study eye, n (%)	3 (5.1)	1 (1.5)	3.48 [0.35; 34.43] 0.286	3.36 [0.36; 31.39] 0.289	0.04 [-0.03; 0.10] 0.269
Pooled Analysis					
Interaction Test:	p = 0.575				
Male					
N'/N	230 / 230	241 / 241			
Any ocular SAE at the study eye, n (%)	7 (3.0)	4 (1.7)	1.93 [0.55; 6.80] 0.305	1.87 [0.56; 6.22] 0.301	0.01 [-0.01; 0.04] 0.307

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any ocular SAE at the study eye, n (%)	5 (3.6)	4 (3.1)	1.14 [0.30; 4.43] 0.845	1.13 [0.33; 3.96] 0.844	0.00 [-0.04; 0.05] 0.846

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 13-3.4 Any serious ocular adverse event at the study eye by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.381**					
KESTREL					
Interaction Test:	N.E.				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any ocular SAE at the study eye, n (%)	2 (2.7)	4 (6.3)	0.42 [0.07; 2.35] 0.322	0.43 [0.08; 2.28] 0.323	-0.04 [-0.11; 0.03] 0.320
> 65 letters					
N'/N	115 / 115	123 / 123			
Any ocular SAE at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE					
Interaction Test:	p = 0.553				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any ocular SAE at the study eye, n (%)	3 (4.6)	2 (2.2)	2.15 [0.35; 13.27] 0.408	2.10 [0.36; 12.21] 0.409	0.02 [-0.04; 0.08] 0.424
> 65 letters					
N'/N	114 / 114	90 / 90			
Any ocular SAE at the study eye, n (%)	1 (0.9)	1 (1.1)	0.79 [0.05; 12.77] 0.867	0.79 [0.05; 12.45] 0.867	-0.00 [-0.03; 0.03] 0.868
Pooled Analysis					
Interaction Test:	p = 0.965				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any ocular SAE at the study eye, n (%)	5 (3.6)	6 (3.9)	0.86 [0.25; 2.98] 0.808	0.90 [0.29; 2.76] 0.853	-0.00 [-0.05; 0.04] 0.855
> 65 letters					
N'/N	229 / 229	213 / 213			
Any ocular SAE at the study eye, n (%)	1 (0.4)	1 (0.5)	0.92 [0.05; 15.35] 0.952	0.79 [0.05; 12.45] 0.867	-0.00 [-0.01; 0.01] 0.867

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.835**					
KESTREL					
Interaction Test:	N.E.				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any ocular SAE at the study eye, n (%)	5 (6.8)	5 (7.8)	0.86 [0.24; 3.10] 0.812	0.86 [0.26; 2.85] 0.812	-0.01 [-0.10; 0.08] 0.812
> 65 letters					
N'/N	115 / 115	123 / 123			
Any ocular SAE at the study eye, n (%)	2 (1.7)	0 (0.0)	N.E.	5.34 [0.26; 110.16] 0.278	0.02 [-0.01; 0.04] 0.154
KITE					
Interaction Test:	p = 0.434				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any ocular SAE at the study eye, n (%)	4 (6.2)	2 (2.2)	2.92 [0.52; 16.43] 0.225	2.80 [0.53; 14.83] 0.226	0.04 [-0.03; 0.11] 0.238
> 65 letters					
N'/N	114 / 114	90 / 90			
Any ocular SAE at the study eye, n (%)	1 (0.9)	1 (1.1)	0.79 [0.05; 12.77] 0.867	0.79 [0.05; 12.45] 0.867	-0.00 [-0.03; 0.03] 0.868
Pooled Analysis					
Interaction Test:	p = 0.533				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any ocular SAE at the study eye, n (%)	9 (6.5)	7 (4.5)	1.44 [0.51; 4.03] 0.488	1.32 [0.52; 3.37] 0.556	0.02 [-0.04; 0.07] 0.563

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any ocular SAE at the study eye, n (%)	3 (1.3)	1 (0.5)	3.19 [0.32; 31.87] 0.323	2.16 [0.34; 13.73] 0.401	0.01 [-0.01; 0.03] 0.358

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 100 / KESTREL: logit(proportion) = treatment [by BCVA].

Table 13-3.5 Any serious ocular adverse event at the study eye by region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.835**					
KESTREL					
Interaction Test:	N.E.				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular SAE at the study eye, n (%)	6 (6.7)	4 (4.8)	1.41 [0.38; 5.19] 0.604	1.38 [0.40; 4.73] 0.605	0.02 [-0.05; 0.09] 0.600
European Region					
N'/N	69 / 69	75 / 75			
Any ocular SAE at the study eye, n (%)	1 (1.4)	1 (1.3)	1.09 [0.07; 17.74] 0.953	1.09 [0.07; 17.04] 0.953	0.00 [-0.04; 0.04] 0.953
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any ocular SAE at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE					
Interaction Test:	N.E.				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular SAE at the study eye, n (%)	2 (7.7)	1 (4.8)	1.67 [0.14; 19.76] 0.686	1.62 [0.16; 16.61] 0.687	0.03 [-0.11; 0.17] 0.675
European Region					
N'/N	135 / 135	132 / 132			
Any ocular SAE at the study eye, n (%)	3 (2.2)	2 (1.5)	1.48 [0.24; 8.98] 0.672	1.47 [0.25; 8.64] 0.672	0.01 [-0.03; 0.04] 0.669
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any ocular SAE at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	N.E.				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular SAE at the study eye, n (%)	6 (6.7)	4 (4.8)	N.E.	1.38 [0.40; 4.73] 0.604	0.02 [-0.05; 0.09] 0.600
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular SAE at the study eye, n (%)	2 (7.7)	1 (4.8)	N.E.	1.62 [0.16; 16.61] 0.686	0.03 [-0.11; 0.17] 0.675
European Region					
N'/N	204 / 204	207 / 207			
Any ocular SAE at the study eye, n (%)	4 (2.0)	3 (1.4)	1.26 [0.24; 6.76] 0.784	1.34 [0.30; 5.95] 0.696	0.01 [-0.02; 0.03] 0.695
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any ocular SAE at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by region].
Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by region].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 13-3.6 Any serious ocular adverse event at the study eye by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.381**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular SAE at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular SAE at the study eye, n (%)	2 (1.1)	4 (2.2)	0.51 [0.09; 2.80] 0.435	0.51 [0.09; 2.76] 0.435	-0.01 [-0.04; 0.02] 0.424
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular SAE at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular SAE at the study eye, n (%)	4 (2.5)	3 (1.7)	1.46 [0.32; 6.63] 0.623	1.45 [0.33; 6.38] 0.623	0.01 [-0.02; 0.04] 0.623
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular SAE at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular SAE at the study eye, n (%)	6 (1.8)	7 (2.0)	0.85 [0.27; 2.67] 0.782	0.91 [0.31; 2.66] 0.858	-0.00 [-0.02; 0.02] 0.858

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.835**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular SAE at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular SAE at the study eye, n (%)	7 (4.0)	5 (2.8)	1.45 [0.45; 4.65] 0.533	1.43 [0.46; 4.43] 0.533	0.01 [-0.03; 0.05] 0.531
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular SAE at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular SAE at the study eye, n (%)	5 (3.1)	3 (1.7)	1.84 [0.43; 7.82] 0.410	1.81 [0.44; 7.46] 0.410	0.01 [-0.02; 0.05] 0.408
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular SAE at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular SAE at the study eye, n (%)	12 (3.6)	8 (2.3)	1.63 [0.65; 4.11] 0.302	1.57 [0.65; 3.79] 0.311	0.01 [-0.01; 0.04] 0.313

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE, Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by diabetes type].
Week 52 / Pooled Analysis, Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 13-3.7 Any serious ocular adverse event at the study eye by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.835**					
KESTREL					
Interaction Test:	p = 0.077				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any ocular SAE at the study eye, n (%)	4 (5.3)	1 (0.9)	5.89 [0.64; 53.77] 0.116	5.63 [0.64; 49.40] 0.119	0.04 [-0.01; 0.10] 0.112
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any ocular SAE at the study eye, n (%)	3 (2.7)	4 (5.0)	0.52 [0.11; 2.40] 0.405	0.54 [0.12; 2.33] 0.405	-0.02 [-0.08; 0.03] 0.419
KITE					
Interaction Test:	N.E.				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any ocular SAE at the study eye, n (%)	4 (4.9)	0 (0.0)	N.E.	10.52 [0.57; 192.50] 0.113	0.05 [0.00; 0.10] 0.040 *
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any ocular SAE at the study eye, n (%)	1 (1.0)	3 (3.5)	0.28 [0.03; 2.79] 0.281	0.29 [0.03; 2.76] 0.282	-0.02 [-0.07; 0.02] 0.267
Pooled Analysis					
Interaction Test:	p = 0.009 *				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any ocular SAE at the study eye, n (%)	8 (5.1)	1 (0.5)	11.26 [1.38; 92.16] 0.024 *	7.38 [1.30; 41.98] 0.008 *	0.05 [0.01; 0.08] 0.011 *

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any ocular SAE at the study eye, n (%)	4 (1.9)	7 (4.2)	0.44 [0.12; 1.55] 0.202	0.44 [0.13; 1.48] 0.172	-0.02 [-0.06; 0.01] 0.189

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KITE: logit(proportion) = treatment [by HbA1c].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 13-3.8 Any serious ocular adverse event at the study eye by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.835**					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any ocular SAE at the study eye, n (%)	6 (5.0)	2 (1.8)	2.84 [0.56; 14.39] 0.207	2.75 [0.57; 13.34] 0.209	0.03 [-0.01; 0.08] 0.178
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any ocular SAE at the study eye, n (%)	1 (3.3)	3 (7.7)	0.41 [0.04; 4.19] 0.455	0.43 [0.05; 3.96] 0.459	-0.04 [-0.15; 0.06] 0.418
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any ocular SAE at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE					
Interaction Test:	N.E.				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any ocular SAE at the study eye, n (%)	2 (2.4)	0 (0.0)	N.E.	5.41 [0.26; 111.04] 0.274	0.02 [-0.01; 0.06] 0.152
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any ocular SAE at the study eye, n (%)	2 (3.9)	2 (4.1)	0.96 [0.13; 7.09] 0.967	0.96 [0.14; 6.56] 0.967	-0.00 [-0.08; 0.08] 0.967
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any ocular SAE at the study eye, n (%)	1 (2.3)	1 (2.5)	0.93 [0.06; 15.36] 0.959	0.93 [0.06; 14.38] 0.959	-0.00 [-0.07; 0.06] 0.959

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.230				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any ocular SAE at the study eye, n (%)	8 (3.9)	2 (1.0)	4.24 [0.86; 20.87] 0.075	3.25 [0.81; 13.02] 0.078	0.03 [-0.00; 0.06] 0.063
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any ocular SAE at the study eye, n (%)	3 (3.7)	5 (5.7)	0.66 [0.15; 2.88] 0.579	0.66 [0.16; 2.76] 0.573	-0.02 [-0.08; 0.04] 0.565
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any ocular SAE at the study eye, n (%)	1 (1.2)	1 (1.3)	0.99 [0.06; 16.16] 0.992	0.93 [0.06; 14.38] 0.959	-0.00 [-0.04; 0.03] 0.959

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by duration of DME].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 13-3.9 Any serious ocular adverse event at the study eye by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.835**					
KESTREL					
Interaction Test:	p = 0.662				
focal					
N'/N	59 / 59	48 / 48			
Any ocular SAE at the study eye, n (%)	1 (1.7)	1 (2.1)	0.81 [0.05; 13.30] 0.883	0.81 [0.05; 12.67] 0.883	-0.00 [-0.06; 0.05] 0.884
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular SAE at the study eye, n (%)	6 (4.7)	4 (3.0)	1.61 [0.44; 5.85] 0.468	1.58 [0.46; 5.48] 0.469	0.02 [-0.03; 0.06] 0.467
KITE					
Interaction Test:	N.E.				
focal					
N'/N	63 / 63	66 / 66			
Any ocular SAE at the study eye, n (%)	4 (6.3)	2 (3.0)	2.17 [0.38; 12.28] 0.381	2.10 [0.40; 11.04] 0.383	0.03 [-0.04; 0.11] 0.373
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular SAE at the study eye, n (%)	1 (0.9)	0 (0.0)	N.E.	2.84 [0.12; 69.09] 0.521	0.01 [-0.01; 0.03] 0.315
Pooled Analysis					
Interaction Test:	p = 0.817				
focal					
N'/N	122 / 122	114 / 114			
Any ocular SAE at the study eye, n (%)	5 (4.1)	3 (2.6)	1.61 [0.37; 7.06] 0.525	1.63 [0.41; 6.57] 0.486	0.02 [-0.03; 0.06] 0.485

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular SAE at the study eye, n (%)	7 (2.9)	4 (1.6)	2.03 [0.54; 7.54] 0.293	1.73 [0.55; 5.48] 0.346	0.01 [-0.01; 0.04] 0.320

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KITE: logit(proportion) = treatment [by DME type].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 13-3.10 Any serious ocular adverse event at the study eye by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 13-3.11 Any serious ocular adverse event at the study eye by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.835**					
KESTREL					
Interaction Test:	p = 0.276				
presence					
N'/N	62 / 62	61 / 61			
Any ocular SAE at the study eye, n (%)	2 (3.2)	3 (4.9)	0.64 [0.10; 4.00] 0.637	0.66 [0.11; 3.79] 0.637	-0.02 [-0.09; 0.05] 0.635
absence					
N'/N	127 / 127	126 / 126			
Any ocular SAE at the study eye, n (%)	5 (3.9)	2 (1.6)	2.54 [0.48; 13.34] 0.271	2.48 [0.49; 12.55] 0.272	0.02 [-0.02; 0.06] 0.253
KITE					
Interaction Test:	p = 0.366				
presence					
N'/N	56 / 56	67 / 67			
Any ocular SAE at the study eye, n (%)	3 (5.4)	1 (1.5)	3.74 [0.38; 36.96] 0.260	3.59 [0.38; 33.55] 0.262	0.04 [-0.03; 0.10] 0.249
absence					
N'/N	123 / 123	114 / 114			
Any ocular SAE at the study eye, n (%)	2 (1.6)	2 (1.8)	0.93 [0.13; 6.68] 0.939	0.93 [0.13; 6.47] 0.939	-0.00 [-0.03; 0.03] 0.939
Pooled Analysis					
Interaction Test:	p = 0.793				
presence					
N'/N	118 / 118	128 / 128			
Any ocular SAE at the study eye, n (%)	5 (4.2)	4 (3.1)	1.37 [0.36; 5.29] 0.646	1.33 [0.37; 4.75] 0.655	0.01 [-0.04; 0.06] 0.659

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular SAE at the study eye, n (%)	7 (2.8)	4 (1.7)	1.75 [0.50; 6.18] 0.383	1.69 [0.50; 5.68] 0.390	0.01 [-0.01; 0.04] 0.388

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 13-3.12 Any serious ocular adverse event at the study eye by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 13-3.13 Any serious ocular adverse event at the study eye by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.835**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any ocular SAE at the study eye, n (%)	0 (0.0)	1 (7.7)	N.E.	0.36 [0.02; 8.05] 0.519	-0.08 [-0.22; 0.07] 0.298
Exposed					
N'/N	177 / 177	174 / 174			
Any ocular SAE at the study eye, n (%)	7 (4.0)	4 (2.3)	1.75 [0.50; 6.09] 0.379	1.72 [0.51; 5.77] 0.380	0.02 [-0.02; 0.05] 0.372
KITE					
Interaction Test:	p = 0.964				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any ocular SAE at the study eye, n (%)	2 (11.8)	1 (8.3)	1.47 [0.12; 18.29] 0.766	1.41 [0.14; 13.86] 0.767	0.03 [-0.18; 0.25] 0.759
Exposed					
N'/N	162 / 162	169 / 169			
Any ocular SAE at the study eye, n (%)	3 (1.9)	2 (1.2)	1.58 [0.26; 9.55] 0.621	1.56 [0.26; 9.24] 0.621	0.01 [-0.02; 0.03] 0.620
Pooled Analysis					
Interaction Test:	p = 0.574				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any ocular SAE at the study eye, n (%)	2 (6.9)	2 (8.0)	0.90 [0.12; 6.93] 0.915	0.83 [0.14; 4.77] 0.837	-0.02 [-0.16; 0.12] 0.799

	Treatment Groups		Comparison		
Any serious ocular adverse event at the study eye by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any ocular SAE at the study eye, n (%)	10 (2.9)	6 (1.7)	1.72 [0.61; 4.89] 0.306	1.67 [0.61; 4.54] 0.310	0.01 [-0.01; 0.03] 0.309

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL: logit(proportion) = treatment [by exposure (week 100)].

Table 13-4.1 Any serious ocular adverse event at the fellow eye (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event at the fellow eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the fellow eye, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular SAE at the fellow eye, n (%)	0 (0.0)	3 (1.6)	N.E.	0.14 [0.01; 2.72] 0.195	-0.02 [-0.03; 0.00] 0.081
KITE, N'/N	179 / 179	181 / 181			
Any ocular SAE at the fellow eye, n (%)	1 (0.6)	1 (0.6)	1.01 [0.06; 16.29] 0.994	1.01 [0.06; 16.04] 0.994	0.00 [-0.02; 0.02] 0.994
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular SAE at the fellow eye, n (%)	1 (0.3)	4 (1.1)	N.E.	0.33 [0.05; 2.09] 0.218	-0.01 [-0.02; 0.00] 0.178
p_H=N.E.					
Any ocular SAE at the fellow eye, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular SAE at the fellow eye, n (%)	4 (2.1)	7 (3.7)	0.56 [0.16; 1.93] 0.356	0.57 [0.17; 1.90] 0.356	-0.02 [-0.05; 0.02] 0.349
KITE, N'/N	179 / 179	181 / 181			
Any ocular SAE at the fellow eye, n (%)	1 (0.6)	2 (1.1)	0.50 [0.05; 5.59] 0.576	0.51 [0.05; 5.53] 0.576	-0.01 [-0.02; 0.01] 0.568

	Treatment Groups		Comparison		
Any serious ocular adverse event at the fellow eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular SAE at the fellow eye, n (%)	5 (1.4)	9 (2.4)	0.53 [0.14; 2.02] 0.352	0.55 [0.19; 1.63] 0.275	-0.01 [-0.03; 0.01] 0.274
p_H=0.942					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-4.2 Any serious ocular adverse event at the fellow eye by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event at the fellow eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.942**					
KESTREL					
Interaction Test:	N.E.				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular SAE at the fellow eye, n (%)	0 (0.0)	2 (2.2)	N.E.	0.18 [0.01; 3.68] 0.265	-0.02 [-0.05; 0.01] 0.153
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular SAE at the fellow eye, n (%)	4 (4.7)	5 (5.3)	0.88 [0.23; 3.39] 0.851	0.88 [0.25; 3.19] 0.851	-0.01 [-0.07; 0.06] 0.851
KITE					
Interaction Test:	N.E.				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular SAE at the fellow eye, n (%)	0 (0.0)	1 (1.0)	N.E.	0.34 [0.01; 8.25] 0.507	-0.01 [-0.03; 0.01] 0.315
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular SAE at the fellow eye, n (%)	1 (1.3)	1 (1.3)	1.00 [0.06; 16.27] 1.000	1.00 [0.06; 15.71] 1.000	0.00 [-0.03; 0.03] 1.000
Pooled Analysis					
Interaction Test:	N.E.				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular SAE at the fellow eye, n (%)	0 (0.0)	3 (1.5)	N.E.	0.24 [0.03; 2.08] 0.157	-0.02 [-0.03; 0.00] 0.079

	Treatment Groups		Comparison		
Any serious ocular adverse event at the fellow eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular SAE at the fellow eye, n (%)	5 (3.0)	6 (3.5)	0.94 [0.20; 4.33] 0.933	0.90 [0.28; 2.89] 0.866	-0.00 [-0.04; 0.03] 0.866

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by age].
Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by age].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 13-4.3 Any serious ocular adverse event at the fellow eye by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event at the fellow eye by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.942**					
KESTREL					
Interaction Test:	N.E.				
Male					
N'/N	110 / 110	126 / 126			
Any ocular SAE at the fellow eye, n (%)	2 (1.8)	7 (5.6)	0.31 [0.06; 1.55] 0.155	0.33 [0.07; 1.54] 0.158	-0.04 [-0.08; 0.01] 0.120
Female					
N'/N	79 / 79	61 / 61			
Any ocular SAE at the fellow eye, n (%)	2 (2.5)	0 (0.0)	N.E.	3.88 [0.19; 79.26] 0.379	0.03 [-0.01; 0.06] 0.152
KITE					
Interaction Test:	N.E.				
Male					
N'/N	120 / 120	115 / 115			
Any ocular SAE at the fellow eye, n (%)	1 (0.8)	0 (0.0)	N.E.	2.88 [0.12; 69.89] 0.516	0.01 [-0.01; 0.02] 0.315
Female					
N'/N	59 / 59	66 / 66			
Any ocular SAE at the fellow eye, n (%)	0 (0.0)	2 (3.0)	N.E.	0.22 [0.01; 4.56] 0.330	-0.03 [-0.07; 0.01] 0.151
Pooled Analysis					
Interaction Test:	p = 0.636				
Male					
N'/N	230 / 230	241 / 241			
Any ocular SAE at the fellow eye, n (%)	3 (1.3)	7 (2.9)	0.45 [0.10; 2.11] 0.309	0.51 [0.14; 1.83] 0.293	-0.01 [-0.04; 0.01] 0.263

	Treatment Groups		Comparison		
Any serious ocular adverse event at the fellow eye by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any ocular SAE at the fellow eye, n (%)	2 (1.4)	2 (1.6)	0.80 [0.09; 6.81] 0.839	0.93 [0.17; 5.00] 0.929	-0.00 [-0.03; 0.03] 0.939

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL: logit(proportion) = treatment [by gender].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 13-4.4 Any serious ocular adverse event at the fellow eye by BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 13-4.5 Any serious ocular adverse event at the fellow eye by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 13-4.6 Any serious ocular adverse event at the fellow eye by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event at the fellow eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.942**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular SAE at the fellow eye, n (%)	0 (0.0)	1 (16.7)	N.E.	0.18 [0.01; 3.85] 0.272	-0.17 [-0.46; 0.13] 0.273
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular SAE at the fellow eye, n (%)	4 (2.3)	6 (3.3)	0.67 [0.19; 2.43] 0.547	0.68 [0.20; 2.37] 0.547	-0.01 [-0.04; 0.02] 0.544
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular SAE at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular SAE at the fellow eye, n (%)	1 (0.6)	2 (1.1)	0.54 [0.05; 6.02] 0.617	0.54 [0.05; 5.94] 0.617	-0.01 [-0.03; 0.01] 0.607
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular SAE at the fellow eye, n (%)	0 (0.0)	1 (7.7)	N.E.	0.18 [0.01; 3.85] 0.223	-0.07 [-0.22; 0.07] 0.313

	Treatment Groups		Comparison		
Any serious ocular adverse event at the fellow eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular SAE at the fellow eye, n (%)	5 (1.5)	8 (2.3)	0.61 [0.16; 2.33] 0.466	0.65 [0.21; 1.96] 0.439	-0.01 [-0.03; 0.01] 0.436

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by diabetes type].
Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 13-4.7 Any serious ocular adverse event at the fellow eye by HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 13-4.8 Any serious ocular adverse event at the fellow eye by duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 13-4.9 Any serious ocular adverse event at the fellow eye by DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 13-4.10 Any serious ocular adverse event at the fellow eye by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 13-4.11 Any serious ocular adverse event at the fellow eye by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event at the fellow eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.942**					
KESTREL					
Interaction Test:	N.E.				
presence					
N'/N	62 / 62	61 / 61			
Any ocular SAE at the fellow eye, n (%)	0 (0.0)	2 (3.3)	N.E.	0.20 [0.01; 4.02] 0.291	-0.03 [-0.08; 0.01] 0.150
absence					
N'/N	127 / 127	126 / 126			
Any ocular SAE at the fellow eye, n (%)	4 (3.1)	5 (4.0)	0.79 [0.21; 3.00] 0.726	0.79 [0.22; 2.89] 0.726	-0.01 [-0.05; 0.04] 0.725
KITE					
Interaction Test:	N.E.				
presence					
N'/N	56 / 56	67 / 67			
Any ocular SAE at the fellow eye, n (%)	0 (0.0)	1 (1.5)	N.E.	0.40 [0.02; 9.57] 0.570	-0.01 [-0.04; 0.01] 0.314
absence					
N'/N	123 / 123	114 / 114			
Any ocular SAE at the fellow eye, n (%)	1 (0.8)	1 (0.9)	0.93 [0.06; 14.98] 0.957	0.93 [0.06; 14.64] 0.957	-0.00 [-0.02; 0.02] 0.957
Pooled Analysis					
Interaction Test:	N.E.				
presence					
N'/N	118 / 118	128 / 128			
Any ocular SAE at the fellow eye, n (%)	0 (0.0)	3 (2.3)	N.E.	0.27 [0.03; 2.32] 0.199	-0.02 [-0.05; 0.00] 0.077

	Treatment Groups		Comparison		
Any serious ocular adverse event at the fellow eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular SAE at the fellow eye, n (%)	5 (2.0)	6 (2.5)	0.85 [0.19; 3.92] 0.837	0.82 [0.25; 2.63] 0.734	-0.00 [-0.03; 0.02] 0.734

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by status of SRF].
Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by status of SRF].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 13-4.12 Any serious ocular adverse event at the fellow eye by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 13-4.13 Any serious ocular adverse event at the fellow eye by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event at the fellow eye by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.942**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any ocular SAE at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Exposed					
N'/N	177 / 177	174 / 174			
Any ocular SAE at the fellow eye, n (%)	4 (2.3)	7 (4.0)	0.55 [0.16; 1.92] 0.350	0.56 [0.17; 1.88] 0.350	-0.02 [-0.05; 0.02] 0.344
KITE					
Interaction Test:	N.E.				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any ocular SAE at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Exposed					
N'/N	162 / 162	169 / 169			
Any ocular SAE at the fellow eye, n (%)	1 (0.6)	2 (1.2)	0.52 [0.05; 5.78] 0.593	0.52 [0.05; 5.70] 0.594	-0.01 [-0.03; 0.01] 0.584
Pooled Analysis					
Interaction Test:	N.E.				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any ocular SAE at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any serious ocular adverse event at the fellow eye by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any ocular SAE at the fellow eye, n (%)	5 (1.5)	9 (2.6)	0.54 [0.14; 2.05] 0.361	0.55 [0.19; 1.63] 0.276	-0.01 [-0.03; 0.01] 0.274

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by exposure (week 100)].
Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by exposure (week 100)].

Table 13-5.1 Any serious non-ocular adverse event (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious non-ocular adverse event (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular SAE, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any non-ocular SAE, n (%)	35 (18.5)	37 (19.8)	0.92 [0.55; 1.54] 0.755	0.94 [0.62; 1.42] 0.755	-0.01 [-0.09; 0.07] 0.755
KITE, N'/N	179 / 179	181 / 181			
Any non-ocular SAE, n (%)	30 (16.8)	37 (20.4)	0.78 [0.46; 1.34] 0.370	0.82 [0.53; 1.27] 0.371	-0.04 [-0.12; 0.04] 0.369
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any non-ocular SAE, n (%)	65 (17.7)	74 (20.1)	0.85 [0.59; 1.23] 0.393	0.88 [0.65; 1.19] 0.397	-0.02 [-0.08; 0.03] 0.396
p_H=0.668					
Any non-ocular SAE, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any non-ocular SAE, n (%)	53 (28.0)	55 (29.4)	0.94 [0.60; 1.46] 0.769	0.95 [0.69; 1.31] 0.769	-0.01 [-0.11; 0.08] 0.769
KITE, N'/N	179 / 179	181 / 181			
Any non-ocular SAE, n (%)	48 (26.8)	58 (32.0)	0.78 [0.49; 1.22] 0.277	0.84 [0.61; 1.15] 0.278	-0.05 [-0.15; 0.04] 0.276
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any non-ocular SAE, n (%)	101 (27.4)	113 (30.7)	0.85 [0.62; 1.17] 0.332	0.89 [0.71; 1.12] 0.331	-0.03 [-0.10; 0.03] 0.330
p_H=0.569					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-5.2 Any serious non-ocular adverse event by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.185				
< 65 years					
N'/N	104 / 104	93 / 93			
Any non-ocular SAE, n (%)	19 (18.3)	13 (14.0)	1.38 [0.64; 2.97] 0.416	1.31 [0.68; 2.50] 0.418	0.04 [-0.06; 0.15] 0.411
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any non-ocular SAE, n (%)	16 (18.8)	24 (25.5)	0.68 [0.33; 1.38] 0.283	0.74 [0.42; 1.29] 0.286	-0.07 [-0.19; 0.05] 0.278
KITE					
Interaction Test:	p = 0.664				
< 65 years					
N'/N	100 / 100	102 / 102			
Any non-ocular SAE, n (%)	18 (18.0)	24 (23.5)	0.71 [0.36; 1.42] 0.334	0.77 [0.44; 1.32] 0.336	-0.06 [-0.17; 0.06] 0.331
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any non-ocular SAE, n (%)	12 (15.2)	13 (16.5)	0.91 [0.39; 2.14] 0.828	0.92 [0.45; 1.90] 0.828	-0.01 [-0.13; 0.10] 0.827
Pooled Analysis					
Interaction Test:	p = 0.549				
< 65 years					
N'/N	204 / 204	195 / 195			
Any non-ocular SAE, n (%)	37 (18.1)	37 (19.0)	0.95 [0.57; 1.57] 0.832	0.96 [0.64; 1.46] 0.860	-0.01 [-0.08; 0.07] 0.860

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any non-ocular SAE, n (%)	28 (17.1)	37 (21.4)	0.75 [0.44; 1.30] 0.311	0.80 [0.52; 1.25] 0.334	-0.04 [-0.13; 0.04] 0.331
Any non-ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.569**					
KESTREL					
Interaction Test:	p = 0.158				
< 65 years					
N'/N	104 / 104	93 / 93			
Any non-ocular SAE, n (%)	32 (30.8)	24 (25.8)	1.28 [0.68; 2.38] 0.441	1.19 [0.76; 1.87] 0.443	0.05 [-0.08; 0.18] 0.439
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any non-ocular SAE, n (%)	21 (24.7)	31 (33.0)	0.67 [0.35; 1.28] 0.225	0.75 [0.47; 1.20] 0.228	-0.08 [-0.21; 0.05] 0.220
KITE					
Interaction Test:	p = 0.141				
< 65 years					
N'/N	100 / 100	102 / 102			
Any non-ocular SAE, n (%)	22 (22.0)	34 (33.3)	0.56 [0.30; 1.06] 0.074	0.66 [0.42; 1.05] 0.077	-0.11 [-0.24; 0.01] 0.069
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any non-ocular SAE, n (%)	26 (32.9)	24 (30.4)	1.12 [0.57; 2.20] 0.732	1.08 [0.68; 1.71] 0.732	0.03 [-0.12; 0.17] 0.732
Pooled Analysis					
Interaction Test:	p = 0.990				
< 65 years					
N'/N	204 / 204	195 / 195			
Any non-ocular SAE, n (%)	54 (26.5)	58 (29.7)	0.85 [0.55; 1.32] 0.482	0.89 [0.65; 1.22] 0.465	-0.03 [-0.12; 0.06] 0.465

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any non-ocular SAE, n (%)	47 (28.7)	55 (31.8)	0.86 [0.54; 1.37] 0.520	0.90 [0.65; 1.25] 0.524	-0.03 [-0.13; 0.07] 0.522

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-5.3 Any serious non-ocular adverse event by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.470				
Male					
N'/N	110 / 110	126 / 126			
Any non-ocular SAE, n (%)	21 (19.1)	28 (22.2)	0.83 [0.44; 1.56] 0.554	0.86 [0.52; 1.42] 0.555	-0.03 [-0.13; 0.07] 0.552
Female					
N'/N	79 / 79	61 / 61			
Any non-ocular SAE, n (%)	14 (17.7)	9 (14.8)	1.24 [0.50; 3.10] 0.639	1.20 [0.56; 2.59] 0.640	0.03 [-0.09; 0.15] 0.635
KITE					
Interaction Test:	p = 0.325				
Male					
N'/N	120 / 120	115 / 115			
Any non-ocular SAE, n (%)	22 (18.3)	22 (19.1)	0.95 [0.49; 1.83] 0.876	0.96 [0.56; 1.63] 0.876	-0.01 [-0.11; 0.09] 0.876
Female					
N'/N	59 / 59	66 / 66			
Any non-ocular SAE, n (%)	8 (13.6)	15 (22.7)	0.53 [0.21; 1.37] 0.191	0.60 [0.27; 1.31] 0.196	-0.09 [-0.23; 0.04] 0.179
Pooled Analysis					
Interaction Test:	p = 0.827				
Male					
N'/N	230 / 230	241 / 241			
Any non-ocular SAE, n (%)	43 (18.7)	50 (20.7)	0.88 [0.56; 1.39] 0.584	0.90 [0.63; 1.31] 0.593	-0.02 [-0.09; 0.05] 0.592

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any non-ocular SAE, n (%)	22 (15.9)	24 (18.9)	0.81 [0.43; 1.53] 0.510	0.85 [0.49; 1.46] 0.551	-0.03 [-0.12; 0.06] 0.549
Any non-ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.569**					
KESTREL					
Interaction Test:	p = 0.995				
Male					
N'/N	110 / 110	126 / 126			
Any non-ocular SAE, n (%)	33 (30.0)	39 (31.0)	0.96 [0.55; 1.67] 0.874	0.97 [0.66; 1.43] 0.874	-0.01 [-0.13; 0.11] 0.874
Female					
N'/N	79 / 79	61 / 61			
Any non-ocular SAE, n (%)	20 (25.3)	16 (26.2)	0.95 [0.44; 2.05] 0.902	0.97 [0.55; 1.70] 0.902	-0.01 [-0.16; 0.14] 0.903
KITE					
Interaction Test:	p = 0.371				
Male					
N'/N	120 / 120	115 / 115			
Any non-ocular SAE, n (%)	34 (28.3)	35 (30.4)	0.90 [0.52; 1.58] 0.724	0.93 [0.63; 1.38] 0.724	-0.02 [-0.14; 0.10] 0.724
Female					
N'/N	59 / 59	66 / 66			
Any non-ocular SAE, n (%)	14 (23.7)	23 (34.8)	0.58 [0.27; 1.28] 0.176	0.68 [0.39; 1.20] 0.182	-0.11 [-0.27; 0.05] 0.168
Pooled Analysis					
Interaction Test:	p = 0.499				
Male					
N'/N	230 / 230	241 / 241			
Any non-ocular SAE, n (%)	67 (29.1)	74 (30.7)	0.93 [0.63; 1.38] 0.715	0.95 [0.72; 1.25] 0.718	-0.02 [-0.10; 0.07] 0.718

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any non-ocular SAE, n (%)	34 (24.6)	39 (30.7)	0.74 [0.43; 1.27] 0.269	0.81 [0.54; 1.21] 0.298	-0.06 [-0.17; 0.05] 0.296

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-5.4 Any serious non-ocular adverse event by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.265				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any non-ocular SAE, n (%)	14 (18.9)	9 (14.1)	1.43 [0.57; 3.56] 0.447	1.35 [0.62; 2.90] 0.449	0.05 [-0.07; 0.17] 0.440
> 65 letters					
N'/N	115 / 115	123 / 123			
Any non-ocular SAE, n (%)	21 (18.3)	28 (22.8)	0.76 [0.40; 1.43] 0.391	0.80 [0.48; 1.33] 0.393	-0.05 [-0.15; 0.06] 0.389
KITE					
Interaction Test:	p = 0.020 *				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any non-ocular SAE, n (%)	6 (9.2)	22 (24.2)	0.32 [0.12; 0.84] 0.021 *	0.38 [0.16; 0.89] 0.025 *	-0.15 [-0.26; -0.04] 0.009 *
> 65 letters					
N'/N	114 / 114	90 / 90			
Any non-ocular SAE, n (%)	24 (21.1)	15 (16.7)	1.33 [0.65; 2.72] 0.430	1.26 [0.71; 2.26] 0.432	0.04 [-0.06; 0.15] 0.423
Pooled Analysis					
Interaction Test:	p = 0.364				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any non-ocular SAE, n (%)	20 (14.4)	31 (20.0)	0.67 [0.36; 1.25] 0.209	0.71 [0.41; 1.23] 0.215	-0.06 [-0.14; 0.03] 0.207

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any non-ocular SAE, n (%)	45 (19.7)	43 (20.2)	0.96 [0.60; 1.54] 0.878	0.98 [0.67; 1.43] 0.911	-0.00 [-0.08; 0.07] 0.910
Any non-ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.569**					
KESTREL					
Interaction Test:	p = 0.445				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any non-ocular SAE, n (%)	20 (27.0)	15 (23.4)	1.21 [0.56; 2.62] 0.629	1.15 [0.65; 2.06] 0.630	0.04 [-0.11; 0.18] 0.627
> 65 letters					
N'/N	115 / 115	123 / 123			
Any non-ocular SAE, n (%)	33 (28.7)	40 (32.5)	0.84 [0.48; 1.45] 0.523	0.88 [0.60; 1.30] 0.524	-0.04 [-0.16; 0.08] 0.522
KITE					
Interaction Test:	p = 0.015 *				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any non-ocular SAE, n (%)	12 (18.5)	34 (37.4)	0.38 [0.18; 0.81] 0.012 *	0.49 [0.28; 0.88] 0.016 *	-0.19 [-0.33; -0.05] 0.007 *
> 65 letters					
N'/N	114 / 114	90 / 90			
Any non-ocular SAE, n (%)	36 (31.6)	24 (26.7)	1.27 [0.69; 2.34] 0.445	1.18 [0.77; 1.83] 0.448	0.05 [-0.08; 0.17] 0.441
Pooled Analysis					
Interaction Test:	p = 0.213				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any non-ocular SAE, n (%)	32 (23.0)	49 (31.6)	0.65 [0.39; 1.10] 0.111	0.73 [0.49; 1.09] 0.119	-0.08 [-0.18; 0.02] 0.115

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any non-ocular SAE, n (%)	69 (30.1)	64 (30.0)	1.00 [0.66; 1.50] 0.989	1.01 [0.75; 1.34] 0.967	0.00 [-0.08; 0.09] 0.967

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-5.5 Any serious non-ocular adverse event by region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.904				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any non-ocular SAE, n (%)	17 (18.9)	17 (20.5)	0.90 [0.43; 1.91] 0.792	0.92 [0.50; 1.68] 0.792	-0.02 [-0.13; 0.10] 0.792
European Region					
N'/N	69 / 69	75 / 75			
Any non-ocular SAE, n (%)	12 (17.4)	15 (20.0)	0.84 [0.36; 1.95] 0.689	0.87 [0.44; 1.73] 0.689	-0.03 [-0.15; 0.10] 0.688
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any non-ocular SAE, n (%)	6 (20.0)	5 (17.2)	1.20 [0.32; 4.47] 0.786	1.16 [0.40; 3.39] 0.786	0.03 [-0.17; 0.23] 0.785
KITE					
Interaction Test:	p = 0.035 *				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any non-ocular SAE, n (%)	5 (19.2)	1 (4.8)	4.76 [0.51; 44.40] 0.171	4.04 [0.51; 31.96] 0.186	0.14 [-0.03; 0.32] 0.109
European Region					
N'/N	135 / 135	132 / 132			
Any non-ocular SAE, n (%)	18 (13.3)	30 (22.7)	0.52 [0.28; 0.99] 0.048 *	0.59 [0.34; 1.00] 0.050 *	-0.09 [-0.19; -0.00] 0.045 *
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any non-ocular SAE, n (%)	7 (38.9)	6 (21.4)	2.33 [0.63; 8.64] 0.204	1.81 [0.73; 4.53] 0.202	0.17 [-0.10; 0.45] 0.208

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.142				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any non-ocular SAE, n (%)	17 (18.9)	17 (20.5)	0.84 [0.35; 2.02] 0.696	0.92 [0.50; 1.68] 0.793	-0.02 [-0.13; 0.10] 0.792
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any non-ocular SAE, n (%)	5 (19.2)	1 (4.8)	5.14 [0.52; 50.42] 0.160	4.04 [0.51; 31.96] 0.144	0.14 [-0.03; 0.32] 0.109
European Region					
N'/N	204 / 204	207 / 207			
Any non-ocular SAE, n (%)	30 (14.7)	45 (21.7)	0.64 [0.37; 1.08] 0.097	0.68 [0.45; 1.03] 0.066	-0.07 [-0.14; 0.00] 0.065
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any non-ocular SAE, n (%)	13 (27.1)	11 (19.3)	1.56 [0.62; 3.92] 0.340	1.47 [0.74; 2.95] 0.277	0.09 [-0.07; 0.25] 0.277
Any non-ocular SAE, Week 100					
Test of heterogeneity in main analysis: $\mathbf{p_H=0.569}$					
KESTREL					
Interaction Test:	p = 0.934				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any non-ocular SAE, n (%)	27 (30.0)	27 (32.5)	0.89 [0.47; 1.69] 0.720	0.92 [0.59; 1.44] 0.720	-0.03 [-0.16; 0.11] 0.720
European Region					
N'/N	69 / 69	75 / 75			
Any non-ocular SAE, n (%)	17 (24.6)	20 (26.7)	0.90 [0.42; 1.90] 0.781	0.92 [0.53; 1.61] 0.781	-0.02 [-0.16; 0.12] 0.780
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any non-ocular SAE, n (%)	9 (30.0)	8 (27.6)	1.13 [0.36; 3.48] 0.838	1.09 [0.49; 2.43] 0.838	0.02 [-0.21; 0.26] 0.838

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.486				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any non-ocular SAE, n (%)	6 (23.1)	3 (14.3)	1.80 [0.39; 8.27] 0.450	1.62 [0.46; 5.70] 0.456	0.09 [-0.13; 0.31] 0.435
European Region					
N'/N	135 / 135	132 / 132			
Any non-ocular SAE, n (%)	35 (25.9)	44 (33.3)	0.70 [0.41; 1.19] 0.186	0.78 [0.54; 1.13] 0.187	-0.07 [-0.18; 0.04] 0.184
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any non-ocular SAE, n (%)	7 (38.9)	11 (39.3)	0.98 [0.29; 3.31] 0.979	0.99 [0.47; 2.07] 0.979	-0.00 [-0.29; 0.28] 0.979
Pooled Analysis					
Interaction Test:	p = 0.678				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any non-ocular SAE, n (%)	27 (30.0)	27 (32.5)	0.80 [0.37; 1.69] 0.553	0.92 [0.59; 1.44] 0.721	-0.03 [-0.16; 0.11] 0.720
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any non-ocular SAE, n (%)	6 (23.1)	3 (14.3)	2.02 [0.42; 9.80] 0.383	1.62 [0.46; 5.70] 0.451	0.09 [-0.13; 0.31] 0.435
European Region					
N'/N	204 / 204	207 / 207			
Any non-ocular SAE, n (%)	52 (25.5)	64 (30.9)	0.79 [0.50; 1.25] 0.316	0.82 [0.60; 1.12] 0.214	-0.06 [-0.14; 0.03] 0.212

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any non-ocular SAE, n (%)	16 (33.3)	19 (33.3)	1.02 [0.45; 2.32] 0.958	1.04 [0.60; 1.79] 0.896	0.01 [-0.17; 0.19] 0.895

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-5.6 Any serious non-ocular adverse event by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.465				
Type 1					
N'/N	12 / 12	6 / 6			
Any non-ocular SAE, n (%)	2 (16.7)	2 (33.3)	0.40 [0.04; 3.90] 0.430	0.50 [0.09; 2.73] 0.423	-0.17 [-0.60; 0.27] 0.450
Type 2					
N'/N	177 / 177	181 / 181			
Any non-ocular SAE, n (%)	33 (18.6)	35 (19.3)	0.96 [0.56; 1.62] 0.867	0.96 [0.63; 1.48] 0.867	-0.01 [-0.09; 0.07] 0.867
KITE					
Interaction Test:	p = 0.916				
Type 1					
N'/N	19 / 19	7 / 7			
Any non-ocular SAE, n (%)	2 (10.5)	1 (14.3)	0.71 [0.05; 9.27] 0.791	0.74 [0.08; 6.91] 0.789	-0.04 [-0.33; 0.26] 0.802
Type 2					
N'/N	160 / 160	174 / 174			
Any non-ocular SAE, n (%)	28 (17.5)	36 (20.7)	0.81 [0.47; 1.41] 0.460	0.85 [0.54; 1.32] 0.461	-0.03 [-0.12; 0.05] 0.458
Pooled Analysis					
Interaction Test:	p = 0.516				
Type 1					
N'/N	31 / 31	13 / 13			
Any non-ocular SAE, n (%)	4 (12.9)	3 (23.1)	0.50 [0.09; 2.65] 0.416	0.58 [0.15; 2.25] 0.447	-0.09 [-0.35; 0.16] 0.469

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any non-ocular SAE, n (%)	61 (18.1)	71 (20.0)	0.88 [0.60; 1.29] 0.518	0.91 [0.66; 1.23] 0.526	-0.02 [-0.08; 0.04] 0.525
Any non-ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.569**					
KESTREL					
Interaction Test:	p = 0.942				
Type 1					
N'/N	12 / 12	6 / 6			
Any non-ocular SAE, n (%)	4 (33.3)	2 (33.3)	1.00 [0.13; 8.00] 1.000	1.00 [0.25; 4.00] 1.000	0.00 [-0.46; 0.46] 1.000
Type 2					
N'/N	177 / 177	181 / 181			
Any non-ocular SAE, n (%)	49 (27.7)	53 (29.3)	0.92 [0.58; 1.46] 0.738	0.95 [0.68; 1.31] 0.738	-0.02 [-0.11; 0.08] 0.738
KITE					
Interaction Test:	p = 0.791				
Type 1					
N'/N	19 / 19	7 / 7			
Any non-ocular SAE, n (%)	3 (15.8)	1 (14.3)	1.12 [0.10; 13.04] 0.925	1.11 [0.14; 8.94] 0.925	0.02 [-0.29; 0.32] 0.923
Type 2					
N'/N	160 / 160	174 / 174			
Any non-ocular SAE, n (%)	45 (28.1)	57 (32.8)	0.80 [0.50; 1.28] 0.359	0.86 [0.62; 1.19] 0.360	-0.05 [-0.14; 0.05] 0.357
Pooled Analysis					
Interaction Test:	p = 0.867				
Type 1					
N'/N	31 / 31	13 / 13			
Any non-ocular SAE, n (%)	7 (22.6)	3 (23.1)	0.99 [0.21; 4.61] 0.985	1.04 [0.32; 3.32] 0.952	0.01 [-0.26; 0.27] 0.950

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any non-ocular SAE, n (%)	94 (27.9)	110 (31.0)	0.86 [0.62; 1.20] 0.373	0.90 [0.71; 1.14] 0.378	-0.03 [-0.10; 0.04] 0.377

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-5.7 Any serious non-ocular adverse event by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.731				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any non-ocular SAE, n (%)	13 (17.1)	19 (17.8)	0.96 [0.44; 2.08] 0.909	0.96 [0.51; 1.83] 0.909	-0.01 [-0.12; 0.10] 0.909
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any non-ocular SAE, n (%)	21 (18.8)	18 (22.5)	0.79 [0.39; 1.61] 0.525	0.83 [0.48; 1.46] 0.524	-0.04 [-0.15; 0.08] 0.529
KITE					
Interaction Test:	p = 0.412				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any non-ocular SAE, n (%)	16 (19.5)	19 (19.8)	0.98 [0.47; 2.06] 0.963	0.99 [0.54; 1.79] 0.963	-0.00 [-0.12; 0.11] 0.963
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any non-ocular SAE, n (%)	14 (14.4)	18 (21.2)	0.63 [0.29; 1.35] 0.236	0.68 [0.36; 1.29] 0.237	-0.07 [-0.18; 0.04] 0.236
Pooled Analysis					
Interaction Test:	p = 0.419				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any non-ocular SAE, n (%)	29 (18.4)	38 (18.7)	0.98 [0.57; 1.67] 0.934	0.98 [0.63; 1.51] 0.910	-0.00 [-0.09; 0.08] 0.910

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any non-ocular SAE, n (%)	35 (16.7)	36 (21.8)	0.72 [0.43; 1.21] 0.213	0.76 [0.50; 1.16] 0.202	-0.05 [-0.13; 0.03] 0.205
Any non-ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.569**					
KESTREL					
Interaction Test:	p = 0.591				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any non-ocular SAE, n (%)	20 (26.3)	28 (26.2)	1.01 [0.52; 1.97] 0.982	1.01 [0.61; 1.65] 0.982	0.00 [-0.13; 0.13] 0.982
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any non-ocular SAE, n (%)	32 (28.6)	27 (33.8)	0.79 [0.42; 1.46] 0.444	0.85 [0.55; 1.29] 0.442	-0.05 [-0.18; 0.08] 0.446
KITE					
Interaction Test:	p = 0.844				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any non-ocular SAE, n (%)	23 (28.0)	31 (32.3)	0.82 [0.43; 1.56] 0.540	0.87 [0.55; 1.36] 0.541	-0.04 [-0.18; 0.09] 0.538
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any non-ocular SAE, n (%)	25 (25.8)	27 (31.8)	0.75 [0.39; 1.42] 0.373	0.81 [0.51; 1.28] 0.373	-0.06 [-0.19; 0.07] 0.373
Pooled Analysis					
Interaction Test:	p = 0.612				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any non-ocular SAE, n (%)	43 (27.2)	59 (29.1)	0.91 [0.57; 1.45] 0.698	0.93 [0.67; 1.30] 0.670	-0.02 [-0.11; 0.07] 0.668

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any non-ocular SAE, n (%)	57 (27.3)	54 (32.7)	0.77 [0.49; 1.21] 0.257	0.83 [0.61; 1.13] 0.243	-0.06 [-0.15; 0.04] 0.243

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-5.8 Any serious non-ocular adverse event by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.345				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any non-ocular SAE, n (%)	19 (15.8)	24 (21.8)	0.67 [0.35; 1.31] 0.247	0.73 [0.42; 1.25] 0.248	-0.06 [-0.16; 0.04] 0.246
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any non-ocular SAE, n (%)	4 (13.3)	5 (12.8)	1.05 [0.26; 4.29] 0.950	1.04 [0.31; 3.54] 0.950	0.01 [-0.16; 0.17] 0.950
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any non-ocular SAE, n (%)	12 (30.8)	8 (21.1)	1.67 [0.59; 4.69] 0.333	1.46 [0.67; 3.17] 0.337	0.10 [-0.10; 0.29] 0.327
KITE					
Interaction Test:	p = 0.569				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any non-ocular SAE, n (%)	17 (20.0)	18 (19.6)	1.03 [0.49; 2.15] 0.942	1.02 [0.56; 1.85] 0.942	0.00 [-0.11; 0.12] 0.942
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any non-ocular SAE, n (%)	6 (11.8)	10 (20.4)	0.52 [0.17; 1.56] 0.244	0.58 [0.23; 1.47] 0.247	-0.09 [-0.23; 0.06] 0.237
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any non-ocular SAE, n (%)	7 (16.3)	9 (22.5)	0.67 [0.22; 2.01] 0.474	0.72 [0.30; 1.76] 0.476	-0.06 [-0.23; 0.11] 0.473

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.715				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any non-ocular SAE, n (%)	36 (17.6)	42 (20.8)	0.80 [0.49; 1.32] 0.390	0.85 [0.57; 1.26] 0.415	-0.03 [-0.11; 0.04] 0.414
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any non-ocular SAE, n (%)	10 (12.3)	15 (17.0)	0.70 [0.29; 1.66] 0.414	0.72 [0.34; 1.49] 0.370	-0.05 [-0.16; 0.06] 0.366
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any non-ocular SAE, n (%)	19 (23.2)	17 (21.8)	1.09 [0.52; 2.29] 0.827	1.07 [0.60; 1.90] 0.826	0.01 [-0.12; 0.14] 0.826
Any non-ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.569**					
KESTREL					
Interaction Test:	p = 0.484				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any non-ocular SAE, n (%)	32 (26.7)	34 (30.9)	0.81 [0.46; 1.44] 0.478	0.86 [0.57; 1.30] 0.478	-0.04 [-0.16; 0.07] 0.478
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any non-ocular SAE, n (%)	6 (20.0)	10 (25.6)	0.73 [0.23; 2.28] 0.583	0.78 [0.32; 1.91] 0.586	-0.06 [-0.25; 0.14] 0.577
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any non-ocular SAE, n (%)	15 (38.5)	11 (28.9)	1.53 [0.59; 3.98] 0.379	1.33 [0.70; 2.51] 0.382	0.10 [-0.11; 0.31] 0.375

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.078				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any non-ocular SAE, n (%)	28 (32.9)	26 (28.3)	1.25 [0.66; 2.37] 0.500	1.17 [0.75; 1.82] 0.500	0.05 [-0.09; 0.18] 0.499
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any non-ocular SAE, n (%)	10 (19.6)	20 (40.8)	0.35 [0.14; 0.87] 0.023 *	0.48 [0.25; 0.92] 0.027 *	-0.21 [-0.39; -0.04] 0.018 *
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any non-ocular SAE, n (%)	10 (23.3)	12 (30.0)	0.71 [0.27; 1.88] 0.488	0.78 [0.38; 1.59] 0.488	-0.07 [-0.26; 0.12] 0.487
Pooled Analysis					
Interaction Test:	p = 0.193				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any non-ocular SAE, n (%)	60 (29.3)	60 (29.7)	0.98 [0.64; 1.50] 0.911	0.99 [0.73; 1.33] 0.936	-0.00 [-0.09; 0.09] 0.936
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any non-ocular SAE, n (%)	16 (19.8)	30 (34.1)	0.48 [0.24; 0.97] 0.042 *	0.57 [0.34; 0.96] 0.031 *	-0.15 [-0.28; -0.02] 0.027 *

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any non-ocular SAE, n (%)	25 (30.5)	23 (29.5)	1.05 [0.53; 2.07] 0.883	1.04 [0.65; 1.66] 0.881	0.01 [-0.13; 0.15] 0.881

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-5.9 Any serious non-ocular adverse event by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.686				
focal					
N'/N	59 / 59	48 / 48			
Any non-ocular SAE, n (%)	7 (11.9)	7 (14.6)	0.79 [0.26; 2.43] 0.679	0.81 [0.31; 2.16] 0.679	-0.03 [-0.16; 0.10] 0.681
diffuse					
N'/N	127 / 127	134 / 134			
Any non-ocular SAE, n (%)	28 (22.0)	29 (21.6)	1.02 [0.57; 1.84] 0.937	1.02 [0.64; 1.61] 0.937	0.00 [-0.10; 0.10] 0.937
KITE					
Interaction Test:	p = 0.822				
focal					
N'/N	63 / 63	66 / 66			
Any non-ocular SAE, n (%)	10 (15.9)	12 (18.2)	0.85 [0.34; 2.13] 0.728	0.87 [0.41; 1.88] 0.728	-0.02 [-0.15; 0.11] 0.727
diffuse					
N'/N	115 / 115	109 / 109			
Any non-ocular SAE, n (%)	20 (17.4)	24 (22.0)	0.75 [0.38; 1.44] 0.384	0.79 [0.46; 1.35] 0.385	-0.05 [-0.15; 0.06] 0.384
Pooled Analysis					
Interaction Test:	p = 0.860				
focal					
N'/N	122 / 122	114 / 114			
Any non-ocular SAE, n (%)	17 (13.9)	19 (16.7)	0.82 [0.40; 1.67] 0.580	0.85 [0.47; 1.55] 0.596	-0.02 [-0.12; 0.07] 0.595

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any non-ocular SAE, n (%)	48 (19.8)	53 (21.8)	0.88 [0.57; 1.37] 0.575	0.91 [0.64; 1.29] 0.604	-0.02 [-0.09; 0.05] 0.603
Any non-ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.569**					
KESTREL					
Interaction Test:	p = 0.339				
focal					
N'/N	59 / 59	48 / 48			
Any non-ocular SAE, n (%)	14 (23.7)	15 (31.3)	0.68 [0.29; 1.61] 0.385	0.76 [0.41; 1.41] 0.385	-0.08 [-0.25; 0.10] 0.387
diffuse					
N'/N	127 / 127	134 / 134			
Any non-ocular SAE, n (%)	39 (30.7)	38 (28.4)	1.12 [0.66; 1.91] 0.677	1.08 [0.74; 1.58] 0.677	0.02 [-0.09; 0.13] 0.677
KITE					
Interaction Test:	p = 0.775				
focal					
N'/N	63 / 63	66 / 66			
Any non-ocular SAE, n (%)	18 (28.6)	21 (31.8)	0.86 [0.40; 1.82] 0.688	0.90 [0.53; 1.52] 0.689	-0.03 [-0.19; 0.13] 0.688
diffuse					
N'/N	115 / 115	109 / 109			
Any non-ocular SAE, n (%)	30 (26.1)	35 (32.1)	0.75 [0.42; 1.33] 0.321	0.81 [0.54; 1.23] 0.322	-0.06 [-0.18; 0.06] 0.321
Pooled Analysis					
Interaction Test:	p = 0.635				
focal					
N'/N	122 / 122	114 / 114			
Any non-ocular SAE, n (%)	32 (26.2)	36 (31.6)	0.78 [0.44; 1.38] 0.393	0.84 [0.56; 1.25] 0.383	-0.05 [-0.17; 0.06] 0.382

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any non-ocular SAE, n (%)	69 (28.5)	73 (30.0)	0.92 [0.62; 1.37] 0.690	0.95 [0.72; 1.25] 0.714	-0.02 [-0.10; 0.07] 0.714

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-5.10 Any serious non-ocular adverse event by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.950				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any non-ocular SAE, n (%)	20 (18.7)	18 (18.8)	1.00 [0.49; 2.02] 0.992	1.00 [0.56; 1.77] 0.992	-0.00 [-0.11; 0.11] 0.992
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any non-ocular SAE, n (%)	13 (18.6)	15 (21.1)	0.85 [0.37; 1.95] 0.704	0.88 [0.45; 1.71] 0.704	-0.03 [-0.16; 0.11] 0.703
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any non-ocular SAE, n (%)	2 (16.7)	4 (20.0)	0.80 [0.12; 5.20] 0.815	0.83 [0.18; 3.88] 0.816	-0.03 [-0.31; 0.24] 0.812
KITE					
Interaction Test:	p = 0.943				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any non-ocular SAE, n (%)	15 (17.6)	17 (20.7)	0.82 [0.38; 1.77] 0.613	0.85 [0.46; 1.59] 0.613	-0.03 [-0.15; 0.09] 0.613
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any non-ocular SAE, n (%)	12 (16.2)	17 (21.5)	0.71 [0.31; 1.60] 0.404	0.75 [0.39; 1.47] 0.406	-0.05 [-0.18; 0.07] 0.400
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any non-ocular SAE, n (%)	3 (15.0)	3 (15.8)	0.94 [0.17; 5.36] 0.946	0.95 [0.22; 4.14] 0.946	-0.01 [-0.23; 0.22] 0.946

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.930				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any non-ocular SAE, n (%)	35 (18.2)	35 (19.7)	0.90 [0.54; 1.52] 0.705	0.93 [0.61; 1.41] 0.727	-0.01 [-0.09; 0.07] 0.727
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any non-ocular SAE, n (%)	25 (17.4)	32 (21.3)	0.78 [0.43; 1.39] 0.396	0.81 [0.51; 1.30] 0.389	-0.04 [-0.13; 0.05] 0.386
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any non-ocular SAE, n (%)	5 (15.6)	7 (17.9)	0.86 [0.24; 3.02] 0.812	0.89 [0.31; 2.58] 0.836	-0.02 [-0.19; 0.16] 0.832
Any non-ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.569**					
KESTREL					
Interaction Test:	p = 0.820				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any non-ocular SAE, n (%)	31 (29.0)	27 (28.1)	1.04 [0.57; 1.92] 0.894	1.03 [0.67; 1.59] 0.894	0.01 [-0.12; 0.13] 0.894
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any non-ocular SAE, n (%)	19 (27.1)	21 (29.6)	0.89 [0.43; 1.85] 0.749	0.92 [0.54; 1.55] 0.749	-0.02 [-0.17; 0.12] 0.748
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any non-ocular SAE, n (%)	3 (25.0)	7 (35.0)	0.62 [0.13; 3.06] 0.556	0.71 [0.23; 2.25] 0.566	-0.10 [-0.42; 0.22] 0.543

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.310				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any non-ocular SAE, n (%)	26 (30.6)	23 (28.0)	1.13 [0.58; 2.20] 0.719	1.09 [0.68; 1.75] 0.719	0.03 [-0.11; 0.16] 0.718
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any non-ocular SAE, n (%)	18 (24.3)	29 (36.7)	0.55 [0.27; 1.12] 0.099	0.66 [0.40; 1.09] 0.103	-0.12 [-0.27; 0.02] 0.093
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any non-ocular SAE, n (%)	4 (20.0)	6 (31.6)	0.54 [0.13; 2.34] 0.411	0.63 [0.21; 1.90] 0.415	-0.12 [-0.39; 0.16] 0.405
Pooled Analysis					
Interaction Test:	p = 0.330				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any non-ocular SAE, n (%)	57 (29.7)	50 (28.1)	1.08 [0.69; 1.69] 0.750	1.06 [0.77; 1.46] 0.733	0.02 [-0.08; 0.11] 0.732
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any non-ocular SAE, n (%)	37 (25.7)	50 (33.3)	0.70 [0.42; 1.15] 0.159	0.77 [0.54; 1.10] 0.154	-0.08 [-0.18; 0.03] 0.151

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any non-ocular SAE, n (%)	7 (21.9)	13 (33.3)	0.56 [0.19; 1.64] 0.293	0.67 [0.30; 1.48] 0.320	-0.11 [-0.32; 0.10] 0.305

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-5.11 Any serious non-ocular adverse event by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.316				
presence					
N'/N	62 / 62	61 / 61			
Any non-ocular SAE, n (%)	13 (21.0)	10 (16.4)	1.35 [0.54; 3.37] 0.516	1.28 [0.61; 2.69] 0.517	0.05 [-0.09; 0.18] 0.514
absence					
N'/N	127 / 127	126 / 126			
Any non-ocular SAE, n (%)	22 (17.3)	27 (21.4)	0.77 [0.41; 1.44] 0.409	0.81 [0.49; 1.34] 0.410	-0.04 [-0.14; 0.06] 0.408
KITE					
Interaction Test:	p = 0.652				
presence					
N'/N	56 / 56	67 / 67			
Any non-ocular SAE, n (%)	9 (16.1)	15 (22.4)	0.66 [0.27; 1.66] 0.380	0.72 [0.34; 1.51] 0.384	-0.06 [-0.20; 0.08] 0.372
absence					
N'/N	123 / 123	114 / 114			
Any non-ocular SAE, n (%)	21 (17.1)	22 (19.3)	0.86 [0.44; 1.67] 0.657	0.88 [0.52; 1.52] 0.657	-0.02 [-0.12; 0.08] 0.657
Pooled Analysis					
Interaction Test:	p = 0.700				
presence					
N'/N	118 / 118	128 / 128			
Any non-ocular SAE, n (%)	22 (18.6)	25 (19.5)	0.94 [0.50; 1.78] 0.856	0.96 [0.57; 1.61] 0.866	-0.01 [-0.11; 0.09] 0.866

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any non-ocular SAE, n (%)	43 (17.2)	49 (20.4)	0.81 [0.51; 1.27] 0.359	0.84 [0.58; 1.22] 0.366	-0.03 [-0.10; 0.04] 0.365
Any non-ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.569**					
KESTREL					
Interaction Test:	p = 0.385				
presence					
N'/N	62 / 62	61 / 61			
Any non-ocular SAE, n (%)	18 (29.0)	15 (24.6)	1.25 [0.56; 2.79] 0.579	1.18 [0.66; 2.12] 0.579	0.04 [-0.11; 0.20] 0.578
absence					
N'/N	127 / 127	126 / 126			
Any non-ocular SAE, n (%)	35 (27.6)	40 (31.7)	0.82 [0.48; 1.40] 0.466	0.87 [0.59; 1.27] 0.467	-0.04 [-0.15; 0.07] 0.466
KITE					
Interaction Test:	p = 0.574				
presence					
N'/N	56 / 56	67 / 67			
Any non-ocular SAE, n (%)	15 (26.8)	24 (35.8)	0.66 [0.30; 1.42] 0.285	0.75 [0.44; 1.28] 0.290	-0.09 [-0.25; 0.07] 0.278
absence					
N'/N	123 / 123	114 / 114			
Any non-ocular SAE, n (%)	33 (26.8)	34 (29.8)	0.86 [0.49; 1.52] 0.609	0.90 [0.60; 1.35] 0.609	-0.03 [-0.14; 0.08] 0.609
Pooled Analysis					
Interaction Test:	p = 0.861				
presence					
N'/N	118 / 118	128 / 128			
Any non-ocular SAE, n (%)	33 (28.0)	39 (30.5)	0.89 [0.51; 1.54] 0.677	0.92 [0.62; 1.37] 0.697	-0.02 [-0.14; 0.09] 0.696

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any non-ocular SAE, n (%)	68 (27.2)	74 (30.8)	0.84 [0.57; 1.24] 0.373	0.88 [0.67; 1.17] 0.379	-0.04 [-0.12; 0.04] 0.378

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-5.12 Any serious non-ocular adverse event by exposure (week 52) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular SAE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.668**					
KESTREL					
Interaction Test:	p = 0.198				
Non-exposed					
N'/N	71 / 71	75 / 75			
Any non-ocular SAE, n (%)	19 (26.8)	16 (21.3)	1.35 [0.63; 2.89] 0.443	1.25 [0.70; 2.24] 0.444	0.05 [-0.08; 0.19] 0.443
Exposed					
N'/N	118 / 118	112 / 112			
Any non-ocular SAE, n (%)	16 (13.6)	21 (18.8)	0.68 [0.33; 1.38] 0.286	0.72 [0.40; 1.31] 0.287	-0.05 [-0.15; 0.04] 0.285
KITE					
Interaction Test:	p = 0.081				
Non-exposed					
N'/N	85 / 85	90 / 90			
Any non-ocular SAE, n (%)	19 (22.4)	17 (18.9)	1.24 [0.59; 2.58] 0.571	1.18 [0.66; 2.12] 0.572	0.03 [-0.09; 0.15] 0.571
Exposed					
N'/N	94 / 94	91 / 91			
Any non-ocular SAE, n (%)	11 (11.7)	20 (22.0)	0.47 [0.21; 1.05] 0.065	0.53 [0.27; 1.05] 0.068	-0.10 [-0.21; 0.00] 0.060
Pooled Analysis					
Interaction Test:	p = 0.031 *				
Non-exposed					
N'/N	156 / 156	165 / 165			
Any non-ocular SAE, n (%)	38 (24.4)	33 (20.0)	1.30 [0.77; 2.21] 0.328	1.22 [0.81; 1.84] 0.348	0.04 [-0.05; 0.13] 0.347

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	212 / 212	203 / 203			
Any non-ocular SAE, n (%)	27 (12.7)	41 (20.2)	0.57 [0.33; 0.97] 0.037 *	0.63 [0.40; 0.99] 0.041 *	-0.07 [-0.15; -0.00] 0.040 *

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 13-5.13 Any serious non-ocular adverse event by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular SAE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.569**					
KESTREL					
Interaction Test:	p = 0.801				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any non-ocular SAE, n (%)	5 (41.7)	5 (38.5)	1.14 [0.23; 5.67] 0.870	1.08 [0.41; 2.83] 0.870	0.03 [-0.35; 0.42] 0.870
Exposed					
N'/N	177 / 177	174 / 174			
Any non-ocular SAE, n (%)	48 (27.1)	50 (28.7)	0.92 [0.58; 1.47] 0.736	0.94 [0.67; 1.32] 0.736	-0.02 [-0.11; 0.08] 0.736
KITE					
Interaction Test:	p = 0.814				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any non-ocular SAE, n (%)	8 (47.1)	6 (50.0)	0.89 [0.20; 3.90] 0.876	0.94 [0.44; 2.01] 0.875	-0.03 [-0.40; 0.34] 0.876
Exposed					
N'/N	162 / 162	169 / 169			
Any non-ocular SAE, n (%)	40 (24.7)	52 (30.8)	0.74 [0.45; 1.20] 0.218	0.80 [0.56; 1.14] 0.220	-0.06 [-0.16; 0.04] 0.216
Pooled Analysis					
Interaction Test:	p = 0.690				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any non-ocular SAE, n (%)	13 (44.8)	11 (44.0)	1.04 [0.35; 3.06] 0.940	1.00 [0.55; 1.81] 0.997	-0.00 [-0.27; 0.27] 0.997

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any non-ocular SAE, n (%)	88 (26.0)	102 (29.7)	0.83 [0.59; 1.16] 0.271	0.87 [0.68; 1.11] 0.271	-0.04 [-0.11; 0.03] 0.270

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

14 Safety analysis: Any severe adverse event

Table 14-1.1 Any severe adverse event (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe adverse event (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any severe AE, n (%)	25 (13.2)	27 (14.4)	0.90 [0.50; 1.62] 0.734	0.92 [0.55; 1.52] 0.734	-0.01 [-0.08; 0.06] 0.734
KITE, N'/N	179 / 179	181 / 181			
Any severe AE, n (%)	22 (12.3)	19 (10.5)	1.19 [0.62; 2.29] 0.593	1.17 [0.66; 2.09] 0.593	0.02 [-0.05; 0.08] 0.592
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any severe AE, n (%)	47 (12.8)	46 (12.5)	1.04 [0.67; 1.60] 0.874	1.02 [0.70; 1.49] 0.916	0.00 [-0.05; 0.05] 0.916
p_H=0.532					
Any severe AE, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any severe AE, n (%)	42 (22.2)	41 (21.9)	1.02 [0.62; 1.66] 0.945	1.01 [0.69; 1.48] 0.945	0.00 [-0.08; 0.09] 0.945
KITE, N'/N	179 / 179	181 / 181			
Any severe AE, n (%)	40 (22.3)	46 (25.4)	0.84 [0.52; 1.37] 0.495	0.88 [0.61; 1.27] 0.496	-0.03 [-0.12; 0.06] 0.494

	Treatment Groups		Comparison		
Any severe adverse event (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any severe AE, n (%)	82 (22.3)	87 (23.6)	0.93 [0.66; 1.31] 0.673	0.94 [0.72; 1.23] 0.664	-0.01 [-0.07; 0.05] 0.663
p_H=0.596					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-1.2 Any severe adverse event by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.532**					
KESTREL					
Interaction Test:	p = 0.705				
< 65 years					
N'/N	104 / 104	93 / 93			
Any severe AE, n (%)	14 (13.5)	15 (16.1)	0.81 [0.37; 1.78] 0.598	0.83 [0.43; 1.64] 0.598	-0.03 [-0.13; 0.07] 0.599
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any severe AE, n (%)	11 (12.9)	12 (12.8)	1.02 [0.42; 2.44] 0.972	1.01 [0.47; 2.18] 0.972	0.00 [-0.10; 0.10] 0.972
KITE					
Interaction Test:	p = 0.386				
< 65 years					
N'/N	100 / 100	102 / 102			
Any severe AE, n (%)	12 (12.0)	8 (7.8)	1.60 [0.63; 4.10] 0.326	1.53 [0.65; 3.58] 0.327	0.04 [-0.04; 0.12] 0.322
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any severe AE, n (%)	10 (12.7)	11 (13.9)	0.90 [0.36; 2.25] 0.815	0.91 [0.41; 2.02] 0.815	-0.01 [-0.12; 0.09] 0.815
Pooled Analysis					
Interaction Test:	p = 0.807				
< 65 years					
N'/N	204 / 204	195 / 195			
Any severe AE, n (%)	26 (12.7)	23 (11.8)	1.09 [0.60; 1.99] 0.774	1.07 [0.63; 1.80] 0.810	0.01 [-0.06; 0.07] 0.810
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any severe AE, n (%)	21 (12.8)	23 (13.3)	0.98 [0.52; 1.85] 0.948	0.96 [0.55; 1.67] 0.892	-0.01 [-0.08; 0.07] 0.891

	Treatment Groups		Comparison		
Any severe adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.596**					
KESTREL					
Interaction Test:	p = 0.566				
< 65 years					
N'/N	104 / 104	93 / 93			
Any severe AE, n (%)	27 (26.0)	22 (23.7)	1.13 [0.59; 2.17] 0.709	1.10 [0.67; 1.79] 0.709	0.02 [-0.10; 0.14] 0.708
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any severe AE, n (%)	15 (17.6)	19 (20.2)	0.85 [0.40; 1.79] 0.663	0.87 [0.47; 1.61] 0.663	-0.03 [-0.14; 0.09] 0.661
KITE					
Interaction Test:	p = 0.640				
< 65 years					
N'/N	100 / 100	102 / 102			
Any severe AE, n (%)	17 (17.0)	22 (21.6)	0.74 [0.37; 1.51] 0.412	0.79 [0.45; 1.39] 0.413	-0.05 [-0.15; 0.06] 0.410
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any severe AE, n (%)	23 (29.1)	24 (30.4)	0.94 [0.48; 1.86] 0.862	0.96 [0.59; 1.55] 0.862	-0.01 [-0.16; 0.13] 0.862
Pooled Analysis					
Interaction Test:	p = 0.891				
< 65 years					
N'/N	204 / 204	195 / 195			
Any severe AE, n (%)	44 (21.6)	44 (22.6)	0.95 [0.59; 1.53] 0.842	0.95 [0.65; 1.37] 0.776	-0.01 [-0.09; 0.07] 0.776

	Treatment Groups		Comparison		
Any severe adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any severe AE, n (%)	38 (23.2)	43 (24.9)	0.91 [0.55; 1.50] 0.706	0.92 [0.63; 1.35] 0.673	-0.02 [-0.11; 0.07] 0.672

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-1.3 Any severe adverse event by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.532**					
KESTREL					
Interaction Test:	p = 0.155				
Male					
N'/N	110 / 110	126 / 126			
Any severe AE, n (%)	16 (14.5)	15 (11.9)	1.26 [0.59; 2.68] 0.550	1.22 [0.63; 2.36] 0.550	0.03 [-0.06; 0.11] 0.551
Female					
N'/N	79 / 79	61 / 61			
Any severe AE, n (%)	9 (11.4)	12 (19.7)	0.52 [0.21; 1.34] 0.178	0.58 [0.26; 1.29] 0.179	-0.08 [-0.20; 0.04] 0.183
KITE					
Interaction Test:	p = 0.868				
Male					
N'/N	120 / 120	115 / 115			
Any severe AE, n (%)	13 (10.8)	10 (8.7)	1.28 [0.54; 3.04] 0.582	1.25 [0.57; 2.73] 0.583	0.02 [-0.05; 0.10] 0.580
Female					
N'/N	59 / 59	66 / 66			
Any severe AE, n (%)	9 (15.3)	9 (13.6)	1.14 [0.42; 3.10] 0.797	1.12 [0.48; 2.63] 0.797	0.02 [-0.11; 0.14] 0.797
Pooled Analysis					
Interaction Test:	p = 0.248				
Male					
N'/N	230 / 230	241 / 241			
Any severe AE, n (%)	29 (12.6)	25 (10.4)	1.27 [0.72; 2.26] 0.406	1.23 [0.74; 2.04] 0.417	0.02 [-0.03; 0.08] 0.416
Female					
N'/N	138 / 138	127 / 127			
Any severe AE, n (%)	18 (13.0)	21 (16.5)	0.75 [0.38; 1.49] 0.418	0.79 [0.44; 1.40] 0.415	-0.04 [-0.12; 0.05] 0.419

	Treatment Groups		Comparison		
Any severe adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.596**					
KESTREL					
Interaction Test:	p = 0.181				
Male					
N'/N	110 / 110	126 / 126			
Any severe AE, n (%)	27 (24.5)	25 (19.8)	1.31 [0.71; 2.43] 0.385	1.24 [0.77; 2.00] 0.385	0.05 [-0.06; 0.15] 0.386
Female					
N'/N	79 / 79	61 / 61			
Any severe AE, n (%)	15 (19.0)	16 (26.2)	0.66 [0.30; 1.47] 0.308	0.72 [0.39; 1.35] 0.307	-0.07 [-0.21; 0.07] 0.311
KITE					
Interaction Test:	p = 0.434				
Male					
N'/N	120 / 120	115 / 115			
Any severe AE, n (%)	26 (21.7)	25 (21.7)	1.00 [0.54; 1.85] 0.989	1.00 [0.61; 1.62] 0.989	-0.00 [-0.11; 0.10] 0.989
Female					
N'/N	59 / 59	66 / 66			
Any severe AE, n (%)	14 (23.7)	21 (31.8)	0.67 [0.30; 1.47] 0.316	0.75 [0.42; 1.33] 0.320	-0.08 [-0.24; 0.08] 0.310
Pooled Analysis					
Interaction Test:	p = 0.122				
Male					
N'/N	230 / 230	241 / 241			
Any severe AE, n (%)	53 (23.0)	50 (20.7)	1.14 [0.74; 1.77] 0.547	1.11 [0.79; 1.56] 0.545	0.02 [-0.05; 0.10] 0.544

	Treatment Groups		Comparison		
Any severe adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any severe AE, n (%)	29 (21.0)	37 (29.1)	0.65 [0.37; 1.14] 0.135	0.74 [0.48; 1.12] 0.153	-0.08 [-0.18; 0.03] 0.152

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-1.4 Any severe adverse event by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.532**					
KESTREL					
Interaction Test:	p = 0.181				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any severe AE, n (%)	11 (14.9)	15 (23.4)	0.57 [0.24; 1.35] 0.202	0.63 [0.31; 1.28] 0.204	-0.09 [-0.22; 0.05] 0.202
> 65 letters					
N'/N	115 / 115	123 / 123			
Any severe AE, n (%)	14 (12.2)	12 (9.8)	1.28 [0.57; 2.90] 0.551	1.25 [0.60; 2.58] 0.551	0.02 [-0.06; 0.10] 0.551
KITE					
Interaction Test:	p = 0.029 *				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any severe AE, n (%)	3 (4.6)	11 (12.1)	0.35 [0.09; 1.32] 0.121	0.38 [0.11; 1.31] 0.127	-0.07 [-0.16; 0.01] 0.082
> 65 letters					
N'/N	114 / 114	90 / 90			
Any severe AE, n (%)	19 (16.7)	8 (8.9)	2.05 [0.85; 4.93] 0.109	1.88 [0.86; 4.08] 0.113	0.08 [-0.01; 0.17] 0.091
Pooled Analysis					
Interaction Test:	p = 0.013 *				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any severe AE, n (%)	14 (10.1)	26 (16.8)	0.54 [0.27; 1.08] 0.082	0.54 [0.29; 1.00] 0.046 *	-0.08 [-0.16; -0.00] 0.041 *
> 65 letters					
N'/N	229 / 229	213 / 213			
Any severe AE, n (%)	33 (14.4)	20 (9.4)	1.72 [0.94; 3.13] 0.076	1.52 [0.90; 2.58] 0.116	0.05 [-0.01; 0.11] 0.111

	Treatment Groups		Comparison		
Any severe adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.596**					
KESTREL					
Interaction Test:	p = 0.245				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any severe AE, n (%)	17 (23.0)	19 (29.7)	0.71 [0.33; 1.51] 0.371	0.77 [0.44; 1.36] 0.371	-0.07 [-0.21; 0.08] 0.372
> 65 letters					
N'/N	115 / 115	123 / 123			
Any severe AE, n (%)	25 (21.7)	22 (17.9)	1.28 [0.67; 2.42] 0.456	1.22 [0.73; 2.03] 0.456	0.04 [-0.06; 0.14] 0.456
KITE					
Interaction Test:	p = 0.124				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any severe AE, n (%)	9 (13.8)	23 (25.3)	0.48 [0.20; 1.11] 0.085	0.55 [0.27; 1.11] 0.093	-0.11 [-0.24; 0.01] 0.068
> 65 letters					
N'/N	114 / 114	90 / 90			
Any severe AE, n (%)	31 (27.2)	23 (25.6)	1.09 [0.58; 2.04] 0.792	1.06 [0.67; 1.69] 0.793	0.02 [-0.11; 0.14] 0.792
Pooled Analysis					
Interaction Test:	p = 0.077				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any severe AE, n (%)	26 (18.7)	42 (27.1)	0.63 [0.36; 1.10] 0.102	0.66 [0.43; 1.03] 0.064	-0.09 [-0.19; 0.00] 0.059

	Treatment Groups		Comparison		
Any severe adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any severe AE, n (%)	56 (24.5)	45 (21.1)	1.20 [0.77; 1.87] 0.427	1.13 [0.80; 1.60] 0.478	0.03 [-0.05; 0.11] 0.477

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-1.5 Any severe adverse event by region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.532**					
KESTREL					
Interaction Test:	p = 0.994				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any severe AE, n (%)	16 (17.8)	16 (19.3)	0.91 [0.42; 1.95] 0.800	0.92 [0.49; 1.72] 0.800	-0.01 [-0.13; 0.10] 0.800
European Region					
N'/N	69 / 69	75 / 75			
Any severe AE, n (%)	8 (11.6)	10 (13.3)	0.85 [0.32; 2.30] 0.753	0.87 [0.36; 2.08] 0.753	-0.02 [-0.13; 0.09] 0.752
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any severe AE, n (%)	1 (3.3)	1 (3.4)	0.97 [0.06; 16.20] 0.981	0.97 [0.06; 14.74] 0.981	-0.00 [-0.09; 0.09] 0.981
KITE					
Interaction Test:	N.E.				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any severe AE, n (%)	3 (11.5)	0 (0.0)	N.E.	5.70 [0.31; 104.62] 0.241	0.12 [-0.01; 0.24] 0.066
European Region					
N'/N	135 / 135	132 / 132			
Any severe AE, n (%)	14 (10.4)	18 (13.6)	0.73 [0.35; 1.54] 0.413	0.76 [0.39; 1.47] 0.413	-0.03 [-0.11; 0.05] 0.411
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any severe AE, n (%)	5 (27.8)	1 (3.6)	10.38 [1.10; 98.20] 0.041 *	7.78 [0.99; 61.25] 0.051	0.24 [0.02; 0.46] 0.030 *

	Treatment Groups		Comparison		
Any severe adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	N.E.				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any severe AE, n (%)	16 (17.8)	16 (19.3)	N.E.	0.92 [0.49; 1.72] 0.800	-0.01 [-0.13; 0.10] 0.800
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any severe AE, n (%)	3 (11.5)	0 (0.0)	N.E.	5.70 [0.31; 104.62] 0.178	0.12 [-0.01; 0.24] 0.066
European Region					
N'/N	204 / 204	207 / 207			
Any severe AE, n (%)	22 (10.8)	28 (13.5)	0.79 [0.42; 1.48] 0.463	0.80 [0.47; 1.35] 0.398	-0.03 [-0.09; 0.04] 0.397
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any severe AE, n (%)	6 (12.5)	2 (3.5)	3.09 [0.51; 18.92] 0.222	3.93 [0.90; 17.19] 0.047 *	0.10 [-0.01; 0.21] 0.064
Any severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.596**					
KESTREL					
Interaction Test:	p = 0.721				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any severe AE, n (%)	28 (31.1)	23 (27.7)	1.18 [0.61; 2.27] 0.624	1.12 [0.71; 1.79] 0.625	0.03 [-0.10; 0.17] 0.623
European Region					
N'/N	69 / 69	75 / 75			
Any severe AE, n (%)	12 (17.4)	15 (20.0)	0.84 [0.36; 1.95] 0.689	0.87 [0.44; 1.73] 0.689	-0.03 [-0.15; 0.10] 0.688
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any severe AE, n (%)	2 (6.7)	3 (10.3)	0.62 [0.10; 4.01] 0.615	0.64 [0.12; 3.58] 0.616	-0.04 [-0.18; 0.11] 0.612

	Treatment Groups		Comparison		
Any severe adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.617				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any severe AE, n (%)	4 (15.4)	3 (14.3)	1.09 [0.22; 5.52] 0.916	1.08 [0.27; 4.29] 0.916	0.01 [-0.19; 0.22] 0.916
European Region					
N'/N	135 / 135	132 / 132			
Any severe AE, n (%)	30 (22.2)	36 (27.3)	0.76 [0.44; 1.33] 0.339	0.81 [0.53; 1.24] 0.340	-0.05 [-0.15; 0.05] 0.338
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any severe AE, n (%)	6 (33.3)	7 (25.0)	1.50 [0.41; 5.51] 0.541	1.33 [0.53; 3.33] 0.538	0.08 [-0.19; 0.35] 0.546
Pooled Analysis					
Interaction Test:	p = 0.822				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any severe AE, n (%)	28 (31.1)	23 (27.7)	1.22 [0.55; 2.72] 0.619	1.12 [0.71; 1.79] 0.625	0.03 [-0.10; 0.17] 0.623
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any severe AE, n (%)	4 (15.4)	3 (14.3)	1.05 [0.19; 5.68] 0.957	1.08 [0.27; 4.29] 0.917	0.01 [-0.19; 0.22] 0.916
European Region					
N'/N	204 / 204	207 / 207			
Any severe AE, n (%)	42 (20.6)	51 (24.6)	0.77 [0.46; 1.28] 0.312	0.83 [0.58; 1.19] 0.310	-0.04 [-0.12; 0.04] 0.308

	Treatment Groups		Comparison		
Any severe adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any severe AE, n (%)	8 (16.7)	10 (17.5)	1.00 [0.36; 2.80] 0.997	1.09 [0.49; 2.43] 0.841	0.01 [-0.13; 0.16] 0.842

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KITE: logit(proportion) = treatment [by region].
Week 52 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by region].

Table 14-1.6 Any severe adverse event by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.532**					
KESTREL					
Interaction Test:	p = 0.640				
Type 1					
N'/N	12 / 12	6 / 6			
Any severe AE, n (%)	1 (8.3)	1 (16.7)	0.45 [0.02; 8.83] 0.602	0.50 [0.04; 6.68] 0.600	-0.08 [-0.42; 0.25] 0.628
Type 2					
N'/N	177 / 177	181 / 181			
Any severe AE, n (%)	24 (13.6)	26 (14.4)	0.94 [0.51; 1.70] 0.826	0.94 [0.56; 1.58] 0.826	-0.01 [-0.08; 0.06] 0.826
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any severe AE, n (%)	0 (0.0)	2 (28.6)	N.E.	0.08 [0.00; 1.49] 0.090	-0.29 [-0.62; 0.05] 0.094
Type 2					
N'/N	160 / 160	174 / 174			
Any severe AE, n (%)	22 (13.8)	17 (9.8)	1.47 [0.75; 2.89] 0.260	1.41 [0.78; 2.55] 0.261	0.04 [-0.03; 0.11] 0.260
Pooled Analysis					
Interaction Test:	p = 0.057				
Type 1					
N'/N	31 / 31	13 / 13			
Any severe AE, n (%)	1 (3.2)	3 (23.1)	0.11 [0.01; 1.19] 0.070	0.19 [0.03; 1.14] 0.046 *	-0.20 [-0.44; 0.04] 0.110
Type 2					
N'/N	337 / 337	355 / 355			
Any severe AE, n (%)	46 (13.6)	43 (12.1)	1.16 [0.74; 1.82] 0.514	1.12 [0.76; 1.66] 0.556	0.02 [-0.03; 0.07] 0.556

	Treatment Groups		Comparison		
Any severe adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.596**					
KESTREL					
Interaction Test:	p = 0.694				
Type 1					
N'/N	12 / 12	6 / 6			
Any severe AE, n (%)	3 (25.0)	1 (16.7)	1.67 [0.13; 20.57] 0.691	1.50 [0.20; 11.54] 0.697	0.08 [-0.30; 0.47] 0.672
Type 2					
N'/N	177 / 177	181 / 181			
Any severe AE, n (%)	39 (22.0)	40 (22.1)	1.00 [0.60; 1.64] 0.988	1.00 [0.68; 1.47] 0.988	-0.00 [-0.09; 0.09] 0.988
KITE					
Interaction Test:	p = 0.322				
Type 1					
N'/N	19 / 19	7 / 7			
Any severe AE, n (%)	2 (10.5)	2 (28.6)	0.29 [0.03; 2.65] 0.275	0.37 [0.06; 2.14] 0.266	-0.18 [-0.54; 0.18] 0.329
Type 2					
N'/N	160 / 160	174 / 174			
Any severe AE, n (%)	38 (23.8)	44 (25.3)	0.92 [0.56; 1.52] 0.744	0.94 [0.64; 1.37] 0.745	-0.02 [-0.11; 0.08] 0.744
Pooled Analysis					
Interaction Test:	p = 0.641				
Type 1					
N'/N	31 / 31	13 / 13			
Any severe AE, n (%)	5 (16.1)	3 (23.1)	0.65 [0.13; 3.23] 0.596	0.72 [0.20; 2.55] 0.621	-0.06 [-0.33; 0.20] 0.637

	Treatment Groups		Comparison		
Any severe adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any severe AE, n (%)	77 (22.8)	84 (23.7)	0.96 [0.67; 1.36] 0.813	0.97 [0.74; 1.27] 0.810	-0.01 [-0.07; 0.06] 0.809

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KITE: logit(proportion) = treatment [by diabetes type].

Table 14-1.7 Any severe adverse event by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.532**					
KESTREL					
Interaction Test:	p = 0.683				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any severe AE, n (%)	8 (10.5)	12 (11.2)	0.93 [0.36; 2.40] 0.883	0.94 [0.40; 2.18] 0.883	-0.01 [-0.10; 0.08] 0.882
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any severe AE, n (%)	16 (14.3)	15 (18.8)	0.72 [0.33; 1.56] 0.408	0.76 [0.40; 1.45] 0.407	-0.04 [-0.15; 0.06] 0.415
KITE					
Interaction Test:	p = 0.541				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any severe AE, n (%)	7 (8.5)	9 (9.4)	0.90 [0.32; 2.54] 0.845	0.91 [0.35; 2.34] 0.846	-0.01 [-0.09; 0.08] 0.845
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any severe AE, n (%)	15 (15.5)	10 (11.8)	1.37 [0.58; 3.24] 0.471	1.31 [0.62; 2.77] 0.472	0.04 [-0.06; 0.14] 0.465
Pooled Analysis					
Interaction Test:	p = 0.911				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any severe AE, n (%)	15 (9.5)	21 (10.3)	0.93 [0.46; 1.87] 0.837	0.93 [0.49; 1.74] 0.811	-0.01 [-0.07; 0.05] 0.809
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any severe AE, n (%)	31 (14.8)	25 (15.2)	0.98 [0.55; 1.73] 0.939	0.97 [0.60; 1.57] 0.905	-0.00 [-0.08; 0.07] 0.906

	Treatment Groups		Comparison		
Any severe adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.596**					
KESTREL					
Interaction Test:	p = 0.240				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any severe AE, n (%)	14 (18.4)	16 (15.0)	1.28 [0.58; 2.82] 0.533	1.23 [0.64; 2.37] 0.532	0.03 [-0.08; 0.14] 0.538
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any severe AE, n (%)	27 (24.1)	25 (31.3)	0.70 [0.37; 1.33] 0.273	0.77 [0.49; 1.22] 0.271	-0.07 [-0.20; 0.06] 0.277
KITE					
Interaction Test:	p = 0.435				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any severe AE, n (%)	15 (18.3)	24 (25.0)	0.67 [0.33; 1.39] 0.283	0.73 [0.41; 1.30] 0.286	-0.07 [-0.19; 0.05] 0.275
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any severe AE, n (%)	25 (25.8)	22 (25.9)	0.99 [0.51; 1.93] 0.987	1.00 [0.61; 1.63] 0.987	-0.00 [-0.13; 0.13] 0.987
Pooled Analysis					
Interaction Test:	p = 0.808				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any severe AE, n (%)	29 (18.4)	40 (19.7)	0.91 [0.54; 1.55] 0.740	0.92 [0.60; 1.41] 0.701	-0.02 [-0.10; 0.07] 0.700

	Treatment Groups		Comparison		
Any severe adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any severe AE, n (%)	52 (24.9)	47 (28.5)	0.84 [0.53; 1.33] 0.452	0.87 [0.62; 1.22] 0.425	-0.04 [-0.13; 0.05] 0.427

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-1.8 Any severe adverse event by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.532**					
KESTREL					
Interaction Test:	p = 0.087				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any severe AE, n (%)	13 (10.8)	17 (15.5)	0.66 [0.31; 1.44] 0.301	0.70 [0.36; 1.38] 0.302	-0.05 [-0.13; 0.04] 0.301
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any severe AE, n (%)	4 (13.3)	8 (20.5)	0.60 [0.16; 2.21] 0.438	0.65 [0.22; 1.96] 0.443	-0.07 [-0.25; 0.10] 0.423
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any severe AE, n (%)	8 (20.5)	2 (5.3)	4.65 [0.92; 23.52] 0.064	3.90 [0.88; 17.18] 0.072	0.15 [0.01; 0.30] 0.040 *
KITE					
Interaction Test:	p = 0.895				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any severe AE, n (%)	10 (11.8)	8 (8.7)	1.40 [0.53; 3.73] 0.501	1.35 [0.56; 3.27] 0.502	0.03 [-0.06; 0.12] 0.501
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any severe AE, n (%)	4 (7.8)	4 (8.2)	0.96 [0.23; 4.06] 0.953	0.96 [0.25; 3.63] 0.953	-0.00 [-0.11; 0.10] 0.953
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any severe AE, n (%)	8 (18.6)	7 (17.5)	1.08 [0.35; 3.30] 0.896	1.06 [0.42; 2.66] 0.896	0.01 [-0.15; 0.18] 0.896

	Treatment Groups		Comparison		
Any severe adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.276				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any severe AE, n (%)	23 (11.2)	25 (12.4)	0.91 [0.49; 1.68] 0.763	0.90 [0.53; 1.52] 0.690	-0.01 [-0.08; 0.05] 0.691
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any severe AE, n (%)	8 (9.9)	12 (13.6)	0.69 [0.27; 1.80] 0.454	0.76 [0.33; 1.78] 0.533	-0.03 [-0.13; 0.06] 0.527
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any severe AE, n (%)	16 (19.5)	9 (11.5)	1.87 [0.77; 4.54] 0.165	1.68 [0.79; 3.58] 0.170	0.08 [-0.03; 0.19] 0.165
Any severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.596**					
KESTREL					
Interaction Test:	p = 0.100				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any severe AE, n (%)	26 (21.7)	27 (24.5)	0.85 [0.46; 1.57] 0.605	0.88 [0.55; 1.42] 0.605	-0.03 [-0.14; 0.08] 0.605
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any severe AE, n (%)	4 (13.3)	9 (23.1)	0.51 [0.14; 1.86] 0.310	0.58 [0.20; 1.70] 0.318	-0.10 [-0.28; 0.08] 0.288
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any severe AE, n (%)	12 (30.8)	5 (13.2)	2.93 [0.92; 9.36] 0.069	2.34 [0.91; 6.00] 0.077	0.18 [-0.00; 0.36] 0.056

	Treatment Groups		Comparison		
Any severe adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.237				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any severe AE, n (%)	21 (24.7)	20 (21.7)	1.18 [0.59; 2.38] 0.640	1.14 [0.66; 1.94] 0.640	0.03 [-0.09; 0.15] 0.641
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any severe AE, n (%)	8 (15.7)	15 (30.6)	0.42 [0.16; 1.11] 0.081	0.51 [0.24; 1.10] 0.086	-0.15 [-0.31; 0.01] 0.073
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any severe AE, n (%)	11 (25.6)	11 (27.5)	0.91 [0.34; 2.40] 0.843	0.93 [0.45; 1.90] 0.843	-0.02 [-0.21; 0.17] 0.843
Pooled Analysis					
Interaction Test:	p = 0.090				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any severe AE, n (%)	47 (22.9)	47 (23.3)	0.98 [0.62; 1.56] 0.935	0.99 [0.69; 1.40] 0.936	-0.00 [-0.09; 0.08] 0.936
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any severe AE, n (%)	12 (14.8)	24 (27.3)	0.47 [0.21; 1.01] 0.054	0.53 [0.29; 1.00] 0.043 *	-0.13 [-0.25; -0.01] 0.038 *

	Treatment Groups		Comparison		
Any severe adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any severe AE, n (%)	23 (28.0)	16 (20.5)	1.52 [0.73; 3.15] 0.264	1.36 [0.78; 2.38] 0.273	0.07 [-0.06; 0.21] 0.270

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-1.9 Any severe adverse event by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.532**					
KESTREL					
Interaction Test:	p = 0.263				
focal					
N'/N	59 / 59	48 / 48			
Any severe AE, n (%)	5 (8.5)	7 (14.6)	0.54 [0.16; 1.83] 0.325	0.58 [0.20; 1.72] 0.326	-0.06 [-0.18; 0.06] 0.329
diffuse					
N'/N	127 / 127	134 / 134			
Any severe AE, n (%)	20 (15.7)	18 (13.4)	1.20 [0.60; 2.40] 0.596	1.17 [0.65; 2.11] 0.597	0.02 [-0.06; 0.11] 0.597
KITE					
Interaction Test:	p = 0.286				
focal					
N'/N	63 / 63	66 / 66			
Any severe AE, n (%)	7 (11.1)	9 (13.6)	0.79 [0.28; 2.27] 0.664	0.81 [0.32; 2.06] 0.664	-0.03 [-0.14; 0.09] 0.663
diffuse					
N'/N	115 / 115	109 / 109			
Any severe AE, n (%)	15 (13.0)	9 (8.3)	1.67 [0.70; 3.98] 0.251	1.58 [0.72; 3.46] 0.253	0.05 [-0.03; 0.13] 0.243
Pooled Analysis					
Interaction Test:	p = 0.128				
focal					
N'/N	122 / 122	114 / 114			
Any severe AE, n (%)	12 (9.8)	16 (14.0)	0.66 [0.30; 1.45] 0.299	0.71 [0.35; 1.42] 0.329	-0.04 [-0.12; 0.04] 0.329
diffuse					
N'/N	242 / 242	243 / 243			
Any severe AE, n (%)	35 (14.5)	27 (11.1)	1.39 [0.81; 2.39] 0.236	1.31 [0.82; 2.10] 0.255	0.03 [-0.02; 0.09] 0.253

	Treatment Groups		Comparison		
Any severe adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.596**					
KESTREL					
Interaction Test:	p = 0.278				
focal					
N'/N	59 / 59	48 / 48			
Any severe AE, n (%)	10 (16.9)	11 (22.9)	0.69 [0.26; 1.79] 0.441	0.74 [0.34; 1.59] 0.441	-0.06 [-0.21; 0.09] 0.444
diffuse					
N'/N	127 / 127	134 / 134			
Any severe AE, n (%)	32 (25.2)	28 (20.9)	1.28 [0.72; 2.27] 0.410	1.21 [0.77; 1.88] 0.410	0.04 [-0.06; 0.15] 0.409
KITE					
Interaction Test:	p = 0.462				
focal					
N'/N	63 / 63	66 / 66			
Any severe AE, n (%)	14 (22.2)	19 (28.8)	0.71 [0.32; 1.57] 0.394	0.77 [0.42; 1.40] 0.396	-0.07 [-0.22; 0.08] 0.391
diffuse					
N'/N	115 / 115	109 / 109			
Any severe AE, n (%)	26 (22.6)	24 (22.0)	1.03 [0.55; 1.94] 0.916	1.03 [0.63; 1.67] 0.916	0.01 [-0.10; 0.11] 0.916
Pooled Analysis					
Interaction Test:	p = 0.186				
focal					
N'/N	122 / 122	114 / 114			
Any severe AE, n (%)	24 (19.7)	30 (26.3)	0.70 [0.38; 1.28] 0.246	0.76 [0.47; 1.22] 0.252	-0.06 [-0.17; 0.04] 0.250

	Treatment Groups		Comparison		
Any severe adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any severe AE, n (%)	58 (24.0)	52 (21.4)	1.15 [0.75; 1.76] 0.513	1.12 [0.81; 1.56] 0.497	0.03 [-0.05; 0.10] 0.497

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-1.10 Any severe adverse event by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.532**					
KESTREL					
Interaction Test:	p = 0.863				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any severe AE, n (%)	11 (10.3)	12 (12.5)	0.80 [0.34; 1.91] 0.619	0.82 [0.38; 1.78] 0.619	-0.02 [-0.11; 0.07] 0.620
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any severe AE, n (%)	11 (15.7)	10 (14.1)	1.14 [0.45; 2.88] 0.786	1.12 [0.51; 2.46] 0.786	0.02 [-0.10; 0.13] 0.786
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any severe AE, n (%)	3 (25.0)	5 (25.0)	1.00 [0.19; 5.22] 1.000	1.00 [0.29; 3.45] 1.000	0.00 [-0.31; 0.31] 1.000
KITE					
Interaction Test:	p = 0.528				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any severe AE, n (%)	9 (10.6)	10 (12.2)	0.85 [0.33; 2.22] 0.744	0.87 [0.37; 2.03] 0.744	-0.02 [-0.11; 0.08] 0.744
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any severe AE, n (%)	10 (13.5)	6 (7.6)	1.90 [0.65; 5.52] 0.238	1.78 [0.68; 4.65] 0.240	0.06 [-0.04; 0.16] 0.233
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any severe AE, n (%)	3 (15.0)	3 (15.8)	0.94 [0.17; 5.36] 0.946	0.95 [0.22; 4.14] 0.946	-0.01 [-0.23; 0.22] 0.946

	Treatment Groups		Comparison		
Any severe adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.525				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any severe AE, n (%)	20 (10.4)	22 (12.4)	0.84 [0.44; 1.60] 0.587	0.84 [0.48; 1.49] 0.557	-0.02 [-0.08; 0.05] 0.557
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any severe AE, n (%)	21 (14.6)	16 (10.7)	1.43 [0.71; 2.87] 0.313	1.36 [0.74; 2.50] 0.319	0.04 [-0.04; 0.11] 0.318
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any severe AE, n (%)	6 (18.8)	8 (20.5)	0.92 [0.28; 3.00] 0.889	0.98 [0.38; 2.53] 0.963	-0.00 [-0.19; 0.18] 0.962
Any severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.596**					
KESTREL					
Interaction Test:	p = 0.777				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any severe AE, n (%)	21 (19.6)	19 (19.8)	0.99 [0.50; 1.98] 0.976	0.99 [0.57; 1.73] 0.976	-0.00 [-0.11; 0.11] 0.976
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any severe AE, n (%)	17 (24.3)	14 (19.7)	1.31 [0.59; 2.91] 0.513	1.23 [0.66; 2.30] 0.514	0.05 [-0.09; 0.18] 0.512
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any severe AE, n (%)	4 (33.3)	8 (40.0)	0.75 [0.17; 3.35] 0.706	0.83 [0.32; 2.18] 0.711	-0.07 [-0.41; 0.28] 0.703

	Treatment Groups		Comparison		
Any severe adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.891				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any severe AE, n (%)	19 (22.4)	19 (23.2)	0.95 [0.46; 1.97] 0.900	0.96 [0.55; 1.69] 0.900	-0.01 [-0.14; 0.12] 0.900
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any severe AE, n (%)	16 (21.6)	21 (26.6)	0.76 [0.36; 1.61] 0.475	0.81 [0.46; 1.44] 0.476	-0.05 [-0.18; 0.09] 0.472
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any severe AE, n (%)	5 (25.0)	6 (31.6)	0.72 [0.18; 2.93] 0.648	0.79 [0.29; 2.17] 0.649	-0.07 [-0.35; 0.22] 0.648
Pooled Analysis					
Interaction Test:	p = 0.834				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any severe AE, n (%)	40 (20.8)	38 (21.3)	0.97 [0.59; 1.59] 0.891	0.98 [0.66; 1.45] 0.914	-0.00 [-0.09; 0.08] 0.914
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any severe AE, n (%)	33 (22.9)	35 (23.3)	0.99 [0.57; 1.70] 0.962	0.98 [0.65; 1.49] 0.937	-0.00 [-0.10; 0.09] 0.937

	Treatment Groups		Comparison		
Any severe adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any severe AE, n (%)	9 (28.1)	14 (35.9)	0.70 [0.25; 1.93] 0.492	0.81 [0.40; 1.63] 0.560	-0.07 [-0.28; 0.15] 0.552

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-1.11 Any severe adverse event by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.532**					
KESTREL					
Interaction Test:	p = 0.933				
presence					
N'/N	62 / 62	61 / 61			
Any severe AE, n (%)	10 (16.1)	11 (18.0)	0.87 [0.34; 2.24] 0.779	0.89 [0.41; 1.95] 0.779	-0.02 [-0.15; 0.11] 0.779
absence					
N'/N	127 / 127	126 / 126			
Any severe AE, n (%)	15 (11.8)	16 (12.7)	0.92 [0.43; 1.95] 0.830	0.93 [0.48; 1.80] 0.830	-0.01 [-0.09; 0.07] 0.830
KITE					
Interaction Test:	p = 0.316				
presence					
N'/N	56 / 56	67 / 67			
Any severe AE, n (%)	5 (8.9)	8 (11.9)	0.72 [0.22; 2.35] 0.590	0.75 [0.26; 2.16] 0.591	-0.03 [-0.14; 0.08] 0.584
absence					
N'/N	123 / 123	114 / 114			
Any severe AE, n (%)	17 (13.8)	11 (9.6)	1.50 [0.67; 3.36] 0.322	1.43 [0.70; 2.93] 0.324	0.04 [-0.04; 0.12] 0.316
Pooled Analysis					
Interaction Test:	p = 0.455				
presence					
N'/N	118 / 118	128 / 128			
Any severe AE, n (%)	15 (12.7)	19 (14.8)	0.83 [0.40; 1.73] 0.625	0.84 [0.45; 1.57] 0.578	-0.02 [-0.11; 0.06] 0.574

	Treatment Groups		Comparison		
Any severe adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any severe AE, n (%)	32 (12.8)	27 (11.3)	1.18 [0.68; 2.04] 0.554	1.14 [0.70; 1.84] 0.597	0.02 [-0.04; 0.07] 0.596
Any severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.596**					
KESTREL					
Interaction Test:	p = 0.707				
presence					
N'/N	62 / 62	61 / 61			
Any severe AE, n (%)	15 (24.2)	16 (26.2)	0.90 [0.40; 2.03] 0.795	0.92 [0.50; 1.70] 0.795	-0.02 [-0.17; 0.13] 0.795
absence					
N'/N	127 / 127	126 / 126			
Any severe AE, n (%)	27 (21.3)	25 (19.8)	1.09 [0.59; 2.01] 0.780	1.07 [0.66; 1.74] 0.780	0.01 [-0.09; 0.11] 0.780
KITE					
Interaction Test:	p = 0.505				
presence					
N'/N	56 / 56	67 / 67			
Any severe AE, n (%)	11 (19.6)	18 (26.9)	0.67 [0.28; 1.56] 0.349	0.73 [0.38; 1.42] 0.353	-0.07 [-0.22; 0.08] 0.341
absence					
N'/N	123 / 123	114 / 114			
Any severe AE, n (%)	29 (23.6)	28 (24.6)	0.95 [0.52; 1.72] 0.859	0.96 [0.61; 1.51] 0.859	-0.01 [-0.12; 0.10] 0.859
Pooled Analysis					
Interaction Test:	p = 0.488				
presence					
N'/N	118 / 118	128 / 128			
Any severe AE, n (%)	26 (22.0)	34 (26.6)	0.79 [0.44; 1.42] 0.426	0.83 [0.53; 1.29] 0.402	-0.05 [-0.15; 0.06] 0.398

	Treatment Groups		Comparison		
Any severe adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any severe AE, n (%)	56 (22.4)	53 (22.1)	1.02 [0.66; 1.56] 0.934	1.01 [0.73; 1.41] 0.945	0.00 [-0.07; 0.08] 0.945

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-1.12 Any severe adverse event by exposure (week 52) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe adverse event by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.532**					
KESTREL					
Interaction Test:	p = 0.160				
Non-exposed					
N'/N	71 / 71	75 / 75			
Any severe AE, n (%)	15 (21.1)	12 (16.0)	1.41 [0.61; 3.26] 0.426	1.32 [0.66; 2.62] 0.427	0.05 [-0.07; 0.18] 0.426
Exposed					
N'/N	118 / 118	112 / 112			
Any severe AE, n (%)	10 (8.5)	15 (13.4)	0.60 [0.26; 1.40] 0.235	0.63 [0.30; 1.35] 0.236	-0.05 [-0.13; 0.03] 0.232
KITE					
Interaction Test:	p = 0.375				
Non-exposed					
N'/N	85 / 85	90 / 90			
Any severe AE, n (%)	15 (17.6)	11 (12.2)	1.54 [0.66; 3.57] 0.316	1.44 [0.70; 2.96] 0.317	0.05 [-0.05; 0.16] 0.314
Exposed					
N'/N	94 / 94	91 / 91			
Any severe AE, n (%)	7 (7.4)	8 (8.8)	0.83 [0.29; 2.40] 0.738	0.85 [0.32; 2.24] 0.738	-0.01 [-0.09; 0.07] 0.738
Pooled Analysis					
Interaction Test:	p = 0.100				
Non-exposed					
N'/N	156 / 156	165 / 165			
Any severe AE, n (%)	30 (19.2)	23 (13.9)	1.47 [0.81; 2.66] 0.205	1.38 [0.84; 2.27] 0.203	0.05 [-0.03; 0.13] 0.202

	Treatment Groups		Comparison		
Any severe adverse event by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	212 / 212	203 / 203			
Any severe AE, n (%)	17 (8.0)	23 (11.3)	0.69 [0.36; 1.35] 0.284	0.71 [0.39; 1.28] 0.252	-0.03 [-0.09; 0.02] 0.252

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-1.13 Any severe adverse event by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe adverse event by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.596**					
KESTREL					
Interaction Test:	p = 0.572				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any severe AE, n (%)	5 (41.7)	4 (30.8)	1.61 [0.31; 8.32] 0.572	1.35 [0.47; 3.89] 0.573	0.11 [-0.27; 0.48] 0.569
Exposed					
N'/N	177 / 177	174 / 174			
Any severe AE, n (%)	37 (20.9)	37 (21.3)	0.98 [0.59; 1.63] 0.934	0.98 [0.66; 1.47] 0.934	-0.00 [-0.09; 0.08] 0.934
KITE					
Interaction Test:	p = 0.086				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any severe AE, n (%)	10 (58.8)	4 (33.3)	2.86 [0.61; 13.33] 0.182	1.76 [0.72; 4.31] 0.213	0.25 [-0.10; 0.61] 0.159
Exposed					
N'/N	162 / 162	169 / 169			
Any severe AE, n (%)	30 (18.5)	42 (24.9)	0.69 [0.41; 1.17] 0.164	0.75 [0.49; 1.13] 0.166	-0.06 [-0.15; 0.03] 0.160
Pooled Analysis					
Interaction Test:	p = 0.088				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any severe AE, n (%)	15 (51.7)	8 (32.0)	2.29 [0.75; 6.97] 0.145	1.58 [0.80; 3.12] 0.174	0.19 [-0.07; 0.45] 0.159

	Treatment Groups		Comparison		
Any severe adverse event by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any severe AE, n (%)	67 (19.8)	79 (23.0)	0.83 [0.57; 1.19] 0.305	0.86 [0.64; 1.15] 0.300	-0.03 [-0.09; 0.03] 0.299

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-2.1 Any severe ocular adverse event (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular severe AE, n (%)	4 (2.1)	10 (5.3)	0.38 [0.12; 1.24] 0.110	0.40 [0.13; 1.24] 0.112	-0.03 [-0.07; 0.01] 0.098
KITE, N'/N	179 / 179	181 / 181			
Any ocular severe AE, n (%)	5 (2.8)	2 (1.1)	2.57 [0.49; 13.43] 0.263	2.53 [0.50; 12.86] 0.264	0.02 [-0.01; 0.05] 0.246
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular severe AE, n (%)	9 (2.4)	12 (3.3)	0.97 [0.36; 2.67] 0.958	0.75 [0.32; 1.75] 0.501	-0.01 [-0.03; 0.02] 0.502
p_H=0.066					
Any ocular severe AE, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular severe AE, n (%)	9 (4.8)	11 (5.9)	0.80 [0.32; 1.98] 0.629	0.81 [0.34; 1.91] 0.629	-0.01 [-0.06; 0.03] 0.628
KITE, N'/N	179 / 179	181 / 181			
Any ocular severe AE, n (%)	7 (3.9)	7 (3.9)	1.01 [0.35; 2.95] 0.983	1.01 [0.36; 2.82] 0.983	0.00 [-0.04; 0.04] 0.983
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular severe AE, n (%)	16 (4.3)	18 (4.9)	0.90 [0.45; 1.80] 0.761	0.89 [0.46; 1.71] 0.722	-0.01 [-0.04; 0.02] 0.722
p_H=0.743					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-2.2 Any severe ocular adverse event by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.066**					
KESTREL					
Interaction Test:	p = 0.994				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular severe AE, n (%)	3 (2.9)	7 (7.5)	0.36 [0.09; 1.45] 0.153	0.38 [0.10; 1.44] 0.155	-0.05 [-0.11; 0.02] 0.146
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular severe AE, n (%)	1 (1.2)	3 (3.2)	0.36 [0.04; 3.54] 0.382	0.37 [0.04; 3.48] 0.383	-0.02 [-0.06; 0.02] 0.350
KITE					
Interaction Test:	N.E.				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular severe AE, n (%)	2 (2.0)	0 (0.0)	N.E.	5.10 [0.25; 104.90] 0.291	0.02 [-0.01; 0.05] 0.153
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular severe AE, n (%)	3 (3.8)	2 (2.5)	1.52 [0.25; 9.35] 0.652	1.50 [0.26; 8.73] 0.652	0.01 [-0.04; 0.07] 0.649
Pooled Analysis					
Interaction Test:	p = 0.727				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular severe AE, n (%)	5 (2.5)	7 (3.6)	0.85 [0.24; 2.99] 0.799	0.68 [0.23; 1.97] 0.474	-0.01 [-0.05; 0.02] 0.461
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular severe AE, n (%)	4 (2.4)	5 (2.9)	1.16 [0.28; 4.90] 0.836	0.84 [0.23; 3.09] 0.788	-0.00 [-0.04; 0.03] 0.786

	Treatment Groups		Comparison		
Any severe ocular adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.743**					
KESTREL					
Interaction Test:	p = 0.926				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular severe AE, n (%)	6 (5.8)	7 (7.5)	0.75 [0.24; 2.32] 0.621	0.77 [0.27; 2.20] 0.621	-0.02 [-0.09; 0.05] 0.622
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular severe AE, n (%)	3 (3.5)	4 (4.3)	0.82 [0.18; 3.79] 0.803	0.83 [0.19; 3.60] 0.803	-0.01 [-0.06; 0.05] 0.802
KITE					
Interaction Test:	p = 0.985				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular severe AE, n (%)	3 (3.0)	3 (2.9)	1.02 [0.20; 5.18] 0.980	1.02 [0.21; 4.93] 0.980	0.00 [-0.05; 0.05] 0.980
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular severe AE, n (%)	4 (5.1)	4 (5.1)	1.00 [0.24; 4.15] 1.000	1.00 [0.26; 3.86] 1.000	0.00 [-0.07; 0.07] 1.000
Pooled Analysis					
Interaction Test:	p = 0.886				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular severe AE, n (%)	9 (4.4)	10 (5.1)	0.86 [0.34; 2.16] 0.743	0.84 [0.35; 2.01] 0.695	-0.01 [-0.05; 0.03] 0.695

	Treatment Groups		Comparison		
Any severe ocular adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular severe AE, n (%)	7 (4.3)	8 (4.6)	0.95 [0.33; 2.70] 0.921	0.92 [0.34; 2.47] 0.864	-0.00 [-0.05; 0.04] 0.864

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KITE: logit(proportion) = treatment [by age].

Table 14-2.3 Any severe ocular adverse event by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.066**					
KESTREL					
Interaction Test:	N.E.				
Male					
N'/N	110 / 110	126 / 126			
Any ocular severe AE, n (%)	4 (3.6)	5 (4.0)	0.91 [0.24; 3.49] 0.894	0.92 [0.25; 3.33] 0.894	-0.00 [-0.05; 0.05] 0.894
Female					
N'/N	79 / 79	61 / 61			
Any ocular severe AE, n (%)	0 (0.0)	5 (8.2)	N.E.	0.07 [0.00; 1.25] 0.071	-0.08 [-0.15; -0.01] 0.020 *
KITE					
Interaction Test:	N.E.				
Male					
N'/N	120 / 120	115 / 115			
Any ocular severe AE, n (%)	2 (1.7)	2 (1.7)	0.96 [0.13; 6.91] 0.966	0.96 [0.14; 6.69] 0.966	-0.00 [-0.03; 0.03] 0.966
Female					
N'/N	59 / 59	66 / 66			
Any ocular severe AE, n (%)	3 (5.1)	0 (0.0)	N.E.	7.82 [0.41; 148.25] 0.171	0.05 [-0.01; 0.11] 0.075
Pooled Analysis					
Interaction Test:	p = 0.564				
Male					
N'/N	230 / 230	241 / 241			
Any ocular severe AE, n (%)	6 (2.6)	7 (2.9)	1.19 [0.35; 4.06] 0.777	0.93 [0.32; 2.72] 0.894	-0.00 [-0.03; 0.03] 0.893

	Treatment Groups		Comparison		
Any severe ocular adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any ocular severe AE, n (%)	3 (2.2)	5 (3.9)	0.70 [0.15; 3.21] 0.641	0.62 [0.19; 1.99] 0.412	-0.02 [-0.06; 0.03] 0.406
Any ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.743**					
KESTREL					
Interaction Test:	p = 0.134				
Male					
N'/N	110 / 110	126 / 126			
Any ocular severe AE, n (%)	7 (6.4)	6 (4.8)	1.36 [0.44; 4.17] 0.592	1.34 [0.46; 3.86] 0.592	0.02 [-0.04; 0.07] 0.594
Female					
N'/N	79 / 79	61 / 61			
Any ocular severe AE, n (%)	2 (2.5)	5 (8.2)	0.29 [0.05; 1.55] 0.149	0.31 [0.06; 1.54] 0.151	-0.06 [-0.13; 0.02] 0.150
KITE					
Interaction Test:	p = 0.479				
Male					
N'/N	120 / 120	115 / 115			
Any ocular severe AE, n (%)	2 (1.7)	3 (2.6)	0.63 [0.10; 3.86] 0.620	0.64 [0.11; 3.75] 0.620	-0.01 [-0.05; 0.03] 0.618
Female					
N'/N	59 / 59	66 / 66			
Any ocular severe AE, n (%)	5 (8.5)	4 (6.1)	1.44 [0.37; 5.62] 0.604	1.40 [0.39; 4.96] 0.604	0.02 [-0.07; 0.12] 0.605
Pooled Analysis					
Interaction Test:	p = 0.533				
Male					
N'/N	230 / 230	241 / 241			
Any ocular severe AE, n (%)	9 (3.9)	9 (3.7)	1.09 [0.42; 2.81] 0.866	1.09 [0.44; 2.67] 0.852	0.00 [-0.03; 0.04] 0.852

	Treatment Groups		Comparison		
Any severe ocular adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any ocular severe AE, n (%)	7 (5.1)	9 (7.1)	0.70 [0.25; 1.95] 0.491	0.75 [0.29; 1.89] 0.536	-0.02 [-0.08; 0.04] 0.544

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE: logit(proportion) = treatment [by gender].

Table 14-2.4 Any severe ocular adverse event by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.066**					
KESTREL					
Interaction Test:	p = 0.046 *				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any ocular severe AE, n (%)	1 (1.4)	8 (12.5)	0.10 [0.01; 0.79] 0.029 *	0.11 [0.01; 0.84] 0.034 *	-0.11 [-0.20; -0.03] 0.010 *
> 65 letters					
N'/N	115 / 115	123 / 123			
Any ocular severe AE, n (%)	3 (2.6)	2 (1.6)	1.62 [0.27; 9.88] 0.601	1.60 [0.27; 9.43] 0.601	0.01 [-0.03; 0.05] 0.600
KITE					
Interaction Test:	p = 0.919				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any ocular severe AE, n (%)	2 (3.1)	1 (1.1)	2.86 [0.25; 32.19] 0.396	2.80 [0.26; 30.23] 0.396	0.02 [-0.03; 0.07] 0.411
> 65 letters					
N'/N	114 / 114	90 / 90			
Any ocular severe AE, n (%)	3 (2.6)	1 (1.1)	2.41 [0.25; 23.52] 0.451	2.37 [0.25; 22.39] 0.452	0.02 [-0.02; 0.05] 0.414
Pooled Analysis					
Interaction Test:	p = 0.051				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any ocular severe AE, n (%)	3 (2.2)	9 (5.8)	0.44 [0.11; 1.78] 0.247	0.35 [0.10; 1.15] 0.067	-0.04 [-0.09; 0.00] 0.073

	Treatment Groups		Comparison		
Any severe ocular adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any ocular severe AE, n (%)	6 (2.6)	3 (1.4)	3.02 [0.65; 13.93] 0.157	1.88 [0.47; 7.54] 0.363	0.01 [-0.01; 0.04] 0.355
Any ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.743**					
KESTREL					
Interaction Test:	p = 0.006 *				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any ocular severe AE, n (%)	2 (2.7)	9 (14.1)	0.17 [0.04; 0.82] 0.027 *	0.19 [0.04; 0.86] 0.031 *	-0.11 [-0.21; -0.02] 0.016 *
> 65 letters					
N'/N	115 / 115	123 / 123			
Any ocular severe AE, n (%)	7 (6.1)	2 (1.6)	3.92 [0.80; 19.28] 0.093	3.74 [0.79; 17.65] 0.095	0.04 [-0.00; 0.09] 0.075
KITE					
Interaction Test:	p = 0.588				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any ocular severe AE, n (%)	3 (4.6)	3 (3.3)	1.42 [0.28; 7.27] 0.674	1.40 [0.29; 6.72] 0.674	0.01 [-0.05; 0.08] 0.681
> 65 letters					
N'/N	114 / 114	90 / 90			
Any ocular severe AE, n (%)	4 (3.5)	4 (4.4)	0.78 [0.19; 3.22] 0.733	0.79 [0.20; 3.07] 0.733	-0.01 [-0.06; 0.04] 0.736
Pooled Analysis					
Interaction Test:	p = 0.051				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any ocular severe AE, n (%)	5 (3.6)	12 (7.7)	0.43 [0.15; 1.26] 0.125	0.44 [0.17; 1.17] 0.087	-0.05 [-0.10; 0.01] 0.090

	Treatment Groups		Comparison		
Any severe ocular adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any ocular severe AE, n (%)	11 (4.8)	6 (2.8)	1.89 [0.67; 5.33] 0.226	1.68 [0.65; 4.36] 0.280	0.02 [-0.02; 0.06] 0.281

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-2.5 Any severe ocular adverse event by region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.743**					
KESTREL					
Interaction Test:	N.E.				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular severe AE, n (%)	7 (7.8)	6 (7.2)	1.08 [0.35; 3.36] 0.891	1.08 [0.38; 3.07] 0.891	0.01 [-0.07; 0.08] 0.891
European Region					
N'/N	69 / 69	75 / 75			
Any ocular severe AE, n (%)	2 (2.9)	4 (5.3)	0.53 [0.09; 2.99] 0.472	0.54 [0.10; 2.87] 0.473	-0.02 [-0.09; 0.04] 0.459
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any ocular severe AE, n (%)	0 (0.0)	1 (3.4)	N.E.	0.32 [0.01; 7.61] 0.483	-0.03 [-0.10; 0.03] 0.309
KITE					
Interaction Test:	p = 0.939				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular severe AE, n (%)	1 (3.8)	1 (4.8)	0.80 [0.05; 13.60] 0.877	0.81 [0.05; 12.16] 0.877	-0.01 [-0.13; 0.11] 0.878
European Region					
N'/N	135 / 135	132 / 132			
Any ocular severe AE, n (%)	5 (3.7)	5 (3.8)	0.98 [0.28; 3.46] 0.971	0.98 [0.29; 3.30] 0.971	-0.00 [-0.05; 0.04] 0.971
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any ocular severe AE, n (%)	1 (5.6)	1 (3.6)	1.59 [0.09; 27.11] 0.749	1.56 [0.10; 23.33] 0.749	0.02 [-0.11; 0.15] 0.758

	Treatment Groups		Comparison		
Any severe ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.821				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular severe AE, n (%)	7 (7.8)	6 (7.2)	1.69 [0.37; 7.71] 0.497	1.08 [0.38; 3.07] 0.891	0.01 [-0.07; 0.08] 0.891
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular severe AE, n (%)	1 (3.8)	1 (4.8)	0.50 [0.02; 10.31] 0.656	0.81 [0.05; 12.16] 0.878	-0.01 [-0.13; 0.11] 0.878
European Region					
N'/N	204 / 204	207 / 207			
Any ocular severe AE, n (%)	7 (3.4)	9 (4.3)	0.65 [0.21; 2.00] 0.457	0.79 [0.30; 2.09] 0.636	-0.01 [-0.05; 0.03] 0.634
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any ocular severe AE, n (%)	1 (2.1)	2 (3.5)	0.61 [0.05; 6.93] 0.688	0.74 [0.11; 5.03] 0.760	-0.01 [-0.08; 0.05] 0.732

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL: logit(proportion) = treatment [by region].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 14-2.6 Any severe ocular adverse event by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.066**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular severe AE, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular severe AE, n (%)	4 (2.3)	10 (5.5)	0.40 [0.12; 1.28] 0.123	0.41 [0.13; 1.28] 0.125	-0.03 [-0.07; 0.01] 0.108
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular severe AE, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular severe AE, n (%)	5 (3.1)	2 (1.1)	2.77 [0.53; 14.50] 0.227	2.72 [0.53; 13.82] 0.228	0.02 [-0.01; 0.05] 0.216
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular severe AE, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular severe AE, n (%)	9 (2.7)	12 (3.4)	1.03 [0.37; 2.82] 0.959	0.78 [0.34; 1.83] 0.572	-0.01 [-0.03; 0.02] 0.572
Any ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.743**					

	Treatment Groups		Comparison		
Any severe ocular adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular severe AE, n (%)	1 (8.3)	0 (0.0)	N.E.	1.62 [0.08; 34.66] 0.759	0.08 [-0.07; 0.24] 0.296
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular severe AE, n (%)	8 (4.5)	11 (6.1)	0.73 [0.29; 1.86] 0.512	0.74 [0.31; 1.81] 0.513	-0.02 [-0.06; 0.03] 0.510
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular severe AE, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular severe AE, n (%)	7 (4.4)	7 (4.0)	1.09 [0.37; 3.18] 0.873	1.09 [0.39; 3.03] 0.873	0.00 [-0.04; 0.05] 0.873
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular severe AE, n (%)	1 (3.2)	0 (0.0)	N.E.	1.62 [0.08; 34.66] 0.761	0.04 [-0.03; 0.10] 0.280

	Treatment Groups		Comparison		
Any severe ocular adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular severe AE, n (%)	15 (4.5)	18 (5.1)	0.89 [0.44; 1.81] 0.747	0.87 [0.45; 1.71] 0.695	-0.01 [-0.04; 0.03] 0.694

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE, Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by diabetes type].
Week 52 / Pooled Analysis, Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 14-2.7 Any severe ocular adverse event by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.066**					
KESTREL					
Interaction Test:	p = 0.726				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any ocular severe AE, n (%)	1 (1.3)	3 (2.8)	0.46 [0.05; 4.53] 0.508	0.47 [0.05; 4.43] 0.509	-0.01 [-0.06; 0.03] 0.471
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any ocular severe AE, n (%)	3 (2.7)	7 (8.8)	0.29 [0.07; 1.15] 0.077	0.31 [0.08; 1.15] 0.079	-0.06 [-0.13; 0.01] 0.084
KITE					
Interaction Test:	p = 0.943				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any ocular severe AE, n (%)	2 (2.4)	1 (1.0)	2.37 [0.21; 26.67] 0.483	2.34 [0.22; 25.36] 0.484	0.01 [-0.03; 0.05] 0.483
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any ocular severe AE, n (%)	3 (3.1)	1 (1.2)	2.68 [0.27; 26.27] 0.397	2.63 [0.28; 24.80] 0.399	0.02 [-0.02; 0.06] 0.364
Pooled Analysis					
Interaction Test:	p = 0.554				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any ocular severe AE, n (%)	3 (1.9)	4 (2.0)	1.31 [0.26; 6.53] 0.743	0.97 [0.21; 4.42] 0.973	-0.00 [-0.03; 0.03] 0.973

	Treatment Groups		Comparison		
Any severe ocular adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any ocular severe AE, n (%)	6 (2.9)	8 (4.8)	0.74 [0.23; 2.43] 0.625	0.57 [0.21; 1.59] 0.279	-0.02 [-0.06; 0.02] 0.300
Any ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.743**					
KESTREL					
Interaction Test:	p = 0.875				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any ocular severe AE, n (%)	2 (2.6)	4 (3.7)	0.70 [0.12; 3.90] 0.680	0.70 [0.13; 3.75] 0.681	-0.01 [-0.06; 0.04] 0.670
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any ocular severe AE, n (%)	6 (5.4)	7 (8.8)	0.59 [0.19; 1.83] 0.361	0.61 [0.21; 1.75] 0.361	-0.03 [-0.11; 0.04] 0.373
KITE					
Interaction Test:	p = 0.784				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any ocular severe AE, n (%)	3 (3.7)	3 (3.1)	1.18 [0.23; 6.00] 0.845	1.17 [0.24; 5.64] 0.844	0.01 [-0.05; 0.06] 0.845
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any ocular severe AE, n (%)	4 (4.1)	4 (4.7)	0.87 [0.21; 3.59] 0.848	0.88 [0.23; 3.40] 0.849	-0.01 [-0.07; 0.05] 0.849
Pooled Analysis					
Interaction Test:	p = 0.700				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any ocular severe AE, n (%)	5 (3.2)	7 (3.4)	0.95 [0.29; 3.06] 0.929	0.92 [0.29; 2.85] 0.880	-0.00 [-0.04; 0.03] 0.879

	Treatment Groups		Comparison		
Any severe ocular adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any ocular severe AE, n (%)	10 (4.8)	11 (6.7)	0.71 [0.29; 1.72] 0.450	0.70 [0.31; 1.61] 0.403	-0.02 [-0.07; 0.03] 0.412

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-2.8 Any severe ocular adverse event by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.066**					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any ocular severe AE, n (%)	3 (2.5)	6 (5.5)	0.44 [0.11; 1.82] 0.260	0.46 [0.12; 1.79] 0.261	-0.03 [-0.08; 0.02] 0.254
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any ocular severe AE, n (%)	0 (0.0)	4 (10.3)	N.E.	0.14 [0.01; 2.56] 0.187	-0.10 [-0.20; -0.01] 0.035 *
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any ocular severe AE, n (%)	1 (2.6)	0 (0.0)	N.E.	2.93 [0.12; 69.64] 0.507	0.03 [-0.02; 0.08] 0.311
KITE					
Interaction Test:	N.E.				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any ocular severe AE, n (%)	1 (1.2)	1 (1.1)	1.08 [0.07; 17.60] 0.955	1.08 [0.07; 17.03] 0.955	0.00 [-0.03; 0.03] 0.955
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any ocular severe AE, n (%)	1 (2.0)	0 (0.0)	N.E.	2.88 [0.12; 69.16] 0.513	0.02 [-0.02; 0.06] 0.313
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any ocular severe AE, n (%)	3 (7.0)	1 (2.5)	2.92 [0.29; 29.34] 0.362	2.79 [0.30; 25.74] 0.365	0.04 [-0.05; 0.13] 0.331

	Treatment Groups		Comparison		
Any severe ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.192				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any ocular severe AE, n (%)	4 (2.0)	7 (3.5)	0.78 [0.20; 3.04] 0.725	0.54 [0.16; 1.80] 0.310	-0.02 [-0.05; 0.02] 0.313
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any ocular severe AE, n (%)	1 (1.2)	4 (4.5)	0.30 [0.03; 2.92] 0.301	0.46 [0.08; 2.50] 0.350	-0.03 [-0.08; 0.02] 0.228
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any ocular severe AE, n (%)	4 (4.9)	1 (1.3)	5.06 [0.52; 49.27] 0.163	2.83 [0.46; 17.49] 0.241	0.04 [-0.02; 0.09] 0.185
Any ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.743**					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any ocular severe AE, n (%)	7 (5.8)	7 (6.4)	0.91 [0.31; 2.69] 0.867	0.92 [0.33; 2.53] 0.867	-0.01 [-0.07; 0.06] 0.867
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any ocular severe AE, n (%)	0 (0.0)	4 (10.3)	N.E.	0.14 [0.01; 2.56] 0.187	-0.10 [-0.20; -0.01] 0.035 *
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any ocular severe AE, n (%)	2 (5.1)	0 (0.0)	N.E.	4.88 [0.24; 98.32] 0.301	0.05 [-0.02; 0.12] 0.147

	Treatment Groups		Comparison		
Any severe ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.301				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any ocular severe AE, n (%)	1 (1.2)	4 (4.3)	0.26 [0.03; 2.39] 0.235	0.27 [0.03; 2.37] 0.238	-0.03 [-0.08; 0.02] 0.191
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any ocular severe AE, n (%)	3 (5.9)	2 (4.1)	1.47 [0.23; 9.19] 0.681	1.44 [0.25; 8.26] 0.682	0.02 [-0.07; 0.10] 0.678
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any ocular severe AE, n (%)	3 (7.0)	1 (2.5)	2.93 [0.29; 29.34] 0.362	2.79 [0.30; 25.74] 0.365	0.04 [-0.05; 0.13] 0.331
Pooled Analysis					
Interaction Test:	p = 0.208				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any ocular severe AE, n (%)	8 (3.9)	11 (5.4)	0.72 [0.28; 1.85] 0.491	0.69 [0.28; 1.70] 0.422	-0.02 [-0.06; 0.02] 0.420
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any ocular severe AE, n (%)	3 (3.7)	6 (6.8)	0.53 [0.13; 2.22] 0.389	0.59 [0.16; 2.21] 0.422	-0.03 [-0.10; 0.04] 0.363

	Treatment Groups		Comparison		
Any severe ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any ocular severe AE, n (%)	5 (6.1)	1 (1.3)	5.08 [0.58; 44.63] 0.142	3.47 [0.59; 20.52] 0.142	0.05 [-0.01; 0.11] 0.102

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE, Week 100 / KESTREL: logit(proportion) = treatment [by duration of DME].

Table 14-2.9 Any severe ocular adverse event by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.066**					
KESTREL					
Interaction Test:	N.E.				
focal					
N'/N	59 / 59	48 / 48			
Any ocular severe AE, n (%)	0 (0.0)	2 (4.2)	N.E.	0.16 [0.01; 3.32] 0.238	-0.04 [-0.10; 0.01] 0.149
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular severe AE, n (%)	4 (3.1)	7 (5.2)	0.59 [0.17; 2.07] 0.409	0.60 [0.18; 2.01] 0.410	-0.02 [-0.07; 0.03] 0.401
KITE					
Interaction Test:	p = 0.857				
focal					
N'/N	63 / 63	66 / 66			
Any ocular severe AE, n (%)	2 (3.2)	1 (1.5)	2.13 [0.19; 24.11] 0.541	2.10 [0.19; 22.54] 0.542	0.02 [-0.04; 0.07] 0.535
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular severe AE, n (%)	3 (2.6)	1 (0.9)	2.89 [0.30; 28.23] 0.361	2.84 [0.30; 26.92] 0.362	0.02 [-0.02; 0.05] 0.332
Pooled Analysis					
Interaction Test:	p = 0.618				
focal					
N'/N	122 / 122	114 / 114			
Any ocular severe AE, n (%)	2 (1.6)	3 (2.6)	0.69 [0.11; 4.38] 0.690	0.67 [0.14; 3.17] 0.611	-0.01 [-0.05; 0.03] 0.618

	Treatment Groups		Comparison		
Any severe ocular adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular severe AE, n (%)	7 (2.9)	8 (3.3)	1.17 [0.37; 3.70] 0.793	0.90 [0.33; 2.45] 0.831	-0.00 [-0.03; 0.03] 0.830
Any ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.743**					
KESTREL					
Interaction Test:	N.E.				
focal					
N'/N	59 / 59	48 / 48			
Any ocular severe AE, n (%)	0 (0.0)	2 (4.2)	N.E.	0.16 [0.01; 3.32] 0.238	-0.04 [-0.10; 0.01] 0.149
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular severe AE, n (%)	9 (7.1)	8 (6.0)	1.20 [0.45; 3.22] 0.715	1.19 [0.47; 2.98] 0.715	0.01 [-0.05; 0.07] 0.715
KITE					
Interaction Test:	p = 0.720				
focal					
N'/N	63 / 63	66 / 66			
Any ocular severe AE, n (%)	4 (6.3)	3 (4.5)	1.42 [0.31; 6.63] 0.653	1.40 [0.33; 5.99] 0.653	0.02 [-0.06; 0.10] 0.652
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular severe AE, n (%)	3 (2.6)	3 (2.8)	0.95 [0.19; 4.79] 0.947	0.95 [0.20; 4.60] 0.947	-0.00 [-0.04; 0.04] 0.947
Pooled Analysis					
Interaction Test:	p = 0.575				
focal					
N'/N	122 / 122	114 / 114			
Any ocular severe AE, n (%)	4 (3.3)	5 (4.4)	0.73 [0.19; 2.78] 0.642	0.80 [0.24; 2.63] 0.713	-0.01 [-0.06; 0.04] 0.726

	Treatment Groups		Comparison		
Any severe ocular adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular severe AE, n (%)	12 (5.0)	11 (4.5)	1.15 [0.49; 2.69] 0.756	1.12 [0.51; 2.48] 0.781	0.01 [-0.03; 0.04] 0.781

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 100 / KESTREL: logit(proportion) = treatment [by DME type].

Table 14-2.10 Any severe ocular adverse event by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.066**					
KESTREL					
Interaction Test:	N.E.				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any ocular severe AE, n (%)	1 (0.9)	5 (5.2)	0.17 [0.02; 1.50] 0.111	0.18 [0.02; 1.51] 0.114	-0.04 [-0.09; 0.01] 0.081
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any ocular severe AE, n (%)	3 (4.3)	1 (1.4)	3.13 [0.32; 30.88] 0.328	3.04 [0.32; 28.55] 0.330	0.03 [-0.03; 0.08] 0.303
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any ocular severe AE, n (%)	0 (0.0)	4 (20.0)	N.E.	0.18 [0.01; 3.07] 0.236	-0.20 [-0.38; -0.02] 0.025 *
KITE					
Interaction Test:	N.E.				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any ocular severe AE, n (%)	3 (3.5)	1 (1.2)	2.96 [0.30; 29.08] 0.351	2.89 [0.31; 27.26] 0.353	0.02 [-0.02; 0.07] 0.324
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any ocular severe AE, n (%)	1 (1.4)	1 (1.3)	1.07 [0.07; 17.40] 0.963	1.07 [0.07; 16.76] 0.963	0.00 [-0.04; 0.04] 0.963
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any ocular severe AE, n (%)	1 (5.0)	0 (0.0)	N.E.	2.86 [0.12; 66.11] 0.512	0.05 [-0.05; 0.15] 0.305

	Treatment Groups		Comparison		
Any severe ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.343				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any ocular severe AE, n (%)	4 (2.1)	6 (3.4)	0.84 [0.21; 3.35] 0.803	0.62 [0.18; 2.14] 0.443	-0.01 [-0.05; 0.02] 0.450
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any ocular severe AE, n (%)	4 (2.8)	2 (1.3)	2.64 [0.44; 15.67] 0.286	2.07 [0.38; 11.17] 0.389	0.01 [-0.02; 0.05] 0.389
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any ocular severe AE, n (%)	1 (3.1)	4 (10.3)	0.35 [0.03; 3.50] 0.369	0.53 [0.09; 2.96] 0.448	-0.06 [-0.17; 0.05] 0.293
Any ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.743**					
KESTREL					
Interaction Test:	p = 0.241				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any ocular severe AE, n (%)	4 (3.7)	6 (6.3)	0.58 [0.16; 2.13] 0.414	0.60 [0.17; 2.06] 0.415	-0.03 [-0.09; 0.04] 0.414
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any ocular severe AE, n (%)	4 (5.7)	1 (1.4)	4.24 [0.46; 38.94] 0.201	4.06 [0.46; 35.40] 0.205	0.04 [-0.02; 0.10] 0.166
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any ocular severe AE, n (%)	1 (8.3)	4 (20.0)	0.36 [0.04; 3.71] 0.393	0.42 [0.05; 3.31] 0.407	-0.12 [-0.35; 0.12] 0.330

	Treatment Groups		Comparison		
Any severe ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	N.E.				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any ocular severe AE, n (%)	4 (4.7)	3 (3.7)	1.30 [0.28; 6.00] 0.736	1.29 [0.30; 5.57] 0.736	0.01 [-0.05; 0.07] 0.735
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any ocular severe AE, n (%)	1 (1.4)	4 (5.1)	0.26 [0.03; 2.35] 0.229	0.27 [0.03; 2.33] 0.232	-0.04 [-0.09; 0.02] 0.186
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any ocular severe AE, n (%)	2 (10.0)	0 (0.0)	N.E.	4.76 [0.24; 93.19] 0.304	0.10 [-0.03; 0.23] 0.136
Pooled Analysis					
Interaction Test:	p = 0.957				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any ocular severe AE, n (%)	8 (4.2)	9 (5.1)	0.83 [0.31; 2.22] 0.703	0.82 [0.33; 2.08] 0.679	-0.01 [-0.05; 0.03] 0.680
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any ocular severe AE, n (%)	5 (3.5)	5 (3.3)	1.05 [0.30; 3.70] 0.944	1.04 [0.30; 3.58] 0.949	0.00 [-0.04; 0.04] 0.949

	Treatment Groups		Comparison		
Any severe ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any ocular severe AE, n (%)	3 (9.4)	4 (10.3)	0.95 [0.20; 4.62] 0.948	1.05 [0.25; 4.47] 0.946	0.01 [-0.13; 0.14] 0.934

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE, Week 100 / KITE: logit(proportion) = treatment [by CSFT].

Table 14-2.11 Any severe ocular adverse event by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.066**					
KESTREL					
Interaction Test:	p = 0.699				
presence					
N'/N	62 / 62	61 / 61			
Any ocular severe AE, n (%)	2 (3.2)	6 (9.8)	0.31 [0.06; 1.58] 0.157	0.33 [0.07; 1.56] 0.162	-0.07 [-0.15; 0.02] 0.135
absence					
N'/N	127 / 127	126 / 126			
Any ocular severe AE, n (%)	2 (1.6)	4 (3.2)	0.49 [0.09; 2.71] 0.412	0.50 [0.09; 2.66] 0.413	-0.02 [-0.05; 0.02] 0.403
KITE					
Interaction Test:	N.E.				
presence					
N'/N	56 / 56	67 / 67			
Any ocular severe AE, n (%)	2 (3.6)	0 (0.0)	N.E.	5.96 [0.29; 121.73] 0.246	0.04 [-0.01; 0.08] 0.150
absence					
N'/N	123 / 123	114 / 114			
Any ocular severe AE, n (%)	3 (2.4)	2 (1.8)	1.40 [0.23; 8.53] 0.715	1.39 [0.24; 8.17] 0.715	0.01 [-0.03; 0.04] 0.712
Pooled Analysis					
Interaction Test:	p = 0.840				
presence					
N'/N	118 / 118	128 / 128			
Any ocular severe AE, n (%)	4 (3.4)	6 (4.7)	0.90 [0.23; 3.57] 0.881	0.72 [0.23; 2.29] 0.578	-0.02 [-0.07; 0.03] 0.545

	Treatment Groups		Comparison		
Any severe ocular adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular severe AE, n (%)	5 (2.0)	6 (2.5)	1.08 [0.29; 4.02] 0.907	0.80 [0.25; 2.61] 0.712	-0.00 [-0.03; 0.02] 0.711
Any ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.743**					
KESTREL					
Interaction Test:	p = 0.324				
presence					
N'/N	62 / 62	61 / 61			
Any ocular severe AE, n (%)	3 (4.8)	6 (9.8)	0.47 [0.11; 1.95] 0.297	0.49 [0.13; 1.88] 0.299	-0.05 [-0.14; 0.04] 0.286
absence					
N'/N	127 / 127	126 / 126			
Any ocular severe AE, n (%)	6 (4.7)	5 (4.0)	1.20 [0.36; 4.04] 0.768	1.19 [0.37; 3.80] 0.768	0.01 [-0.04; 0.06] 0.768
KITE					
Interaction Test:	p = 0.400				
presence					
N'/N	56 / 56	67 / 67			
Any ocular severe AE, n (%)	2 (3.6)	1 (1.5)	2.44 [0.22; 27.69] 0.470	2.39 [0.22; 25.70] 0.471	0.02 [-0.04; 0.08] 0.472
absence					
N'/N	123 / 123	114 / 114			
Any ocular severe AE, n (%)	5 (4.1)	6 (5.3)	0.76 [0.23; 2.57] 0.662	0.77 [0.24; 2.46] 0.662	-0.01 [-0.07; 0.04] 0.663
Pooled Analysis					
Interaction Test:	p = 0.736				
presence					
N'/N	118 / 118	128 / 128			
Any ocular severe AE, n (%)	5 (4.2)	7 (5.5)	0.76 [0.23; 2.49] 0.655	0.74 [0.25; 2.23] 0.592	-0.01 [-0.07; 0.04] 0.592

	Treatment Groups		Comparison		
Any severe ocular adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular severe AE, n (%)	11 (4.4)	11 (4.6)	0.98 [0.41; 2.33] 0.968	0.96 [0.42; 2.17] 0.920	-0.00 [-0.04; 0.03] 0.920

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KITE: logit(proportion) = treatment [by status of SRF].

Table 14-2.12 Any severe ocular adverse event by exposure (week 52) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.066**					
KESTREL					
Interaction Test:	p = 0.517				
Non-exposed					
N'/N	71 / 71	75 / 75			
Any ocular severe AE, n (%)	2 (2.8)	7 (9.3)	0.28 [0.06; 1.40] 0.122	0.30 [0.06; 1.40] 0.127	-0.07 [-0.14; 0.01] 0.094
Exposed					
N'/N	118 / 118	112 / 112			
Any ocular severe AE, n (%)	2 (1.7)	3 (2.7)	0.63 [0.10; 3.82] 0.612	0.63 [0.11; 3.72] 0.612	-0.01 [-0.05; 0.03] 0.611
KITE					
Interaction Test:	p = 0.405				
Non-exposed					
N'/N	85 / 85	90 / 90			
Any ocular severe AE, n (%)	4 (4.7)	1 (1.1)	4.40 [0.48; 40.14] 0.190	4.24 [0.48; 37.14] 0.193	0.04 [-0.01; 0.09] 0.158
Exposed					
N'/N	94 / 94	91 / 91			
Any ocular severe AE, n (%)	1 (1.1)	1 (1.1)	0.97 [0.06; 15.71] 0.982	0.97 [0.06; 15.25] 0.982	-0.00 [-0.03; 0.03] 0.982
Pooled Analysis					
Interaction Test:	p = 0.934				
Non-exposed					
N'/N	156 / 156	165 / 165			
Any ocular severe AE, n (%)	6 (3.8)	8 (4.8)	0.97 [0.30; 3.17] 0.960	0.79 [0.28; 2.24] 0.660	-0.01 [-0.05; 0.03] 0.660

	Treatment Groups		Comparison		
Any severe ocular adverse event by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	212 / 212	203 / 203			
Any ocular severe AE, n (%)	3 (1.4)	4 (2.0)	1.05 [0.21; 5.25] 0.953	0.72 [0.16; 3.15] 0.658	-0.01 [-0.03; 0.02] 0.658

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-2.13 Any severe ocular adverse event by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.743**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any ocular severe AE, n (%)	0 (0.0)	1 (7.7)	N.E.	0.36 [0.02; 8.05] 0.519	-0.08 [-0.22; 0.07] 0.298
Exposed					
N'/N	177 / 177	174 / 174			
Any ocular severe AE, n (%)	9 (5.1)	10 (5.7)	0.88 [0.35; 2.22] 0.784	0.88 [0.37; 2.12] 0.784	-0.01 [-0.05; 0.04] 0.784
KITE					
Interaction Test:	N.E.				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any ocular severe AE, n (%)	3 (17.6)	0 (0.0)	N.E.	5.06 [0.28; 89.70] 0.269	0.18 [-0.00; 0.36] 0.056
Exposed					
N'/N	162 / 162	169 / 169			
Any ocular severe AE, n (%)	4 (2.5)	7 (4.1)	0.59 [0.17; 2.04] 0.401	0.60 [0.18; 2.00] 0.402	-0.02 [-0.06; 0.02] 0.393
Pooled Analysis					
Interaction Test:	p = 0.290				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any ocular severe AE, n (%)	3 (10.3)	1 (4.0)	2.90 [0.28; 29.92] 0.372	1.71 [0.30; 9.78] 0.540	0.06 [-0.08; 0.19] 0.400

	Treatment Groups		Comparison		
Any severe ocular adverse event by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any ocular severe AE, n (%)	13 (3.8)	17 (5.0)	0.77 [0.37; 1.63] 0.498	0.77 [0.38; 1.56] 0.463	-0.01 [-0.04; 0.02] 0.462

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by exposure (week 100)].

Table 14-3.1 Any severe ocular adverse event at the study eye (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the study eye, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular severe AE at the study eye, n (%)	2 (1.1)	6 (3.2)	0.32 [0.06; 1.62] 0.169	0.33 [0.07; 1.61] 0.171	-0.02 [-0.05; 0.01] 0.148
KITE, N'/N	179 / 179	181 / 181			
Any ocular severe AE at the study eye, n (%)	5 (2.8)	1 (0.6)	5.17 [0.60; 44.72] 0.135	5.06 [0.60; 42.85] 0.137	0.02 [-0.00; 0.05] 0.097
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular severe AE at the study eye, n (%)	7 (1.9)	7 (1.9)	1.26 [0.33; 4.80] 0.738	1.00 [0.35; 2.82] 0.998	-0.00 [-0.02; 0.02] 0.998
p_H=0.044 *					
Any ocular severe AE at the study eye, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular severe AE at the study eye, n (%)	5 (2.6)	7 (3.7)	0.70 [0.22; 2.24] 0.547	0.71 [0.23; 2.19] 0.547	-0.01 [-0.05; 0.02] 0.545
KITE, N'/N	179 / 179	181 / 181			
Any ocular severe AE at the study eye, n (%)	6 (3.4)	4 (2.2)	1.53 [0.43; 5.53] 0.513	1.52 [0.44; 5.28] 0.513	0.01 [-0.02; 0.05] 0.510

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular severe AE at the study eye, n (%) p_H=0.374	11 (3.0)	11 (3.0)	1.03 [0.43; 2.44] 0.951	1.00 [0.44; 2.27] 0.999	-0.00 [-0.02; 0.02] 0.999

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-3.2 Any severe ocular adverse event at the study eye by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.374**					
KESTREL					
Interaction Test:	p = 0.934				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular severe AE at the study eye, n (%)	3 (2.9)	4 (4.3)	0.66 [0.14; 3.03] 0.594	0.67 [0.15; 2.92] 0.594	-0.01 [-0.07; 0.04] 0.596
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular severe AE at the study eye, n (%)	2 (2.4)	3 (3.2)	0.73 [0.12; 4.48] 0.735	0.74 [0.13; 4.31] 0.735	-0.01 [-0.06; 0.04] 0.732
KITE					
Interaction Test:	p = 0.772				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular severe AE at the study eye, n (%)	2 (2.0)	1 (1.0)	2.06 [0.18; 23.10] 0.557	2.04 [0.19; 22.14] 0.558	0.01 [-0.02; 0.04] 0.550
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular severe AE at the study eye, n (%)	4 (5.1)	3 (3.8)	1.35 [0.29; 6.24] 0.700	1.33 [0.31; 5.76] 0.700	0.01 [-0.05; 0.08] 0.699
Pooled Analysis					
Interaction Test:	p = 0.875				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular severe AE at the study eye, n (%)	5 (2.5)	5 (2.6)	0.96 [0.27; 3.40] 0.952	0.93 [0.28; 3.13] 0.908	-0.00 [-0.03; 0.03] 0.908

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular severe AE at the study eye, n (%)	6 (3.7)	6 (3.5)	1.10 [0.34; 3.56] 0.868	1.04 [0.34; 3.18] 0.941	0.00 [-0.04; 0.04] 0.941

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 14-3.3 Any severe ocular adverse event at the study eye by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.374**					
KESTREL					
Interaction Test:	N.E.				
Male					
N'/N	110 / 110	126 / 126			
Any ocular severe AE at the study eye, n (%)	5 (4.5)	4 (3.2)	1.45 [0.38; 5.55] 0.585	1.43 [0.39; 5.20] 0.585	0.01 [-0.04; 0.06] 0.587
Female					
N'/N	79 / 79	61 / 61			
Any ocular severe AE at the study eye, n (%)	0 (0.0)	3 (4.9)	N.E.	0.11 [0.01; 2.10] 0.143	-0.05 [-0.10; 0.01] 0.076
KITE					
Interaction Test:	p = 0.508				
Male					
N'/N	120 / 120	115 / 115			
Any ocular severe AE at the study eye, n (%)	2 (1.7)	2 (1.7)	0.96 [0.13; 6.91] 0.966	0.96 [0.14; 6.69] 0.966	-0.00 [-0.03; 0.03] 0.966
Female					
N'/N	59 / 59	66 / 66			
Any ocular severe AE at the study eye, n (%)	4 (6.8)	2 (3.0)	2.33 [0.41; 13.20] 0.340	2.24 [0.43; 11.77] 0.342	0.04 [-0.04; 0.11] 0.336
Pooled Analysis					
Interaction Test:	p = 0.554				
Male					
N'/N	230 / 230	241 / 241			
Any ocular severe AE at the study eye, n (%)	7 (3.0)	6 (2.5)	1.27 [0.41; 3.90] 0.681	1.26 [0.43; 3.69] 0.667	0.01 [-0.02; 0.04] 0.668

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any ocular severe AE at the study eye, n (%)	4 (2.9)	5 (3.9)	0.75 [0.20; 2.87] 0.673	0.80 [0.25; 2.56] 0.705	-0.01 [-0.05; 0.04] 0.730

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL: logit(proportion) = treatment [by gender].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 14-3.4 Any severe ocular adverse event at the study eye by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.374**					
KESTREL					
Interaction Test:	p = 0.081				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any ocular severe AE at the study eye, n (%)	2 (2.7)	6 (9.4)	0.27 [0.05; 1.38] 0.115	0.29 [0.06; 1.38] 0.119	-0.07 [-0.15; 0.01] 0.104
> 65 letters					
N'/N	115 / 115	123 / 123			
Any ocular severe AE at the study eye, n (%)	3 (2.6)	1 (0.8)	3.27 [0.34; 31.87] 0.308	3.21 [0.34; 30.41] 0.310	0.02 [-0.02; 0.05] 0.289
KITE					
Interaction Test:	p = 0.231				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any ocular severe AE at the study eye, n (%)	3 (4.6)	1 (1.1)	4.35 [0.44; 42.84] 0.207	4.20 [0.45; 39.48] 0.209	0.04 [-0.02; 0.09] 0.213
> 65 letters					
N'/N	114 / 114	90 / 90			
Any ocular severe AE at the study eye, n (%)	3 (2.6)	3 (3.3)	0.78 [0.15; 3.98] 0.769	0.79 [0.16; 3.82] 0.769	-0.01 [-0.05; 0.04] 0.771
Pooled Analysis					
Interaction Test:	p = 0.441				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any ocular severe AE at the study eye, n (%)	5 (3.6)	7 (4.5)	0.78 [0.24; 2.52] 0.676	0.74 [0.25; 2.13] 0.570	-0.01 [-0.06; 0.03] 0.582

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any ocular severe AE at the study eye, n (%)	6 (2.6)	4 (1.9)	1.55 [0.42; 5.74] 0.516	1.33 [0.39; 4.53] 0.647	0.01 [-0.02; 0.03] 0.648

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 14-3.5 Any severe ocular adverse event at the study eye by region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.374**					
KESTREL					
Interaction Test:	N.E.				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular severe AE at the study eye, n (%)	4 (4.4)	4 (4.8)	0.92 [0.22; 3.80] 0.907	0.92 [0.24; 3.57] 0.907	-0.00 [-0.07; 0.06] 0.907
European Region					
N'/N	69 / 69	75 / 75			
Any ocular severe AE at the study eye, n (%)	1 (1.4)	3 (4.0)	0.35 [0.04; 3.48] 0.372	0.36 [0.04; 3.40] 0.374	-0.03 [-0.08; 0.03] 0.341
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any ocular severe AE at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE					
Interaction Test:	N.E.				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular severe AE at the study eye, n (%)	1 (3.8)	0 (0.0)	N.E.	2.44 [0.10; 57.08] 0.578	0.04 [-0.04; 0.11] 0.308
European Region					
N'/N	135 / 135	132 / 132			
Any ocular severe AE at the study eye, n (%)	4 (3.0)	3 (2.3)	1.31 [0.29; 5.98] 0.725	1.30 [0.30; 5.71] 0.725	0.01 [-0.03; 0.05] 0.724
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any ocular severe AE at the study eye, n (%)	1 (5.6)	1 (3.6)	1.59 [0.09; 27.11] 0.749	1.56 [0.10; 23.33] 0.749	0.02 [-0.11; 0.15] 0.758

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	N.E.				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular severe AE at the study eye, n (%)	4 (4.4)	4 (4.8)	N.E.	0.92 [0.24; 3.57] 0.907	-0.00 [-0.07; 0.06] 0.907
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular severe AE at the study eye, n (%)	1 (3.8)	0 (0.0)	N.E.	2.44 [0.10; 57.08] 0.567	0.04 [-0.04; 0.11] 0.308
European Region					
N'/N	204 / 204	207 / 207			
Any ocular severe AE at the study eye, n (%)	5 (2.5)	6 (2.9)	0.67 [0.17; 2.68] 0.573	0.85 [0.26; 2.76] 0.781	-0.00 [-0.04; 0.03] 0.780
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any ocular severe AE at the study eye, n (%)	1 (2.1)	1 (1.8)	N.E.	1.56 [0.10; 23.33] 0.750	0.01 [-0.04; 0.06] 0.755

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by region].
Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by region].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 14-3.6 Any severe ocular adverse event at the study eye by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.044 ***					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular severe AE at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular severe AE at the study eye, n (%)	2 (1.1)	6 (3.3)	0.33 [0.07; 1.67] 0.182	0.34 [0.07; 1.67] 0.184	-0.02 [-0.05; 0.01] 0.159
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular severe AE at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular severe AE at the study eye, n (%)	5 (3.1)	1 (0.6)	5.58 [0.64; 48.29] 0.118	5.44 [0.64; 46.04] 0.120	0.03 [-0.00; 0.05] 0.087
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular severe AE at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular severe AE at the study eye, n (%)	7 (2.1)	7 (2.0)	1.33 [0.35; 5.06] 0.680	1.05 [0.37; 2.94] 0.927	0.00 [-0.02; 0.02] 0.927

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.374**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular severe AE at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular severe AE at the study eye, n (%)	5 (2.8)	7 (3.9)	0.72 [0.22; 2.32] 0.585	0.73 [0.24; 2.26] 0.585	-0.01 [-0.05; 0.03] 0.583
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular severe AE at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular severe AE at the study eye, n (%)	6 (3.8)	4 (2.3)	1.66 [0.46; 5.98] 0.441	1.63 [0.47; 5.68] 0.442	0.01 [-0.02; 0.05] 0.441
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular severe AE at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular severe AE at the study eye, n (%)	11 (3.3)	11 (3.1)	1.08 [0.46; 2.58] 0.854	1.05 [0.46; 2.39] 0.905	0.00 [-0.02; 0.03] 0.905

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE, Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by diabetes type].
Week 52 / Pooled Analysis, Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 14-3.7 Any severe ocular adverse event at the study eye by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.374**					
KESTREL					
Interaction Test:	p = 0.630				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any ocular severe AE at the study eye, n (%)	2 (2.6)	3 (2.8)	0.94 [0.15; 5.75] 0.944	0.94 [0.16; 5.48] 0.944	-0.00 [-0.05; 0.05] 0.944
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any ocular severe AE at the study eye, n (%)	3 (2.7)	4 (5.0)	0.52 [0.11; 2.40] 0.405	0.54 [0.12; 2.33] 0.405	-0.02 [-0.08; 0.03] 0.419
KITE					
Interaction Test:	p = 0.321				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any ocular severe AE at the study eye, n (%)	3 (3.7)	1 (1.0)	3.61 [0.37; 35.37] 0.271	3.51 [0.37; 33.12] 0.273	0.03 [-0.02; 0.07] 0.259
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any ocular severe AE at the study eye, n (%)	3 (3.1)	3 (3.5)	0.87 [0.17; 4.44] 0.869	0.88 [0.18; 4.23] 0.869	-0.00 [-0.06; 0.05] 0.870
Pooled Analysis					
Interaction Test:	p = 0.308				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any ocular severe AE at the study eye, n (%)	5 (3.2)	4 (2.0)	1.69 [0.44; 6.50] 0.448	1.63 [0.44; 6.12] 0.463	0.01 [-0.02; 0.05] 0.472

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any ocular severe AE at the study eye, n (%)	6 (2.9)	7 (4.2)	0.68 [0.22; 2.09] 0.504	0.67 [0.23; 1.96] 0.467	-0.01 [-0.05; 0.02] 0.477

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 14-3.8 Any severe ocular adverse event at the study eye by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.374**					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any ocular severe AE at the study eye, n (%)	4 (3.3)	3 (2.7)	1.23 [0.27; 5.62] 0.790	1.22 [0.28; 5.34] 0.790	0.01 [-0.04; 0.05] 0.788
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any ocular severe AE at the study eye, n (%)	0 (0.0)	4 (10.3)	N.E.	0.14 [0.01; 2.56] 0.187	-0.10 [-0.20; -0.01] 0.035 *
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any ocular severe AE at the study eye, n (%)	1 (2.6)	0 (0.0)	N.E.	2.93 [0.12; 69.64] 0.507	0.03 [-0.02; 0.08] 0.311
KITE					
Interaction Test:	p = 0.587				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any ocular severe AE at the study eye, n (%)	1 (1.2)	2 (2.2)	0.54 [0.05; 6.02] 0.613	0.54 [0.05; 5.86] 0.613	-0.01 [-0.05; 0.03] 0.603
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any ocular severe AE at the study eye, n (%)	2 (3.9)	1 (2.0)	1.96 [0.17; 22.33] 0.588	1.92 [0.18; 20.52] 0.589	0.02 [-0.05; 0.09] 0.579
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any ocular severe AE at the study eye, n (%)	3 (7.0)	1 (2.5)	2.93 [0.29; 29.34] 0.362	2.79 [0.30; 25.74] 0.365	0.04 [-0.05; 0.13] 0.331

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.267				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any ocular severe AE at the study eye, n (%)	5 (2.4)	5 (2.5)	1.06 [0.30; 3.80] 0.926	0.96 [0.28; 3.31] 0.953	-0.00 [-0.03; 0.03] 0.952
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any ocular severe AE at the study eye, n (%)	2 (2.5)	5 (5.7)	0.41 [0.08; 2.19] 0.295	0.51 [0.11; 2.38] 0.378	-0.03 [-0.09; 0.03] 0.308
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any ocular severe AE at the study eye, n (%)	4 (4.9)	1 (1.3)	4.02 [0.44; 37.14] 0.220	2.83 [0.46; 17.49] 0.241	0.04 [-0.02; 0.09] 0.185

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL: logit(proportion) = treatment [by duration of DME].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 14-3.9 Any severe ocular adverse event at the study eye by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.374**					
KESTREL					
Interaction Test:	N.E.				
focal					
N'/N	59 / 59	48 / 48			
Any ocular severe AE at the study eye, n (%)	0 (0.0)	2 (4.2)	N.E.	0.16 [0.01; 3.32] 0.238	-0.04 [-0.10; 0.01] 0.149
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular severe AE at the study eye, n (%)	5 (3.9)	4 (3.0)	1.33 [0.35; 5.08] 0.675	1.32 [0.36; 4.80] 0.675	0.01 [-0.03; 0.05] 0.675
KITE					
Interaction Test:	p = 0.479				
focal					
N'/N	63 / 63	66 / 66			
Any ocular severe AE at the study eye, n (%)	3 (4.8)	3 (4.5)	1.05 [0.20; 5.41] 0.953	1.05 [0.22; 5.00] 0.953	0.00 [-0.07; 0.07] 0.953
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular severe AE at the study eye, n (%)	3 (2.6)	1 (0.9)	2.89 [0.30; 28.24] 0.361	2.84 [0.30; 26.92] 0.362	0.02 [-0.02; 0.05] 0.332
Pooled Analysis					
Interaction Test:	p = 0.220				
focal					
N'/N	122 / 122	114 / 114			
Any ocular severe AE at the study eye, n (%)	3 (2.5)	5 (4.4)	0.53 [0.12; 2.29] 0.398	0.62 [0.17; 2.25] 0.463	-0.02 [-0.06; 0.03] 0.464

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular severe AE at the study eye, n (%)	8 (3.3)	5 (2.1)	1.70 [0.54; 5.37] 0.366	1.64 [0.54; 4.95] 0.378	0.01 [-0.02; 0.04] 0.377

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL: logit(proportion) = treatment [by DME type].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 14-3.10 Any severe ocular adverse event at the study eye by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.374**					
KESTREL					
Interaction Test:	N.E.				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any ocular severe AE at the study eye, n (%)	3 (2.8)	5 (5.2)	0.53 [0.12; 2.26] 0.387	0.54 [0.13; 2.19] 0.387	-0.02 [-0.08; 0.03] 0.386
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any ocular severe AE at the study eye, n (%)	1 (1.4)	0 (0.0)	N.E.	3.04 [0.13; 73.43] 0.493	0.01 [-0.01; 0.04] 0.314
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any ocular severe AE at the study eye, n (%)	1 (8.3)	2 (10.0)	0.82 [0.07; 10.12] 0.876	0.83 [0.08; 8.24] 0.876	-0.02 [-0.22; 0.19] 0.873
KITE					
Interaction Test:	N.E.				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any ocular severe AE at the study eye, n (%)	3 (3.5)	2 (2.4)	1.46 [0.24; 8.99] 0.681	1.45 [0.25; 8.44] 0.681	0.01 [-0.04; 0.06] 0.678
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any ocular severe AE at the study eye, n (%)	1 (1.4)	2 (2.5)	0.53 [0.05; 5.94] 0.605	0.53 [0.05; 5.76] 0.605	-0.01 [-0.06; 0.03] 0.595
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any ocular severe AE at the study eye, n (%)	2 (10.0)	0 (0.0)	N.E.	4.76 [0.24; 93.19] 0.304	0.10 [-0.03; 0.23] 0.136

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.749				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any ocular severe AE at the study eye, n (%)	6 (3.1)	7 (3.9)	0.82 [0.27; 2.54] 0.737	0.79 [0.27; 2.30] 0.668	-0.01 [-0.05; 0.03] 0.669
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any ocular severe AE at the study eye, n (%)	2 (1.4)	2 (1.3)	1.05 [0.14; 7.56] 0.965	1.05 [0.18; 6.01] 0.960	0.00 [-0.03; 0.03] 0.958
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any ocular severe AE at the study eye, n (%)	3 (9.4)	2 (5.1)	1.92 [0.29; 12.47] 0.495	1.83 [0.34; 9.81] 0.474	0.05 [-0.07; 0.17] 0.423

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by CSFT].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 14-3.11 Any severe ocular adverse event at the study eye by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.374**					
KESTREL					
Interaction Test:	p = 0.911				
presence					
N'/N	62 / 62	61 / 61			
Any ocular severe AE at the study eye, n (%)	2 (3.2)	3 (4.9)	0.64 [0.10; 4.00] 0.637	0.66 [0.11; 3.79] 0.637	-0.02 [-0.09; 0.05] 0.635
absence					
N'/N	127 / 127	126 / 126			
Any ocular severe AE at the study eye, n (%)	3 (2.4)	4 (3.2)	0.74 [0.16; 3.37] 0.695	0.74 [0.17; 3.26] 0.695	-0.01 [-0.05; 0.03] 0.694
KITE					
Interaction Test:	p = 0.644				
presence					
N'/N	56 / 56	67 / 67			
Any ocular severe AE at the study eye, n (%)	2 (3.6)	1 (1.5)	2.44 [0.22; 27.69] 0.470	2.39 [0.22; 25.70] 0.471	0.02 [-0.04; 0.08] 0.472
absence					
N'/N	123 / 123	114 / 114			
Any ocular severe AE at the study eye, n (%)	4 (3.3)	3 (2.6)	1.24 [0.27; 5.68] 0.778	1.24 [0.28; 5.40] 0.778	0.01 [-0.04; 0.05] 0.777
Pooled Analysis					
Interaction Test:	p = 0.908				
presence					
N'/N	118 / 118	128 / 128			
Any ocular severe AE at the study eye, n (%)	4 (3.4)	4 (3.1)	1.10 [0.27; 4.54] 0.893	1.06 [0.28; 4.06] 0.935	0.00 [-0.04; 0.05] 0.935

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular severe AE at the study eye, n (%)	7 (2.8)	7 (2.9)	0.99 [0.34; 2.92] 0.990	0.96 [0.34; 2.70] 0.937	-0.00 [-0.03; 0.03] 0.937

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 14-3.12 Any severe ocular adverse event at the study eye by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 14-3.13 Any severe ocular adverse event at the study eye by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.374**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any ocular severe AE at the study eye, n (%)	0 (0.0)	1 (7.7)	N.E.	0.36 [0.02; 8.05] 0.519	-0.08 [-0.22; 0.07] 0.298
Exposed					
N'/N	177 / 177	174 / 174			
Any ocular severe AE at the study eye, n (%)	5 (2.8)	6 (3.4)	0.81 [0.24; 2.72] 0.738	0.82 [0.25; 2.63] 0.738	-0.01 [-0.04; 0.03] 0.738
KITE					
Interaction Test:	N.E.				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any ocular severe AE at the study eye, n (%)	3 (17.6)	0 (0.0)	N.E.	5.06 [0.28; 89.70] 0.269	0.18 [-0.00; 0.36] 0.056
Exposed					
N'/N	162 / 162	169 / 169			
Any ocular severe AE at the study eye, n (%)	3 (1.9)	4 (2.4)	0.78 [0.17; 3.53] 0.745	0.78 [0.18; 3.44] 0.745	-0.01 [-0.04; 0.03] 0.744
Pooled Analysis					
Interaction Test:	p = 0.340				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any ocular severe AE at the study eye, n (%)	3 (10.3)	1 (4.0)	2.83 [0.27; 29.45] 0.385	1.71 [0.30; 9.78] 0.540	0.06 [-0.08; 0.19] 0.400

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any ocular severe AE at the study eye, n (%)	8 (2.4)	10 (2.9)	0.83 [0.32; 2.16] 0.703	0.80 [0.32; 2.01] 0.642	-0.01 [-0.03; 0.02] 0.642

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by exposure (week 100)].

Table 14-4.1 Any severe ocular adverse event at the fellow eye (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the fellow eye, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular severe AE at the fellow eye, n (%)	2 (1.1)	4 (2.1)	0.49 [0.09; 2.70] 0.413	0.49 [0.09; 2.67] 0.413	-0.01 [-0.04; 0.01] 0.403
KITE, N'/N	179 / 179	181 / 181			
Any ocular severe AE at the fellow eye, n (%)	1 (0.6)	1 (0.6)	1.01 [0.06; 16.29] 0.994	1.01 [0.06; 16.04] 0.994	0.00 [-0.02; 0.02] 0.994
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular severe AE at the fellow eye, n (%)	3 (0.8)	5 (1.4)	0.70 [0.14; 3.52] 0.663	0.60 [0.14; 2.47] 0.473	-0.01 [-0.02; 0.01] 0.472
p_H=0.663					
Any ocular severe AE at the fellow eye, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular severe AE at the fellow eye, n (%)	4 (2.1)	7 (3.7)	0.56 [0.16; 1.93] 0.356	0.57 [0.17; 1.90] 0.356	-0.02 [-0.05; 0.02] 0.349
KITE, N'/N	179 / 179	181 / 181			
Any ocular severe AE at the fellow eye, n (%)	2 (1.1)	5 (2.8)	0.40 [0.08; 2.08] 0.274	0.40 [0.08; 2.06] 0.275	-0.02 [-0.04; 0.01] 0.256

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular severe AE at the fellow eye, n (%)	6 (1.6)	12 (3.3)	0.47 [0.17; 1.32] 0.153	0.50 [0.19; 1.31] 0.151	-0.02 [-0.04; 0.01] 0.150
p_H=0.751					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-4.2 Any severe ocular adverse event at the fellow eye by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.751**					
KESTREL					
Interaction Test:	p = 0.974				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular severe AE at the fellow eye, n (%)	3 (2.9)	5 (5.4)	0.52 [0.12; 2.25] 0.384	0.54 [0.13; 2.18] 0.385	-0.02 [-0.08; 0.03] 0.383
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular severe AE at the fellow eye, n (%)	1 (1.2)	2 (2.1)	0.55 [0.05; 6.15] 0.626	0.55 [0.05; 5.99] 0.626	-0.01 [-0.05; 0.03] 0.615
KITE					
Interaction Test:	p = 0.795				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular severe AE at the fellow eye, n (%)	1 (1.0)	2 (2.0)	0.51 [0.05; 5.66] 0.580	0.51 [0.05; 5.54] 0.580	-0.01 [-0.04; 0.02] 0.571
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular severe AE at the fellow eye, n (%)	1 (1.3)	3 (3.8)	0.32 [0.03; 3.19] 0.335	0.33 [0.04; 3.14] 0.337	-0.03 [-0.07; 0.02] 0.310
Pooled Analysis					
Interaction Test:	p = 0.819				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular severe AE at the fellow eye, n (%)	4 (2.0)	7 (3.6)	0.51 [0.14; 1.83] 0.302	0.53 [0.16; 1.77] 0.295	-0.02 [-0.05; 0.02] 0.298

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular severe AE at the fellow eye, n (%)	2 (1.2)	5 (2.9)	0.40 [0.07; 2.16] 0.288	0.42 [0.08; 2.12] 0.277	-0.02 [-0.05; 0.01] 0.271

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 14-4.3 Any severe ocular adverse event at the fellow eye by gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 14-4.4 Any severe ocular adverse event at the fellow eye by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.751**					
KESTREL					
Interaction Test:	N.E.				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any ocular severe AE at the fellow eye, n (%)	0 (0.0)	5 (7.8)	N.E.	0.08 [0.00; 1.40] 0.083	-0.08 [-0.14; -0.01] 0.020 *
> 65 letters					
N'/N	115 / 115	123 / 123			
Any ocular severe AE at the fellow eye, n (%)	4 (3.5)	2 (1.6)	2.18 [0.39; 12.14] 0.374	2.14 [0.40; 11.46] 0.375	0.02 [-0.02; 0.06] 0.367
KITE					
Interaction Test:	N.E.				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any ocular severe AE at the fellow eye, n (%)	0 (0.0)	3 (3.3)	N.E.	0.20 [0.01; 3.79] 0.283	-0.03 [-0.07; 0.00] 0.078
> 65 letters					
N'/N	114 / 114	90 / 90			
Any ocular severe AE at the fellow eye, n (%)	2 (1.8)	2 (2.2)	0.79 [0.11; 5.69] 0.811	0.79 [0.11; 5.50] 0.811	-0.00 [-0.04; 0.03] 0.813
Pooled Analysis					
Interaction Test:	N.E.				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any ocular severe AE at the fellow eye, n (%)	0 (0.0)	8 (5.2)	N.E.	0.12 [0.02; 0.89] 0.012 *	-0.05 [-0.09; -0.02] 0.003 *

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any ocular severe AE at the fellow eye, n (%)	6 (2.6)	4 (1.9)	1.32 [0.36; 4.88] 0.675	1.42 [0.41; 4.85] 0.579	0.01 [-0.02; 0.04] 0.580

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by BCVA].
Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by BCVA].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 14-4.5 Any severe ocular adverse event at the fellow eye by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 14-4.6 Any severe ocular adverse event at the fellow eye by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.751**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular severe AE at the fellow eye, n (%)	1 (8.3)	0 (0.0)	N.E.	1.62 [0.08; 34.66] 0.759	0.08 [-0.07; 0.24] 0.296
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular severe AE at the fellow eye, n (%)	3 (1.7)	7 (3.9)	0.43 [0.11; 1.68] 0.225	0.44 [0.12; 1.67] 0.226	-0.02 [-0.06; 0.01] 0.209
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular severe AE at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular severe AE at the fellow eye, n (%)	2 (1.3)	5 (2.9)	0.43 [0.08; 2.24] 0.314	0.44 [0.09; 2.21] 0.316	-0.02 [-0.05; 0.01] 0.292
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular severe AE at the fellow eye, n (%)	1 (3.2)	0 (0.0)	N.E.	1.62 [0.08; 34.66] 0.761	0.04 [-0.03; 0.10] 0.280

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular severe AE at the fellow eye, n (%)	5 (1.5)	12 (3.4)	0.43 [0.15; 1.25] 0.120	0.44 [0.16; 1.23] 0.106	-0.02 [-0.04; 0.00] 0.101

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by diabetes type].
Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 14-4.7 Any severe ocular adverse event at the fellow eye by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.751**					
KESTREL					
Interaction Test:	N.E.				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any ocular severe AE at the fellow eye, n (%)	0 (0.0)	3 (2.8)	N.E.	0.20 [0.01; 3.82] 0.285	-0.03 [-0.06; 0.00] 0.079
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any ocular severe AE at the fellow eye, n (%)	3 (2.7)	4 (5.0)	0.52 [0.11; 2.40] 0.405	0.54 [0.12; 2.33] 0.405	-0.02 [-0.08; 0.03] 0.419
KITE					
Interaction Test:	N.E.				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any ocular severe AE at the fellow eye, n (%)	0 (0.0)	2 (2.1)	N.E.	0.23 [0.01; 4.80] 0.346	-0.02 [-0.05; 0.01] 0.153
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any ocular severe AE at the fellow eye, n (%)	2 (2.1)	3 (3.5)	0.58 [0.09; 3.53] 0.550	0.58 [0.10; 3.41] 0.551	-0.01 [-0.06; 0.03] 0.552
Pooled Analysis					
Interaction Test:	N.E.				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any ocular severe AE at the fellow eye, n (%)	0 (0.0)	5 (2.5)	N.E.	0.22 [0.03; 1.78] 0.115	-0.02 [-0.05; -0.00] 0.024 *

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any ocular severe AE at the fellow eye, n (%)	5 (2.4)	7 (4.2)	0.55 [0.17; 1.79] 0.318	0.56 [0.18; 1.72] 0.302	-0.02 [-0.06; 0.02] 0.316

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by HbA1c].
Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by HbA1c].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 14-4.8 Any severe ocular adverse event at the fellow eye by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.751**					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any ocular severe AE at the fellow eye, n (%)	3 (2.5)	4 (3.6)	0.68 [0.15; 3.11] 0.618	0.69 [0.16; 3.00] 0.618	-0.01 [-0.06; 0.03] 0.619
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any ocular severe AE at the fellow eye, n (%)	0 (0.0)	3 (7.7)	N.E.	0.18 [0.01; 3.44] 0.257	-0.08 [-0.16; 0.01] 0.071
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any ocular severe AE at the fellow eye, n (%)	1 (2.6)	0 (0.0)	N.E.	2.93 [0.12; 69.64] 0.507	0.03 [-0.02; 0.08] 0.311
KITE					
Interaction Test:	N.E.				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any ocular severe AE at the fellow eye, n (%)	0 (0.0)	3 (3.3)	N.E.	0.15 [0.01; 2.95] 0.214	-0.03 [-0.07; 0.00] 0.078
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any ocular severe AE at the fellow eye, n (%)	1 (2.0)	2 (4.1)	0.47 [0.04; 5.36] 0.543	0.48 [0.04; 5.13] 0.544	-0.02 [-0.09; 0.05] 0.536
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any ocular severe AE at the fellow eye, n (%)	1 (2.3)	0 (0.0)	N.E.	2.80 [0.12; 66.70] 0.525	0.02 [-0.02; 0.07] 0.312

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	N.E.				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any ocular severe AE at the fellow eye, n (%)	3 (1.5)	7 (3.5)	N.E.	0.45 [0.13; 1.60] 0.205	-0.02 [-0.05; 0.01] 0.178
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any ocular severe AE at the fellow eye, n (%)	1 (1.2)	5 (5.7)	N.E.	0.30 [0.05; 1.86] 0.170	-0.04 [-0.10; 0.01] 0.109
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any ocular severe AE at the fellow eye, n (%)	2 (2.4)	0 (0.0)	N.E.	2.86 [0.30; 26.92] 0.338	0.02 [-0.01; 0.06] 0.152

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by duration of DME].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 14-4.9 Any severe ocular adverse event at the fellow eye by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.751**					
KESTREL					
Interaction Test:	N.E.				
focal					
N'/N	59 / 59	48 / 48			
Any ocular severe AE at the fellow eye, n (%)	0 (0.0)	1 (2.1)	N.E.	0.27 [0.01; 6.53] 0.422	-0.02 [-0.06; 0.02] 0.312
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular severe AE at the fellow eye, n (%)	4 (3.1)	5 (3.7)	0.84 [0.22; 3.20] 0.797	0.84 [0.23; 3.07] 0.797	-0.01 [-0.05; 0.04] 0.796
KITE					
Interaction Test:	p = 0.508				
focal					
N'/N	63 / 63	66 / 66			
Any ocular severe AE at the fellow eye, n (%)	1 (1.6)	1 (1.5)	1.05 [0.06; 17.13] 0.974	1.05 [0.07; 16.39] 0.974	0.00 [-0.04; 0.04] 0.974
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular severe AE at the fellow eye, n (%)	1 (0.9)	3 (2.8)	0.31 [0.03; 3.03] 0.314	0.32 [0.03; 2.99] 0.315	-0.02 [-0.05; 0.02] 0.293
Pooled Analysis					
Interaction Test:	p = 0.821				
focal					
N'/N	122 / 122	114 / 114			
Any ocular severe AE at the fellow eye, n (%)	1 (0.8)	2 (1.8)	0.44 [0.04; 4.98] 0.508	0.56 [0.08; 4.03] 0.561	-0.01 [-0.04; 0.02] 0.548

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular severe AE at the fellow eye, n (%)	5 (2.1)	8 (3.3)	0.60 [0.19; 1.94] 0.395	0.64 [0.21; 1.91] 0.421	-0.01 [-0.04; 0.02] 0.420

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL: logit(proportion) = treatment [by DME type].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 14-4.10 Any severe ocular adverse event at the fellow eye by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 14-4.11 Any severe ocular adverse event at the fellow eye by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.751**					
KESTREL					
Interaction Test:	p = 0.303				
presence					
N'/N	62 / 62	61 / 61			
Any ocular severe AE at the fellow eye, n (%)	1 (1.6)	4 (6.6)	0.23 [0.03; 2.15] 0.199	0.25 [0.03; 2.14] 0.204	-0.05 [-0.12; 0.02] 0.164
absence					
N'/N	127 / 127	126 / 126			
Any ocular severe AE at the fellow eye, n (%)	3 (2.4)	3 (2.4)	0.99 [0.20; 5.01] 0.992	0.99 [0.20; 4.82] 0.992	-0.00 [-0.04; 0.04] 0.992
KITE					
Interaction Test:	N.E.				
presence					
N'/N	56 / 56	67 / 67			
Any ocular severe AE at the fellow eye, n (%)	0 (0.0)	1 (1.5)	N.E.	0.40 [0.02; 9.57] 0.570	-0.01 [-0.04; 0.01] 0.314
absence					
N'/N	123 / 123	114 / 114			
Any ocular severe AE at the fellow eye, n (%)	2 (1.6)	4 (3.5)	0.45 [0.08; 2.53] 0.368	0.46 [0.09; 2.48] 0.369	-0.02 [-0.06; 0.02] 0.362
Pooled Analysis					
Interaction Test:	p = 0.338				
presence					
N'/N	118 / 118	128 / 128			
Any ocular severe AE at the fellow eye, n (%)	1 (0.8)	5 (3.9)	0.20 [0.02; 1.76] 0.146	0.28 [0.05; 1.68] 0.138	-0.03 [-0.07; 0.01] 0.093

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular severe AE at the fellow eye, n (%)	5 (2.0)	7 (2.9)	0.66 [0.20; 2.17] 0.492	0.69 [0.22; 2.12] 0.511	-0.01 [-0.04; 0.02] 0.513

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KITE: logit(proportion) = treatment [by status of SRF].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 14-4.12 Any severe ocular adverse event at the fellow eye by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 14-4.13 Any severe ocular adverse event at the fellow eye by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular severe AE at the fellow eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.751**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any ocular severe AE at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Exposed					
N'/N	177 / 177	174 / 174			
Any ocular severe AE at the fellow eye, n (%)	4 (2.3)	7 (4.0)	0.55 [0.16; 1.92] 0.350	0.56 [0.17; 1.88] 0.350	-0.02 [-0.05; 0.02] 0.344
KITE					
Interaction Test:	N.E.				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any ocular severe AE at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Exposed					
N'/N	162 / 162	169 / 169			
Any ocular severe AE at the fellow eye, n (%)	2 (1.2)	5 (3.0)	0.41 [0.08; 2.14] 0.291	0.42 [0.08; 2.12] 0.292	-0.02 [-0.05; 0.01] 0.271
Pooled Analysis					
Interaction Test:	N.E.				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any ocular severe AE at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any ocular severe AE at the fellow eye, n (%)	6 (1.8)	12 (3.5)	0.48 [0.17; 1.34] 0.159	0.50 [0.19; 1.32] 0.156	-0.02 [-0.04; 0.01] 0.154

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by exposure (week 100)].
Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by exposure (week 100)].

Table 14-5.1 Any severe non-ocular adverse event (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe non-ocular adverse event (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular severe AE, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any non-ocular severe AE, n (%)	21 (11.1)	18 (9.6)	1.17 [0.60; 2.28] 0.637	1.15 [0.64; 2.10] 0.637	0.01 [-0.05; 0.08] 0.636
KITE, N'/N	179 / 179	181 / 181			
Any non-ocular severe AE, n (%)	17 (9.5)	17 (9.4)	1.01 [0.50; 2.05] 0.973	1.01 [0.53; 1.92] 0.973	0.00 [-0.06; 0.06] 0.973
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any non-ocular severe AE, n (%)	38 (10.3)	35 (9.5)	1.09 [0.67; 1.77] 0.723	1.09 [0.70; 1.68] 0.713	0.01 [-0.04; 0.05] 0.713
p_H=0.765					
Any non-ocular severe AE, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any non-ocular severe AE, n (%)	36 (19.0)	33 (17.6)	1.10 [0.65; 1.85] 0.726	1.08 [0.70; 1.65] 0.726	0.01 [-0.06; 0.09] 0.726
KITE, N'/N	179 / 179	181 / 181			
Any non-ocular severe AE, n (%)	33 (18.4)	40 (22.1)	0.80 [0.48; 1.33] 0.388	0.83 [0.55; 1.26] 0.389	-0.04 [-0.12; 0.05] 0.387
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any non-ocular severe AE, n (%)	69 (18.8)	73 (19.8)	0.94 [0.65; 1.35] 0.734	0.95 [0.70; 1.27] 0.712	-0.01 [-0.07; 0.05] 0.711
p_H=0.392					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-5.2 Any severe non-ocular adverse event by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.765**					
KESTREL					
Interaction Test:	p = 0.866				
< 65 years					
N'/N	104 / 104	93 / 93			
Any non-ocular severe AE, n (%)	11 (10.6)	8 (8.6)	1.26 [0.48; 3.27] 0.640	1.23 [0.52; 2.93] 0.640	0.02 [-0.06; 0.10] 0.637
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any non-ocular severe AE, n (%)	10 (11.8)	10 (10.6)	1.12 [0.44; 2.84] 0.811	1.11 [0.48; 2.53] 0.811	0.01 [-0.08; 0.10] 0.812
KITE					
Interaction Test:	p = 0.453				
< 65 years					
N'/N	100 / 100	102 / 102			
Any non-ocular severe AE, n (%)	10 (10.0)	8 (7.8)	1.31 [0.49; 3.46] 0.592	1.28 [0.52; 3.10] 0.592	0.02 [-0.06; 0.10] 0.591
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any non-ocular severe AE, n (%)	7 (8.9)	9 (11.4)	0.76 [0.27; 2.14] 0.599	0.78 [0.30; 1.99] 0.599	-0.03 [-0.12; 0.07] 0.598
Pooled Analysis					
Interaction Test:	p = 0.525				
< 65 years					
N'/N	204 / 204	195 / 195			
Any non-ocular severe AE, n (%)	21 (10.3)	16 (8.2)	1.28 [0.65; 2.53] 0.479	1.25 [0.67; 2.33] 0.478	0.02 [-0.04; 0.08] 0.476

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any non-ocular severe AE, n (%)	17 (10.4)	19 (11.0)	0.93 [0.47; 1.87] 0.845	0.95 [0.51; 1.75] 0.861	-0.01 [-0.07; 0.06] 0.861
Any non-ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.392**					
KESTREL					
Interaction Test:	p = 0.344				
< 65 years					
N'/N	104 / 104	93 / 93			
Any non-ocular severe AE, n (%)	23 (22.1)	16 (17.2)	1.37 [0.67; 2.78] 0.389	1.29 [0.72; 2.28] 0.391	0.05 [-0.06; 0.16] 0.384
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any non-ocular severe AE, n (%)	13 (15.3)	17 (18.1)	0.82 [0.37; 1.80] 0.618	0.85 [0.44; 1.64] 0.619	-0.03 [-0.14; 0.08] 0.616
KITE					
Interaction Test:	p = 0.697				
< 65 years					
N'/N	100 / 100	102 / 102			
Any non-ocular severe AE, n (%)	14 (14.0)	19 (18.6)	0.71 [0.33; 1.51] 0.375	0.75 [0.40; 1.42] 0.376	-0.05 [-0.15; 0.06] 0.372
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any non-ocular severe AE, n (%)	19 (24.1)	21 (26.6)	0.87 [0.43; 1.79] 0.715	0.90 [0.53; 1.55] 0.715	-0.03 [-0.16; 0.11] 0.714
Pooled Analysis					
Interaction Test:	p = 0.625				
< 65 years					
N'/N	204 / 204	195 / 195			
Any non-ocular severe AE, n (%)	37 (18.1)	35 (17.9)	1.03 [0.62; 1.72] 0.910	1.00 [0.66; 1.53] 0.985	0.00 [-0.07; 0.08] 0.984

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any non-ocular severe AE, n (%)	32 (19.5)	38 (22.0)	0.86 [0.51; 1.45] 0.569	0.88 [0.58; 1.33] 0.545	-0.03 [-0.11; 0.06] 0.543

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-5.3 Any severe non-ocular adverse event by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.765**					
KESTREL					
Interaction Test:	p = 0.713				
Male					
N'/N	110 / 110	126 / 126			
Any non-ocular severe AE, n (%)	12 (10.9)	11 (8.7)	1.28 [0.54; 3.03] 0.574	1.25 [0.57; 2.72] 0.574	0.02 [-0.05; 0.10] 0.576
Female					
N'/N	79 / 79	61 / 61			
Any non-ocular severe AE, n (%)	9 (11.4)	7 (11.5)	0.99 [0.35; 2.83] 0.988	0.99 [0.39; 2.51] 0.988	-0.00 [-0.11; 0.11] 0.988
KITE					
Interaction Test:	p = 0.393				
Male					
N'/N	120 / 120	115 / 115			
Any non-ocular severe AE, n (%)	11 (9.2)	8 (7.0)	1.35 [0.52; 3.49] 0.536	1.32 [0.55; 3.16] 0.536	0.02 [-0.05; 0.09] 0.533
Female					
N'/N	59 / 59	66 / 66			
Any non-ocular severe AE, n (%)	6 (10.2)	9 (13.6)	0.72 [0.24; 2.15] 0.553	0.75 [0.28; 1.97] 0.554	-0.03 [-0.15; 0.08] 0.548
Pooled Analysis					
Interaction Test:	p = 0.375				
Male					
N'/N	230 / 230	241 / 241			
Any non-ocular severe AE, n (%)	23 (10.0)	19 (7.9)	1.30 [0.69; 2.46] 0.416	1.28 [0.72; 2.29] 0.405	0.02 [-0.03; 0.07] 0.405

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any non-ocular severe AE, n (%)	15 (10.9)	16 (12.6)	0.83 [0.39; 1.77] 0.636	0.86 [0.44; 1.69] 0.671	-0.02 [-0.09; 0.06] 0.670
Any non-ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.392**					
KESTREL					
Interaction Test:	p = 0.934				
Male					
N'/N	110 / 110	126 / 126			
Any non-ocular severe AE, n (%)	21 (19.1)	22 (17.5)	1.12 [0.58; 2.16] 0.746	1.09 [0.64; 1.88] 0.746	0.02 [-0.08; 0.12] 0.747
Female					
N'/N	79 / 79	61 / 61			
Any non-ocular severe AE, n (%)	15 (19.0)	11 (18.0)	1.07 [0.45; 2.52] 0.885	1.05 [0.52; 2.13] 0.886	0.01 [-0.12; 0.14] 0.885
KITE					
Interaction Test:	p = 0.244				
Male					
N'/N	120 / 120	115 / 115			
Any non-ocular severe AE, n (%)	24 (20.0)	23 (20.0)	1.00 [0.53; 1.90] 1.000	1.00 [0.60; 1.67] 1.000	0.00 [-0.10; 0.10] 1.000
Female					
N'/N	59 / 59	66 / 66			
Any non-ocular severe AE, n (%)	9 (15.3)	17 (25.8)	0.52 [0.21; 1.27] 0.152	0.59 [0.29; 1.23] 0.158	-0.11 [-0.24; 0.03] 0.141
Pooled Analysis					
Interaction Test:	p = 0.374				
Male					
N'/N	230 / 230	241 / 241			
Any non-ocular severe AE, n (%)	45 (19.6)	45 (18.7)	1.06 [0.67; 1.69] 0.793	1.04 [0.72; 1.51] 0.823	0.01 [-0.06; 0.08] 0.822

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any non-ocular severe AE, n (%)	24 (17.4)	28 (22.0)	0.75 [0.41; 1.38] 0.360	0.79 [0.48; 1.31] 0.362	-0.04 [-0.14; 0.05] 0.360

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-5.4 Any severe non-ocular adverse event by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.765**					
KESTREL					
Interaction Test:	p = 0.897				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any non-ocular severe AE, n (%)	10 (13.5)	8 (12.5)	1.09 [0.40; 2.96] 0.860	1.08 [0.45; 2.57] 0.860	0.01 [-0.10; 0.12] 0.860
> 65 letters					
N'/N	115 / 115	123 / 123			
Any non-ocular severe AE, n (%)	11 (9.6)	10 (8.1)	1.20 [0.49; 2.93] 0.697	1.18 [0.52; 2.67] 0.697	0.01 [-0.06; 0.09] 0.697
KITE					
Interaction Test:	p = 0.019 *				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any non-ocular severe AE, n (%)	1 (1.5)	10 (11.0)	0.13 [0.02; 1.01] 0.052	0.14 [0.02; 1.07] 0.058	-0.09 [-0.17; -0.02] 0.009 *
> 65 letters					
N'/N	114 / 114	90 / 90			
Any non-ocular severe AE, n (%)	16 (14.0)	7 (7.8)	1.94 [0.76; 4.93] 0.166	1.80 [0.78; 4.20] 0.170	0.06 [-0.02; 0.15] 0.146
Pooled Analysis					
Interaction Test:	p = 0.092				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any non-ocular severe AE, n (%)	11 (7.9)	18 (11.6)	0.64 [0.29; 1.42] 0.275	0.62 [0.29; 1.31] 0.202	-0.04 [-0.11; 0.02] 0.188

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any non-ocular severe AE, n (%)	27 (11.8)	17 (8.0)	1.55 [0.82; 2.94] 0.181	1.46 [0.81; 2.61] 0.203	0.04 [-0.02; 0.09] 0.197
Any non-ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.392**					
KESTREL					
Interaction Test:	p = 0.794				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any non-ocular severe AE, n (%)	15 (20.3)	13 (20.3)	1.00 [0.43; 2.29] 0.995	1.00 [0.51; 1.94] 0.995	-0.00 [-0.13; 0.13] 0.995
> 65 letters					
N'/N	115 / 115	123 / 123			
Any non-ocular severe AE, n (%)	21 (18.3)	20 (16.3)	1.15 [0.59; 2.26] 0.683	1.12 [0.64; 1.96] 0.683	0.02 [-0.08; 0.12] 0.683
KITE					
Interaction Test:	p = 0.041 *				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any non-ocular severe AE, n (%)	6 (9.2)	21 (23.1)	0.34 [0.13; 0.90] 0.029 *	0.40 [0.17; 0.94] 0.035 *	-0.14 [-0.25; -0.03] 0.015 *
> 65 letters					
N'/N	114 / 114	90 / 90			
Any non-ocular severe AE, n (%)	27 (23.7)	19 (21.1)	1.16 [0.60; 2.26] 0.663	1.12 [0.67; 1.88] 0.663	0.03 [-0.09; 0.14] 0.661
Pooled Analysis					
Interaction Test:	p = 0.135				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any non-ocular severe AE, n (%)	21 (15.1)	34 (21.9)	0.65 [0.36; 1.19] 0.164	0.67 [0.40; 1.11] 0.113	-0.07 [-0.16; 0.02] 0.105

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any non-ocular severe AE, n (%)	48 (21.0)	39 (18.3)	1.17 [0.73; 1.87] 0.516	1.12 [0.77; 1.64] 0.551	0.02 [-0.05; 0.10] 0.549

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-5.5 Any severe non-ocular adverse event by region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.765**					
KESTREL					
Interaction Test:	p = 0.978				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any non-ocular severe AE, n (%)	13 (14.4)	10 (12.0)	1.23 [0.51; 2.98] 0.643	1.20 [0.56; 2.59] 0.644	0.02 [-0.08; 0.12] 0.642
European Region					
N'/N	69 / 69	75 / 75			
Any non-ocular severe AE, n (%)	7 (10.1)	7 (9.3)	1.10 [0.36; 3.30] 0.870	1.09 [0.40; 2.94] 0.870	0.01 [-0.09; 0.11] 0.870
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any non-ocular severe AE, n (%)	1 (3.3)	1 (3.4)	0.97 [0.06; 16.20] 0.981	0.97 [0.06; 14.74] 0.981	-0.00 [-0.09; 0.09] 0.981
KITE					
Interaction Test:	N.E.				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any non-ocular severe AE, n (%)	2 (7.7)	0 (0.0)	N.E.	4.07 [0.21; 80.51] 0.356	0.08 [-0.03; 0.18] 0.141
European Region					
N'/N	135 / 135	132 / 132			
Any non-ocular severe AE, n (%)	11 (8.1)	16 (12.1)	0.64 [0.29; 1.44] 0.285	0.67 [0.32; 1.39] 0.286	-0.04 [-0.11; 0.03] 0.282
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any non-ocular severe AE, n (%)	4 (22.2)	1 (3.6)	7.71 [0.79; 75.75] 0.080	6.22 [0.75; 51.31] 0.089	0.19 [-0.02; 0.39] 0.073

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	N.E.				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any non-ocular severe AE, n (%)	13 (14.4)	10 (12.0)	N.E.	1.20 [0.56; 2.59] 0.644	0.02 [-0.08; 0.12] 0.642
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any non-ocular severe AE, n (%)	2 (7.7)	0 (0.0)	N.E.	4.07 [0.21; 80.51] 0.315	0.08 [-0.03; 0.18] 0.141
European Region					
N'/N	204 / 204	207 / 207			
Any non-ocular severe AE, n (%)	18 (8.8)	23 (11.1)	0.84 [0.42; 1.68] 0.630	0.79 [0.44; 1.42] 0.438	-0.02 [-0.08; 0.04] 0.437
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any non-ocular severe AE, n (%)	5 (10.4)	2 (3.5)	2.67 [0.43; 16.54] 0.290	3.25 [0.71; 14.89] 0.107	0.08 [-0.02; 0.18] 0.130
Any non-ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.392**					
KESTREL					
Interaction Test:	p = 0.771				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any non-ocular severe AE, n (%)	23 (25.6)	18 (21.7)	1.24 [0.61; 2.51] 0.550	1.18 [0.69; 2.02] 0.551	0.04 [-0.09; 0.17] 0.549
European Region					
N'/N	69 / 69	75 / 75			
Any non-ocular severe AE, n (%)	11 (15.9)	12 (16.0)	1.00 [0.41; 2.43] 0.992	1.00 [0.47; 2.11] 0.992	-0.00 [-0.12; 0.12] 0.992
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any non-ocular severe AE, n (%)	2 (6.7)	3 (10.3)	0.62 [0.10; 4.01] 0.615	0.64 [0.12; 3.58] 0.616	-0.04 [-0.18; 0.11] 0.612

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.603				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any non-ocular severe AE, n (%)	3 (11.5)	2 (9.5)	1.24 [0.19; 8.20] 0.824	1.21 [0.22; 6.59] 0.824	0.02 [-0.16; 0.20] 0.822
European Region					
N'/N	135 / 135	132 / 132			
Any non-ocular severe AE, n (%)	25 (18.5)	32 (24.2)	0.71 [0.39; 1.28] 0.255	0.76 [0.48; 1.22] 0.256	-0.06 [-0.16; 0.04] 0.253
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any non-ocular severe AE, n (%)	5 (27.8)	6 (21.4)	1.41 [0.36; 5.55] 0.623	1.30 [0.46; 3.63] 0.621	0.06 [-0.19; 0.32] 0.628
Pooled Analysis					
Interaction Test:	p = 0.884				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any non-ocular severe AE, n (%)	23 (25.6)	18 (21.7)	1.17 [0.50; 2.73] 0.725	1.18 [0.69; 2.02] 0.551	0.04 [-0.09; 0.17] 0.549
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any non-ocular severe AE, n (%)	3 (11.5)	2 (9.5)	1.32 [0.19; 9.33] 0.780	1.21 [0.22; 6.59] 0.826	0.02 [-0.16; 0.20] 0.822
European Region					
N'/N	204 / 204	207 / 207			
Any non-ocular severe AE, n (%)	36 (17.6)	44 (21.3)	0.81 [0.47; 1.39] 0.436	0.82 [0.56; 1.22] 0.339	-0.04 [-0.11; 0.04] 0.337

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any non-ocular severe AE, n (%)	7 (14.6)	9 (15.8)	0.97 [0.33; 2.86] 0.959	1.04 [0.43; 2.50] 0.932	0.01 [-0.13; 0.14] 0.932

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KITE: logit(proportion) = treatment [by region].
Week 52 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by region].

Table 14-5.6 Any severe non-ocular adverse event by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.765**					
KESTREL					
Interaction Test:	p = 0.522				
Type 1					
N'/N	12 / 12	6 / 6			
Any non-ocular severe AE, n (%)	1 (8.3)	1 (16.7)	0.45 [0.02; 8.83] 0.602	0.50 [0.04; 6.68] 0.600	-0.08 [-0.42; 0.25] 0.628
Type 2					
N'/N	177 / 177	181 / 181			
Any non-ocular severe AE, n (%)	20 (11.3)	17 (9.4)	1.23 [0.62; 2.43] 0.554	1.20 [0.65; 2.22] 0.554	0.02 [-0.04; 0.08] 0.554
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any non-ocular severe AE, n (%)	0 (0.0)	2 (28.6)	N.E.	0.08 [0.00; 1.49] 0.090	-0.29 [-0.62; 0.05] 0.094
Type 2					
N'/N	160 / 160	174 / 174			
Any non-ocular severe AE, n (%)	17 (10.6)	15 (8.6)	1.26 [0.61; 2.62] 0.535	1.23 [0.64; 2.39] 0.535	0.02 [-0.04; 0.08] 0.535
Pooled Analysis					
Interaction Test:	p = 0.053				
Type 1					
N'/N	31 / 31	13 / 13			
Any non-ocular severe AE, n (%)	1 (3.2)	3 (23.1)	0.11 [0.01; 1.21] 0.071	0.19 [0.03; 1.14] 0.046 *	-0.20 [-0.44; 0.04] 0.110

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any non-ocular severe AE, n (%)	37 (11.0)	32 (9.0)	1.24 [0.75; 2.04] 0.399	1.22 [0.78; 1.91] 0.392	0.02 [-0.03; 0.06] 0.392
Any non-ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.392**					
KESTREL					
Interaction Test:	p = 0.733				
Type 1					
N'/N	12 / 12	6 / 6			
Any non-ocular severe AE, n (%)	3 (25.0)	1 (16.7)	1.67 [0.14; 20.59] 0.690	1.50 [0.20; 11.54] 0.697	0.08 [-0.30; 0.47] 0.672
Type 2					
N'/N	177 / 177	181 / 181			
Any non-ocular severe AE, n (%)	33 (18.6)	32 (17.7)	1.07 [0.62; 1.83] 0.813	1.05 [0.68; 1.64] 0.813	0.01 [-0.07; 0.09] 0.813
KITE					
Interaction Test:	p = 0.353				
Type 1					
N'/N	19 / 19	7 / 7			
Any non-ocular severe AE, n (%)	2 (10.5)	2 (28.6)	0.29 [0.03; 2.65] 0.275	0.37 [0.06; 2.14] 0.266	-0.18 [-0.54; 0.18] 0.329
Type 2					
N'/N	160 / 160	174 / 174			
Any non-ocular severe AE, n (%)	31 (19.4)	38 (21.8)	0.86 [0.51; 1.46] 0.579	0.89 [0.58; 1.35] 0.579	-0.02 [-0.11; 0.06] 0.578
Pooled Analysis					
Interaction Test:	p = 0.652				
Type 1					
N'/N	31 / 31	13 / 13			
Any non-ocular severe AE, n (%)	5 (16.1)	3 (23.1)	0.66 [0.13; 3.28] 0.607	0.72 [0.20; 2.55] 0.621	-0.06 [-0.33; 0.20] 0.637

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any non-ocular severe AE, n (%)	64 (19.0)	70 (19.7)	0.96 [0.66; 1.40] 0.831	0.97 [0.71; 1.31] 0.819	-0.01 [-0.07; 0.05] 0.819

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KITE: logit(proportion) = treatment [by diabetes type].

Table 14-5.7 Any severe non-ocular adverse event by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.765**					
KESTREL					
Interaction Test:	p = 0.927				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any non-ocular severe AE, n (%)	7 (9.2)	9 (8.4)	1.10 [0.39; 3.11] 0.851	1.10 [0.43; 2.81] 0.850	0.01 [-0.08; 0.09] 0.851
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any non-ocular severe AE, n (%)	13 (11.6)	9 (11.3)	1.04 [0.42; 2.56] 0.939	1.03 [0.46; 2.30] 0.939	0.00 [-0.09; 0.09] 0.939
KITE					
Interaction Test:	p = 0.497				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any non-ocular severe AE, n (%)	5 (6.1)	8 (8.3)	0.71 [0.22; 2.28] 0.569	0.73 [0.25; 2.15] 0.570	-0.02 [-0.10; 0.05] 0.563
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any non-ocular severe AE, n (%)	12 (12.4)	9 (10.6)	1.19 [0.48; 2.99] 0.707	1.17 [0.52; 2.64] 0.708	0.02 [-0.07; 0.11] 0.706
Pooled Analysis					
Interaction Test:	p = 0.692				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any non-ocular severe AE, n (%)	12 (7.6)	17 (8.4)	0.90 [0.42; 1.95] 0.792	0.91 [0.45; 1.85] 0.805	-0.01 [-0.06; 0.05] 0.804

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any non-ocular severe AE, n (%)	25 (12.0)	18 (10.9)	1.10 [0.58; 2.10] 0.762	1.10 [0.62; 1.94] 0.751	0.01 [-0.05; 0.08] 0.749
Any non-ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.392**					
KESTREL					
Interaction Test:	p = 0.197				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any non-ocular severe AE, n (%)	13 (17.1)	13 (12.1)	1.49 [0.65; 3.43] 0.346	1.41 [0.69; 2.86] 0.345	0.05 [-0.06; 0.15] 0.354
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any non-ocular severe AE, n (%)	22 (19.6)	20 (25.0)	0.73 [0.37; 1.46] 0.377	0.79 [0.46; 1.34] 0.375	-0.05 [-0.17; 0.07] 0.382
KITE					
Interaction Test:	p = 0.281				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any non-ocular severe AE, n (%)	12 (14.6)	22 (22.9)	0.58 [0.27; 1.25] 0.164	0.64 [0.34; 1.21] 0.169	-0.08 [-0.20; 0.03] 0.153
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any non-ocular severe AE, n (%)	21 (21.6)	18 (21.2)	1.03 [0.51; 2.09] 0.938	1.02 [0.59; 1.79] 0.938	0.00 [-0.11; 0.12] 0.938
Pooled Analysis					
Interaction Test:	p = 0.935				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any non-ocular severe AE, n (%)	25 (15.8)	35 (17.2)	0.90 [0.51; 1.58] 0.723	0.91 [0.57; 1.44] 0.677	-0.02 [-0.09; 0.06] 0.677

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any non-ocular severe AE, n (%)	43 (20.6)	38 (23.0)	0.88 [0.53; 1.44] 0.600	0.89 [0.61; 1.31] 0.564	-0.02 [-0.11; 0.06] 0.565

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-5.8 Any severe non-ocular adverse event by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.765**					
KESTREL					
Interaction Test:	p = 0.208				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any non-ocular severe AE, n (%)	10 (8.3)	12 (10.9)	0.74 [0.31; 1.79] 0.508	0.76 [0.34; 1.70] 0.508	-0.03 [-0.10; 0.05] 0.509
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any non-ocular severe AE, n (%)	4 (13.3)	4 (10.3)	1.35 [0.31; 5.89] 0.693	1.30 [0.35; 4.78] 0.693	0.03 [-0.12; 0.19] 0.696
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any non-ocular severe AE, n (%)	7 (17.9)	2 (5.3)	3.94 [0.76; 20.34] 0.102	3.41 [0.76; 15.39] 0.111	0.13 [-0.01; 0.27] 0.075
KITE					
Interaction Test:	p = 0.646				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any non-ocular severe AE, n (%)	9 (10.6)	7 (7.6)	1.44 [0.51; 4.05] 0.492	1.39 [0.54; 3.57] 0.492	0.03 [-0.06; 0.11] 0.492
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any non-ocular severe AE, n (%)	3 (5.9)	4 (8.2)	0.70 [0.15; 3.32] 0.656	0.72 [0.17; 3.06] 0.657	-0.02 [-0.12; 0.08] 0.656
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any non-ocular severe AE, n (%)	5 (11.6)	6 (15.0)	0.75 [0.21; 2.67] 0.651	0.78 [0.26; 2.34] 0.652	-0.03 [-0.18; 0.11] 0.652

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.738				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any non-ocular severe AE, n (%)	19 (9.3)	19 (9.4)	0.97 [0.49; 1.90] 0.922	0.98 [0.54; 1.80] 0.956	-0.00 [-0.06; 0.06] 0.956
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any non-ocular severe AE, n (%)	7 (8.6)	8 (9.1)	0.97 [0.33; 2.81] 0.950	0.99 [0.38; 2.57] 0.979	-0.00 [-0.09; 0.09] 0.979
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any non-ocular severe AE, n (%)	12 (14.6)	8 (10.3)	1.50 [0.58; 3.91] 0.402	1.42 [0.61; 3.30] 0.407	0.04 [-0.06; 0.15] 0.406
Any non-ocular severe AE, Week 100 Test of heterogeneity in main analysis: **p_H=0.392**					
KESTREL					
Interaction Test:	p = 0.378				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any non-ocular severe AE, n (%)	22 (18.3)	22 (20.0)	0.90 [0.47; 1.73] 0.748	0.92 [0.54; 1.56] 0.748	-0.02 [-0.12; 0.09] 0.749
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any non-ocular severe AE, n (%)	4 (13.3)	6 (15.4)	0.85 [0.22; 3.32] 0.811	0.87 [0.27; 2.80] 0.811	-0.02 [-0.19; 0.15] 0.809
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any non-ocular severe AE, n (%)	10 (25.6)	5 (13.2)	2.28 [0.70; 7.43] 0.173	1.95 [0.73; 5.17] 0.180	0.12 [-0.05; 0.30] 0.160

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.081				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any non-ocular severe AE, n (%)	20 (23.5)	17 (18.5)	1.36 [0.66; 2.81] 0.410	1.27 [0.72; 2.26] 0.410	0.05 [-0.07; 0.17] 0.410
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any non-ocular severe AE, n (%)	5 (9.8)	13 (26.5)	0.30 [0.10; 0.92] 0.036 *	0.37 [0.14; 0.96] 0.041 *	-0.17 [-0.32; -0.02] 0.027 *
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any non-ocular severe AE, n (%)	8 (18.6)	10 (25.0)	0.69 [0.24; 1.96] 0.481	0.74 [0.33; 1.70] 0.482	-0.06 [-0.24; 0.11] 0.480
Pooled Analysis					
Interaction Test:	p = 0.197				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any non-ocular severe AE, n (%)	42 (20.5)	39 (19.3)	1.08 [0.66; 1.75] 0.770	1.06 [0.72; 1.57] 0.752	0.01 [-0.07; 0.09] 0.752
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any non-ocular severe AE, n (%)	9 (11.1)	19 (21.6)	0.46 [0.19; 1.10] 0.080	0.51 [0.25; 1.05] 0.061	-0.11 [-0.22; 0.00] 0.057

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any non-ocular severe AE, n (%)	18 (22.0)	15 (19.2)	1.19 [0.55; 2.58] 0.652	1.14 [0.62; 2.10] 0.675	0.03 [-0.10; 0.15] 0.675

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-5.9 Any severe non-ocular adverse event by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.765**					
KESTREL					
Interaction Test:	p = 0.433				
focal					
N'/N	59 / 59	48 / 48			
Any non-ocular severe AE, n (%)	5 (8.5)	5 (10.4)	0.80 [0.22; 2.93] 0.732	0.81 [0.25; 2.65] 0.732	-0.02 [-0.13; 0.09] 0.734
diffuse					
N'/N	127 / 127	134 / 134			
Any non-ocular severe AE, n (%)	16 (12.6)	12 (9.0)	1.47 [0.66; 3.23] 0.344	1.41 [0.69; 2.86] 0.345	0.04 [-0.04; 0.11] 0.343
KITE					
Interaction Test:	p = 0.264				
focal					
N'/N	63 / 63	66 / 66			
Any non-ocular severe AE, n (%)	5 (7.9)	8 (12.1)	0.62 [0.19; 2.02] 0.433	0.65 [0.23; 1.89] 0.435	-0.04 [-0.15; 0.06] 0.427
diffuse					
N'/N	115 / 115	109 / 109			
Any non-ocular severe AE, n (%)	12 (10.4)	8 (7.3)	1.47 [0.58; 3.75] 0.419	1.42 [0.60; 3.34] 0.420	0.03 [-0.04; 0.11] 0.414
Pooled Analysis					
Interaction Test:	p = 0.169				
focal					
N'/N	122 / 122	114 / 114			
Any non-ocular severe AE, n (%)	10 (8.2)	13 (11.4)	0.69 [0.29; 1.65] 0.404	0.72 [0.33; 1.59] 0.414	-0.03 [-0.11; 0.04] 0.413

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any non-ocular severe AE, n (%)	28 (11.6)	20 (8.2)	1.46 [0.79; 2.67] 0.225	1.41 [0.82; 2.44] 0.212	0.03 [-0.02; 0.09] 0.211
Any non-ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.392**					
KESTREL					
Interaction Test:	p = 0.570				
focal					
N'/N	59 / 59	48 / 48			
Any non-ocular severe AE, n (%)	10 (16.9)	9 (18.8)	0.88 [0.33; 2.39] 0.809	0.90 [0.40; 2.04] 0.808	-0.02 [-0.16; 0.13] 0.809
diffuse					
N'/N	127 / 127	134 / 134			
Any non-ocular severe AE, n (%)	26 (20.5)	23 (17.2)	1.24 [0.67; 2.32] 0.494	1.19 [0.72; 1.98] 0.495	0.03 [-0.06; 0.13] 0.494
KITE					
Interaction Test:	p = 0.355				
focal					
N'/N	63 / 63	66 / 66			
Any non-ocular severe AE, n (%)	10 (15.9)	16 (24.2)	0.59 [0.24; 1.42] 0.239	0.65 [0.32; 1.33] 0.243	-0.08 [-0.22; 0.05] 0.232
diffuse					
N'/N	115 / 115	109 / 109			
Any non-ocular severe AE, n (%)	23 (20.0)	22 (20.2)	0.99 [0.51; 1.90] 0.973	0.99 [0.59; 1.67] 0.973	-0.00 [-0.11; 0.10] 0.973
Pooled Analysis					
Interaction Test:	p = 0.282				
focal					
N'/N	122 / 122	114 / 114			
Any non-ocular severe AE, n (%)	20 (16.4)	25 (21.9)	0.72 [0.37; 1.38] 0.320	0.75 [0.44; 1.28] 0.293	-0.05 [-0.15; 0.05] 0.292

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any non-ocular severe AE, n (%)	49 (20.2)	45 (18.5)	1.11 [0.71; 1.74] 0.650	1.09 [0.76; 1.57] 0.637	0.02 [-0.05; 0.09] 0.637

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-5.10 Any severe non-ocular adverse event by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.765**					
KESTREL					
Interaction Test:	p = 0.548				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any non-ocular severe AE, n (%)	10 (9.3)	7 (7.3)	1.31 [0.48; 3.59] 0.599	1.28 [0.51; 3.23] 0.599	0.02 [-0.06; 0.10] 0.595
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any non-ocular severe AE, n (%)	8 (11.4)	9 (12.7)	0.89 [0.32; 2.45] 0.820	0.90 [0.37; 2.20] 0.820	-0.01 [-0.12; 0.09] 0.820
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any non-ocular severe AE, n (%)	3 (25.0)	2 (10.0)	3.00 [0.42; 21.31] 0.272	2.50 [0.49; 12.89] 0.273	0.15 [-0.13; 0.43] 0.290
KITE					
Interaction Test:	p = 0.276				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any non-ocular severe AE, n (%)	6 (7.1)	9 (11.0)	0.62 [0.21; 1.82] 0.380	0.64 [0.24; 1.73] 0.381	-0.04 [-0.13; 0.05] 0.377
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any non-ocular severe AE, n (%)	9 (12.2)	5 (6.3)	2.05 [0.65; 6.43] 0.219	1.92 [0.67; 5.47] 0.221	0.06 [-0.03; 0.15] 0.213
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any non-ocular severe AE, n (%)	2 (10.0)	3 (15.8)	0.59 [0.09; 4.01] 0.592	0.63 [0.12; 3.38] 0.593	-0.06 [-0.27; 0.15] 0.589

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.771				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any non-ocular severe AE, n (%)	16 (8.3)	16 (9.0)	0.91 [0.44; 1.88] 0.790	0.93 [0.48; 1.81] 0.826	-0.01 [-0.06; 0.05] 0.826
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any non-ocular severe AE, n (%)	17 (11.8)	14 (9.3)	1.30 [0.62; 2.75] 0.492	1.26 [0.65; 2.46] 0.498	0.02 [-0.05; 0.09] 0.498
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any non-ocular severe AE, n (%)	5 (15.6)	5 (12.8)	1.29 [0.34; 4.95] 0.706	1.25 [0.41; 3.77] 0.701	0.03 [-0.14; 0.20] 0.708
Any non-ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.392**					
KESTREL					
Interaction Test:	p = 0.865				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any non-ocular severe AE, n (%)	19 (17.8)	14 (14.6)	1.26 [0.60; 2.69] 0.541	1.22 [0.65; 2.29] 0.542	0.03 [-0.07; 0.13] 0.539
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any non-ocular severe AE, n (%)	14 (20.0)	13 (18.3)	1.12 [0.48; 2.58] 0.799	1.09 [0.55; 2.15] 0.799	0.02 [-0.11; 0.15] 0.799
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any non-ocular severe AE, n (%)	3 (25.0)	6 (30.0)	0.78 [0.15; 3.93] 0.761	0.83 [0.25; 2.73] 0.763	-0.05 [-0.37; 0.27] 0.757

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.620				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any non-ocular severe AE, n (%)	15 (17.6)	16 (19.5)	0.88 [0.40; 1.93] 0.757	0.90 [0.48; 1.71] 0.757	-0.02 [-0.14; 0.10] 0.757
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any non-ocular severe AE, n (%)	15 (20.3)	18 (22.8)	0.86 [0.40; 1.87] 0.706	0.89 [0.48; 1.63] 0.706	-0.03 [-0.16; 0.11] 0.705
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any non-ocular severe AE, n (%)	3 (15.0)	6 (31.6)	0.38 [0.08; 1.82] 0.228	0.48 [0.14; 1.63] 0.238	-0.17 [-0.43; 0.10] 0.213
Pooled Analysis					
Interaction Test:	p = 0.537				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any non-ocular severe AE, n (%)	34 (17.7)	30 (16.9)	1.06 [0.62; 1.82] 0.841	1.05 [0.67; 1.65] 0.820	0.01 [-0.07; 0.09] 0.820
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any non-ocular severe AE, n (%)	29 (20.1)	31 (20.7)	0.98 [0.56; 1.74] 0.957	0.98 [0.62; 1.53] 0.916	-0.00 [-0.10; 0.09] 0.916

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any non-ocular severe AE, n (%)	6 (18.8)	12 (30.8)	0.52 [0.17; 1.61] 0.259	0.63 [0.27; 1.46] 0.276	-0.12 [-0.32; 0.09] 0.262

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-5.11 Any severe non-ocular adverse event by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.765**					
KESTREL					
Interaction Test:	p = 0.750				
presence					
N'/N	62 / 62	61 / 61			
Any non-ocular severe AE, n (%)	8 (12.9)	6 (9.8)	1.36 [0.44; 4.18] 0.593	1.31 [0.48; 3.56] 0.594	0.03 [-0.08; 0.14] 0.592
absence					
N'/N	127 / 127	126 / 126			
Any non-ocular severe AE, n (%)	13 (10.2)	12 (9.5)	1.08 [0.47; 2.48] 0.849	1.07 [0.51; 2.26] 0.849	0.01 [-0.07; 0.08] 0.849
KITE					
Interaction Test:	p = 0.125				
presence					
N'/N	56 / 56	67 / 67			
Any non-ocular severe AE, n (%)	3 (5.4)	8 (11.9)	0.42 [0.11; 1.66] 0.214	0.45 [0.12; 1.61] 0.219	-0.07 [-0.16; 0.03] 0.186
absence					
N'/N	123 / 123	114 / 114			
Any non-ocular severe AE, n (%)	14 (11.4)	9 (7.9)	1.50 [0.62; 3.61] 0.367	1.44 [0.65; 3.20] 0.369	0.03 [-0.04; 0.11] 0.361
Pooled Analysis					
Interaction Test:	p = 0.427				
presence					
N'/N	118 / 118	128 / 128			
Any non-ocular severe AE, n (%)	11 (9.3)	14 (10.9)	0.83 [0.36; 1.91] 0.664	0.84 [0.39; 1.80] 0.654	-0.02 [-0.09; 0.06] 0.650

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any non-ocular severe AE, n (%)	27 (10.8)	21 (8.8)	1.26 [0.69; 2.30] 0.451	1.24 [0.72; 2.13] 0.446	0.02 [-0.03; 0.07] 0.443
Any non-ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.392**					
KESTREL					
Interaction Test:	p = 0.758				
presence					
N'/N	62 / 62	61 / 61			
Any non-ocular severe AE, n (%)	12 (19.4)	12 (19.7)	0.98 [0.40; 2.39] 0.965	0.98 [0.48; 2.02] 0.965	-0.00 [-0.14; 0.14] 0.965
absence					
N'/N	127 / 127	126 / 126			
Any non-ocular severe AE, n (%)	24 (18.9)	21 (16.7)	1.17 [0.61; 2.22] 0.643	1.13 [0.67; 1.93] 0.643	0.02 [-0.07; 0.12] 0.642
KITE					
Interaction Test:	p = 0.345				
presence					
N'/N	56 / 56	67 / 67			
Any non-ocular severe AE, n (%)	9 (16.1)	17 (25.4)	0.56 [0.23; 1.39] 0.212	0.63 [0.31; 1.31] 0.218	-0.09 [-0.23; 0.05] 0.199
absence					
N'/N	123 / 123	114 / 114			
Any non-ocular severe AE, n (%)	24 (19.5)	23 (20.2)	0.96 [0.51; 1.82] 0.898	0.97 [0.58; 1.61] 0.898	-0.01 [-0.11; 0.10] 0.898
Pooled Analysis					
Interaction Test:	p = 0.379				
presence					
N'/N	118 / 118	128 / 128			
Any non-ocular severe AE, n (%)	21 (17.8)	29 (22.7)	0.75 [0.40; 1.40] 0.368	0.79 [0.47; 1.31] 0.353	-0.05 [-0.15; 0.05] 0.349

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any non-ocular severe AE, n (%)	48 (19.2)	44 (18.3)	1.06 [0.67; 1.67] 0.801	1.05 [0.72; 1.51] 0.814	0.01 [-0.06; 0.08] 0.814

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-5.12 Any severe non-ocular adverse event by exposure (week 52) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular severe AE, Week 52					
Test of heterogeneity in main analysis: **p_H=0.765**					
KESTREL					
Interaction Test:	p = 0.017 *				
Non-exposed					
N'/N	71 / 71	75 / 75			
Any non-ocular severe AE, n (%)	13 (18.3)	5 (6.7)	3.14 [1.06; 9.32] 0.039 *	2.75 [1.03; 7.31] 0.043 *	0.12 [0.01; 0.22] 0.032 *
Exposed					
N'/N	118 / 118	112 / 112			
Any non-ocular severe AE, n (%)	8 (6.8)	13 (11.6)	0.55 [0.22; 1.39] 0.209	0.58 [0.25; 1.36] 0.211	-0.05 [-0.12; 0.03] 0.205
KITE					
Interaction Test:	p = 0.614				
Non-exposed					
N'/N	85 / 85	90 / 90			
Any non-ocular severe AE, n (%)	11 (12.9)	10 (11.1)	1.19 [0.48; 2.96] 0.710	1.16 [0.52; 2.60] 0.710	0.02 [-0.08; 0.11] 0.710
Exposed					
N'/N	94 / 94	91 / 91			
Any non-ocular severe AE, n (%)	6 (6.4)	7 (7.7)	0.82 [0.26; 2.53] 0.728	0.83 [0.29; 2.38] 0.728	-0.01 [-0.09; 0.06] 0.728
Pooled Analysis					
Interaction Test:	p = 0.036 *				
Non-exposed					
N'/N	156 / 156	165 / 165			
Any non-ocular severe AE, n (%)	24 (15.4)	15 (9.1)	1.83 [0.92; 3.64] 0.084	1.69 [0.92; 3.11] 0.085	0.06 [-0.01; 0.13] 0.086

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	212 / 212	203 / 203			
Any non-ocular severe AE, n (%)	14 (6.6)	20 (9.9)	0.63 [0.31; 1.30] 0.213	0.67 [0.35; 1.29] 0.227	-0.03 [-0.09; 0.02] 0.227

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 14-5.13 Any severe non-ocular adverse event by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular severe AE, Week 100					
Test of heterogeneity in main analysis: **p_H=0.392**					
KESTREL					
Interaction Test:	p = 0.359				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any non-ocular severe AE, n (%)	5 (41.7)	3 (23.1)	2.38 [0.42; 13.39] 0.325	1.81 [0.55; 5.98] 0.333	0.19 [-0.18; 0.55] 0.313
Exposed					
N'/N	177 / 177	174 / 174			
Any non-ocular severe AE, n (%)	31 (17.5)	30 (17.2)	1.02 [0.59; 1.77] 0.946	1.02 [0.64; 1.60] 0.946	0.00 [-0.08; 0.08] 0.946
KITE					
Interaction Test:	p = 0.413				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any non-ocular severe AE, n (%)	7 (41.2)	4 (33.3)	1.40 [0.30; 6.53] 0.669	1.24 [0.46; 3.30] 0.673	0.08 [-0.28; 0.43] 0.665
Exposed					
N'/N	162 / 162	169 / 169			
Any non-ocular severe AE, n (%)	26 (16.0)	36 (21.3)	0.71 [0.40; 1.23] 0.222	0.75 [0.48; 1.19] 0.224	-0.05 [-0.14; 0.03] 0.219
Pooled Analysis					
Interaction Test:	p = 0.215				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any non-ocular severe AE, n (%)	12 (41.4)	7 (28.0)	1.83 [0.58; 5.77] 0.300	1.45 [0.68; 3.09] 0.333	0.13 [-0.12; 0.38] 0.319

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any non-ocular severe AE, n (%)	57 (16.8)	66 (19.2)	0.85 [0.58; 1.26] 0.426	0.87 [0.63; 1.21] 0.414	-0.02 [-0.08; 0.03] 0.413

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

15 Safety analysis: Any adverse event leading to study drug discontinuation

Table 15-1.1 Any adverse event leading to study drug discontinuation (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any AE leading to study drug discontinuation, n (%)	4 (2.1)	7 (3.7)	0.56 [0.16; 1.93] 0.356	0.57 [0.17; 1.90] 0.356	-0.02 [-0.05; 0.02] 0.349
KITE, N'/N	179 / 179	181 / 181			
Any AE leading to study drug discontinuation, n (%)	10 (5.6)	8 (4.4)	1.28 [0.49; 3.32] 0.612	1.26 [0.51; 3.13] 0.612	0.01 [-0.03; 0.06] 0.612
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any AE leading to study drug discontinuation, n (%)	14 (3.8)	15 (4.1)	0.84 [0.38; 1.84] 0.657	0.94 [0.46; 1.91] 0.856	-0.00 [-0.03; 0.03] 0.856
p_H=0.298					
Any AE leading to study drug discontinuation, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any AE leading to study drug discontinuation, n (%)	5 (2.6)	9 (4.8)	0.54 [0.18; 1.63] 0.274	0.55 [0.19; 1.61] 0.275	-0.02 [-0.06; 0.02] 0.267
KITE, N'/N	179 / 179	181 / 181			
Any AE leading to study drug discontinuation, n (%)	15 (8.4)	8 (4.4)	1.98 [0.82; 4.79] 0.131	1.90 [0.82; 4.36] 0.132	0.04 [-0.01; 0.09] 0.124

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any AE leading to study drug discontinuation, n (%) p_H=0.072	20 (5.4)	17 (4.6)	1.02 [0.50; 2.08] 0.962	1.18 [0.63; 2.21] 0.606	0.01 [-0.02; 0.04] 0.607

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 15-1.2 Any adverse event leading to study drug discontinuation by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.298**					
KESTREL					
Interaction Test:	p = 0.243				
< 65 years					
N'/N	104 / 104	93 / 93			
Any AE leading to study drug discontinuation, n (%)	1 (1.0)	4 (4.3)	0.22 [0.02; 1.97] 0.174	0.22 [0.03; 1.96] 0.177	-0.03 [-0.08; 0.01] 0.148
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any AE leading to study drug discontinuation, n (%)	3 (3.5)	3 (3.2)	1.11 [0.22; 5.65] 0.900	1.11 [0.23; 5.33] 0.900	0.00 [-0.05; 0.06] 0.900
KITE					
Interaction Test:	p = 0.367				
< 65 years					
N'/N	100 / 100	102 / 102			
Any AE leading to study drug discontinuation, n (%)	7 (7.0)	4 (3.9)	1.84 [0.52; 6.51] 0.341	1.79 [0.54; 5.91] 0.343	0.03 [-0.03; 0.09] 0.335
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any AE leading to study drug discontinuation, n (%)	3 (3.8)	4 (5.1)	0.74 [0.16; 3.42] 0.700	0.75 [0.17; 3.24] 0.700	-0.01 [-0.08; 0.05] 0.699
Pooled Analysis					
Interaction Test:	p = 0.936				
< 65 years					
N'/N	204 / 204	195 / 195			
Any AE leading to study drug discontinuation, n (%)	8 (3.9)	8 (4.1)	0.86 [0.30; 2.43] 0.775	0.98 [0.38; 2.53] 0.965	-0.00 [-0.04; 0.04] 0.966

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any AE leading to study drug discontinuation, n (%)	6 (3.7)	7 (4.0)	0.81 [0.26; 2.53] 0.714	0.90 [0.31; 2.61] 0.844	-0.00 [-0.05; 0.04] 0.843
Any AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.072**					
KESTREL					
Interaction Test:	p = 0.451				
< 65 years					
N'/N	104 / 104	93 / 93			
Any AE leading to study drug discontinuation, n (%)	2 (1.9)	5 (5.4)	0.35 [0.07; 1.82] 0.210	0.36 [0.07; 1.80] 0.212	-0.03 [-0.09; 0.02] 0.201
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any AE leading to study drug discontinuation, n (%)	3 (3.5)	4 (4.3)	0.82 [0.18; 3.79] 0.803	0.83 [0.19; 3.60] 0.803	-0.01 [-0.06; 0.05] 0.802
KITE					
Interaction Test:	p = 0.454				
< 65 years					
N'/N	100 / 100	102 / 102			
Any AE leading to study drug discontinuation, n (%)	8 (8.0)	3 (2.9)	2.87 [0.74; 11.14] 0.128	2.72 [0.74; 9.96] 0.131	0.05 [-0.01; 0.11] 0.112
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any AE leading to study drug discontinuation, n (%)	7 (8.9)	5 (6.3)	1.44 [0.44; 4.74] 0.550	1.40 [0.46; 4.22] 0.550	0.03 [-0.06; 0.11] 0.548
Pooled Analysis					
Interaction Test:	p = 1.000				
< 65 years					
N'/N	204 / 204	195 / 195			
Any AE leading to study drug discontinuation, n (%)	10 (4.9)	8 (4.1)	1.02 [0.38; 2.76] 0.963	1.21 [0.49; 2.97] 0.679	0.01 [-0.03; 0.05] 0.681

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any AE leading to study drug discontinuation, n (%)	10 (6.1)	9 (5.2)	1.02 [0.39; 2.69] 0.961	1.15 [0.48; 2.77] 0.749	0.01 [-0.04; 0.06] 0.749

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 15-1.3 Any adverse event leading to study drug discontinuation by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.298**					
KESTREL					
Interaction Test:	p = 0.927				
Male					
N'/N	110 / 110	126 / 126			
Any AE leading to study drug discontinuation, n (%)	2 (1.8)	4 (3.2)	0.56 [0.10; 3.14] 0.514	0.57 [0.11; 3.07] 0.515	-0.01 [-0.05; 0.03] 0.501
Female					
N'/N	79 / 79	61 / 61			
Any AE leading to study drug discontinuation, n (%)	2 (2.5)	3 (4.9)	0.50 [0.08; 3.10] 0.459	0.51 [0.09; 2.99] 0.459	-0.02 [-0.09; 0.04] 0.468
KITE					
Interaction Test:	p = 0.042 *				
Male					
N'/N	120 / 120	115 / 115			
Any AE leading to study drug discontinuation, n (%)	3 (2.5)	6 (5.2)	0.47 [0.11; 1.91] 0.288	0.48 [0.12; 1.87] 0.290	-0.03 [-0.08; 0.02] 0.280
Female					
N'/N	59 / 59	66 / 66			
Any AE leading to study drug discontinuation, n (%)	7 (11.9)	2 (3.0)	4.31 [0.86; 21.63] 0.076	3.92 [0.85; 18.11] 0.081	0.09 [-0.00; 0.18] 0.061
Pooled Analysis					
Interaction Test:	p = 0.100				
Male					
N'/N	230 / 230	241 / 241			
Any AE leading to study drug discontinuation, n (%)	5 (2.2)	10 (4.1)	0.43 [0.14; 1.34] 0.145	0.51 [0.18; 1.48] 0.209	-0.02 [-0.05; 0.01] 0.205

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any AE leading to study drug discontinuation, n (%)	9 (6.5)	5 (3.9)	1.61 [0.51; 5.05] 0.419	1.73 [0.62; 4.85] 0.287	0.03 [-0.03; 0.08] 0.294
Any AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.072**					
KESTREL					
Interaction Test:	p = 0.925				
Male					
N'/N	110 / 110	126 / 126			
Any AE leading to study drug discontinuation, n (%)	3 (2.7)	6 (4.8)	0.56 [0.14; 2.30] 0.421	0.57 [0.15; 2.24] 0.423	-0.02 [-0.07; 0.03] 0.407
Female					
N'/N	79 / 79	61 / 61			
Any AE leading to study drug discontinuation, n (%)	2 (2.5)	3 (4.9)	0.50 [0.08; 3.10] 0.459	0.51 [0.09; 2.99] 0.459	-0.02 [-0.09; 0.04] 0.468
KITE					
Interaction Test:	p = 0.037 *				
Male					
N'/N	120 / 120	115 / 115			
Any AE leading to study drug discontinuation, n (%)	5 (4.2)	6 (5.2)	0.79 [0.23; 2.66] 0.704	0.80 [0.25; 2.54] 0.704	-0.01 [-0.06; 0.04] 0.704
Female					
N'/N	59 / 59	66 / 66			
Any AE leading to study drug discontinuation, n (%)	10 (16.9)	2 (3.0)	6.53 [1.37; 31.17] 0.019 *	5.59 [1.28; 24.50] 0.022 *	0.14 [0.03; 0.24] 0.009 *
Pooled Analysis					
Interaction Test:	p = 0.062				
Male					
N'/N	230 / 230	241 / 241			
Any AE leading to study drug discontinuation, n (%)	8 (3.5)	12 (5.0)	0.54 [0.21; 1.44] 0.220	0.69 [0.29; 1.67] 0.408	-0.02 [-0.05; 0.02] 0.404

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any AE leading to study drug discontinuation, n (%)	12 (8.7)	5 (3.9)	2.10 [0.70; 6.32] 0.184	2.33 [0.88; 6.19] 0.076	0.05 [-0.01; 0.11] 0.080

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 15-1.4 Any adverse event leading to study drug discontinuation by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.298**					
KESTREL					
Interaction Test:	p = 0.956				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any AE leading to study drug discontinuation, n (%)	2 (2.7)	3 (4.7)	0.56 [0.09; 3.49] 0.539	0.58 [0.10; 3.34] 0.539	-0.02 [-0.08; 0.04] 0.541
> 65 letters					
N'/N	115 / 115	123 / 123			
Any AE leading to study drug discontinuation, n (%)	2 (1.7)	4 (3.3)	0.53 [0.09; 2.93] 0.464	0.53 [0.10; 2.86] 0.465	-0.02 [-0.05; 0.02] 0.452
KITE					
Interaction Test:	p = 0.084				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any AE leading to study drug discontinuation, n (%)	2 (3.1)	6 (6.6)	0.45 [0.09; 2.30] 0.338	0.47 [0.10; 2.24] 0.341	-0.04 [-0.10; 0.03] 0.297
> 65 letters					
N'/N	114 / 114	90 / 90			
Any AE leading to study drug discontinuation, n (%)	8 (7.0)	2 (2.2)	3.32 [0.69; 16.03] 0.135	3.16 [0.69; 14.51] 0.139	0.05 [-0.01; 0.10] 0.093
Pooled Analysis					
Interaction Test:	p = 0.156				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any AE leading to study drug discontinuation, n (%)	4 (2.9)	9 (5.8)	0.44 [0.13; 1.51] 0.192	0.51 [0.16; 1.64] 0.250	-0.03 [-0.07; 0.02] 0.237

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any AE leading to study drug discontinuation, n (%)	10 (4.4)	6 (2.8)	1.40 [0.48; 4.05] 0.540	1.50 [0.53; 4.19] 0.439	0.01 [-0.02; 0.05] 0.429
Any AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.072**					
KESTREL					
Interaction Test:	p = 0.718				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any AE leading to study drug discontinuation, n (%)	2 (2.7)	4 (6.3)	0.42 [0.07; 2.35] 0.322	0.43 [0.08; 2.28] 0.323	-0.04 [-0.11; 0.03] 0.320
> 65 letters					
N'/N	115 / 115	123 / 123			
Any AE leading to study drug discontinuation, n (%)	3 (2.6)	5 (4.1)	0.63 [0.15; 2.71] 0.537	0.64 [0.16; 2.62] 0.537	-0.01 [-0.06; 0.03] 0.530
KITE					
Interaction Test:	p = 0.115				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any AE leading to study drug discontinuation, n (%)	4 (6.2)	6 (6.6)	0.93 [0.25; 3.43] 0.912	0.93 [0.27; 3.18] 0.912	-0.00 [-0.08; 0.07] 0.912
> 65 letters					
N'/N	114 / 114	90 / 90			
Any AE leading to study drug discontinuation, n (%)	11 (9.6)	2 (2.2)	4.70 [1.01; 21.77] 0.048 *	4.34 [0.99; 19.10] 0.052	0.07 [0.01; 0.14] 0.019 *
Pooled Analysis					
Interaction Test:	p = 0.132				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any AE leading to study drug discontinuation, n (%)	6 (4.3)	10 (6.5)	0.56 [0.19; 1.65] 0.294	0.70 [0.27; 1.85] 0.473	-0.02 [-0.07; 0.03] 0.472

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any AE leading to study drug discontinuation, n (%)	14 (6.1)	7 (3.3)	1.66 [0.63; 4.39] 0.307	1.81 [0.72; 4.57] 0.197	0.03 [-0.01; 0.06] 0.186

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 15-1.5 Any adverse event leading to study drug discontinuation by region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.298**					
KESTREL					
Interaction Test:	N.E.				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any AE leading to study drug discontinuation, n (%)	2 (2.2)	3 (3.6)	0.61 [0.10; 3.72] 0.589	0.61 [0.11; 3.59] 0.589	-0.01 [-0.06; 0.04] 0.588
European Region					
N'/N	69 / 69	75 / 75			
Any AE leading to study drug discontinuation, n (%)	0 (0.0)	4 (5.3)	N.E.	0.12 [0.01; 2.20] 0.153	-0.05 [-0.10; -0.00] 0.040 *
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any AE leading to study drug discontinuation, n (%)	2 (6.7)	0 (0.0)	N.E.	4.84 [0.24; 96.66] 0.302	0.07 [-0.02; 0.16] 0.143
KITE					
Interaction Test:	N.E.				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any AE leading to study drug discontinuation, n (%)	0 (0.0)	1 (4.8)	N.E.	0.27 [0.01; 6.34] 0.417	-0.05 [-0.14; 0.04] 0.306
European Region					
N'/N	135 / 135	132 / 132			
Any AE leading to study drug discontinuation, n (%)	6 (4.4)	4 (3.0)	1.49 [0.41; 5.40] 0.545	1.47 [0.42; 5.08] 0.546	0.01 [-0.03; 0.06] 0.542
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any AE leading to study drug discontinuation, n (%)	4 (22.2)	3 (10.7)	2.38 [0.46; 12.20] 0.298	2.07 [0.52; 8.20] 0.298	0.12 [-0.11; 0.34] 0.313

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	N.E.				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any AE leading to study drug discontinuation, n (%)	2 (2.2)	3 (3.6)	N.E.	0.61 [0.11; 3.59] 0.586	-0.01 [-0.06; 0.04] 0.588
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any AE leading to study drug discontinuation, n (%)	0 (0.0)	1 (4.8)	N.E.	0.27 [0.01; 6.34] 0.387	-0.05 [-0.14; 0.04] 0.306
European Region					
N'/N	204 / 204	207 / 207			
Any AE leading to study drug discontinuation, n (%)	6 (2.9)	8 (3.9)	N.E.	0.77 [0.28; 2.14] 0.617	-0.01 [-0.04; 0.03] 0.595
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any AE leading to study drug discontinuation, n (%)	6 (12.5)	3 (5.3)	N.E.	2.57 [0.73; 8.98] 0.129	0.09 [-0.02; 0.20] 0.112
Any AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: $\mathbf{p_H=0.072}$					
KESTREL					
Interaction Test:	N.E.				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any AE leading to study drug discontinuation, n (%)	2 (2.2)	3 (3.6)	0.61 [0.10; 3.72] 0.589	0.61 [0.11; 3.59] 0.589	-0.01 [-0.06; 0.04] 0.588
European Region					
N'/N	69 / 69	75 / 75			
Any AE leading to study drug discontinuation, n (%)	1 (1.4)	6 (8.0)	0.17 [0.02; 1.44] 0.104	0.18 [0.02; 1.47] 0.109	-0.07 [-0.13; 0.00] 0.057
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any AE leading to study drug discontinuation, n (%)	2 (6.7)	0 (0.0)	N.E.	4.84 [0.24; 96.66] 0.302	0.07 [-0.02; 0.16] 0.143

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	N.E.				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any AE leading to study drug discontinuation, n (%)	0 (0.0)	2 (9.5)	N.E.	0.16 [0.01; 3.22] 0.233	-0.10 [-0.22; 0.03] 0.137
European Region					
N'/N	135 / 135	132 / 132			
Any AE leading to study drug discontinuation, n (%)	10 (7.4)	3 (2.3)	3.44 [0.92; 12.79] 0.065	3.26 [0.92; 11.58] 0.068	0.05 [0.00; 0.10] 0.048 *
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any AE leading to study drug discontinuation, n (%)	5 (27.8)	3 (10.7)	3.21 [0.66; 15.57] 0.149	2.59 [0.70; 9.54] 0.152	0.17 [-0.07; 0.41] 0.157
Pooled Analysis					
Interaction Test:	N.E.				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any AE leading to study drug discontinuation, n (%)	2 (2.2)	3 (3.6)	N.E.	0.61 [0.11; 3.59] 0.586	-0.01 [-0.06; 0.04] 0.588
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any AE leading to study drug discontinuation, n (%)	0 (0.0)	2 (9.5)	N.E.	0.16 [0.01; 3.22] 0.172	-0.10 [-0.22; 0.03] 0.137
European Region					
N'/N	204 / 204	207 / 207			
Any AE leading to study drug discontinuation, n (%)	11 (5.4)	9 (4.3)	0.74 [0.21; 2.63] 0.642	1.24 [0.52; 3.00] 0.624	0.01 [-0.03; 0.05] 0.623

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any AE leading to study drug discontinuation, n (%)	7 (14.6)	3 (5.3)	N.E.	2.99 [0.90; 9.99] 0.063	0.11 [-0.00; 0.22] 0.054

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE, Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by region].
Week 52 / Pooled Analysis, Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by region].

Table 15-1.6 Any adverse event leading to study drug discontinuation by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.298**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	177 / 177	181 / 181			
Any AE leading to study drug discontinuation, n (%)	4 (2.3)	7 (3.9)	0.57 [0.17; 2.00] 0.384	0.58 [0.17; 1.96] 0.384	-0.02 [-0.05; 0.02] 0.376
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	160 / 160	174 / 174			
Any AE leading to study drug discontinuation, n (%)	10 (6.3)	8 (4.6)	1.38 [0.53; 3.60] 0.506	1.36 [0.55; 3.36] 0.506	0.02 [-0.03; 0.07] 0.506
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	337 / 337	355 / 355			
Any AE leading to study drug discontinuation, n (%)	14 (4.2)	15 (4.2)	0.88 [0.40; 1.95] 0.759	0.99 [0.49; 2.02] 0.981	-0.00 [-0.03; 0.03] 0.981

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.072**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	177 / 177	181 / 181			
Any AE leading to study drug discontinuation, n (%)	5 (2.8)	9 (5.0)	0.56 [0.18; 1.69] 0.301	0.57 [0.19; 1.66] 0.302	-0.02 [-0.06; 0.02] 0.292
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any AE leading to study drug discontinuation, n (%)	1 (5.3)	0 (0.0)	N.E.	1.20 [0.05; 26.47] 0.908	0.05 [-0.05; 0.15] 0.304
Type 2					
N'/N	160 / 160	174 / 174			
Any AE leading to study drug discontinuation, n (%)	14 (8.8)	8 (4.6)	1.99 [0.81; 4.88] 0.133	1.90 [0.82; 4.42] 0.134	0.04 [-0.01; 0.10] 0.130
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any AE leading to study drug discontinuation, n (%)	1 (3.2)	0 (0.0)	N.E.	1.20 [0.05; 26.47] 0.909	0.03 [-0.03; 0.09] 0.335

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any AE leading to study drug discontinuation, n (%)	19 (5.6)	17 (4.8)	1.04 [0.51; 2.13] 0.919	1.19 [0.63; 2.24] 0.598	0.01 [-0.02; 0.04] 0.600

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE, Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by diabetes type].
Week 52 / Pooled Analysis, Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 15-1.7 Any adverse event leading to study drug discontinuation by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.298**					
KESTREL					
Interaction Test:	p = 0.434				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any AE leading to study drug discontinuation, n (%)	2 (2.6)	3 (2.8)	0.94 [0.15; 5.75] 0.944	0.94 [0.16; 5.48] 0.944	-0.00 [-0.05; 0.05] 0.944
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any AE leading to study drug discontinuation, n (%)	2 (1.8)	4 (5.0)	0.35 [0.06; 1.93] 0.226	0.36 [0.07; 1.90] 0.228	-0.03 [-0.09; 0.02] 0.241
KITE					
Interaction Test:	p = 0.899				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any AE leading to study drug discontinuation, n (%)	4 (4.9)	4 (4.2)	1.18 [0.29; 4.87] 0.820	1.17 [0.30; 4.54] 0.820	0.01 [-0.05; 0.07] 0.820
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any AE leading to study drug discontinuation, n (%)	6 (6.2)	4 (4.7)	1.34 [0.36; 4.90] 0.663	1.31 [0.38; 4.50] 0.663	0.01 [-0.05; 0.08] 0.659
Pooled Analysis					
Interaction Test:	p = 0.707				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any AE leading to study drug discontinuation, n (%)	6 (3.8)	7 (3.4)	0.96 [0.30; 3.03] 0.945	1.08 [0.37; 3.15] 0.892	0.00 [-0.04; 0.04] 0.892

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any AE leading to study drug discontinuation, n (%)	8 (3.8)	8 (4.8)	0.72 [0.26; 2.02] 0.533	0.81 [0.32; 2.09] 0.670	-0.01 [-0.05; 0.03] 0.675
Any AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.072**					
KESTREL					
Interaction Test:	p = 0.240				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any AE leading to study drug discontinuation, n (%)	3 (3.9)	4 (3.7)	1.06 [0.23; 4.87] 0.942	1.06 [0.24; 4.58] 0.942	0.00 [-0.05; 0.06] 0.942
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any AE leading to study drug discontinuation, n (%)	2 (1.8)	5 (6.3)	0.27 [0.05; 1.44] 0.126	0.29 [0.06; 1.44] 0.128	-0.04 [-0.10; 0.01] 0.134
KITE					
Interaction Test:	p = 0.298				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any AE leading to study drug discontinuation, n (%)	5 (6.1)	5 (5.2)	1.18 [0.33; 4.23] 0.798	1.17 [0.35; 3.90] 0.797	0.01 [-0.06; 0.08] 0.798
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any AE leading to study drug discontinuation, n (%)	10 (10.3)	3 (3.5)	3.14 [0.84; 11.82] 0.090	2.92 [0.83; 10.27] 0.095	0.07 [-0.00; 0.14] 0.065
Pooled Analysis					
Interaction Test:	p = 0.885				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any AE leading to study drug discontinuation, n (%)	8 (5.1)	9 (4.4)	0.95 [0.34; 2.64] 0.922	1.12 [0.44; 2.85] 0.808	0.01 [-0.04; 0.05] 0.809

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any AE leading to study drug discontinuation, n (%)	12 (5.7)	8 (4.8)	1.05 [0.40; 2.72] 0.921	1.22 [0.52; 2.86] 0.647	0.01 [-0.04; 0.06] 0.650

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 15-1.8 Any adverse event leading to study drug discontinuation by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.298**					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any AE leading to study drug discontinuation, n (%)	1 (0.8)	3 (2.7)	0.30 [0.03; 2.92] 0.300	0.31 [0.03; 2.89] 0.301	-0.02 [-0.05; 0.02] 0.282
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any AE leading to study drug discontinuation, n (%)	3 (10.0)	4 (10.3)	0.97 [0.20; 4.71] 0.972	0.98 [0.24; 4.03] 0.972	-0.00 [-0.15; 0.14] 0.972
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE					
Interaction Test:	N.E.				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any AE leading to study drug discontinuation, n (%)	3 (3.5)	2 (2.2)	1.65 [0.27; 10.10] 0.590	1.62 [0.28; 9.48] 0.590	0.01 [-0.04; 0.06] 0.590
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any AE leading to study drug discontinuation, n (%)	0 (0.0)	3 (6.1)	N.E.	0.14 [0.01; 2.59] 0.185	-0.06 [-0.13; 0.01] 0.074
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any AE leading to study drug discontinuation, n (%)	7 (16.3)	3 (7.5)	2.40 [0.57; 10.00] 0.230	2.17 [0.60; 7.82] 0.236	0.09 [-0.05; 0.23] 0.210

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.218				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any AE leading to study drug discontinuation, n (%)	4 (2.0)	5 (2.5)	0.76 [0.20; 2.90] 0.686	0.81 [0.22; 2.91] 0.742	-0.00 [-0.03; 0.02] 0.744
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any AE leading to study drug discontinuation, n (%)	3 (3.7)	7 (8.0)	0.36 [0.09; 1.53] 0.168	0.55 [0.17; 1.81] 0.321	-0.04 [-0.11; 0.03] 0.295
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any AE leading to study drug discontinuation, n (%)	7 (8.5)	3 (3.8)	2.08 [0.50; 8.59] 0.311	2.17 [0.60; 7.82] 0.222	0.05 [-0.03; 0.12] 0.215
Any AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.072**					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any AE leading to study drug discontinuation, n (%)	2 (1.7)	4 (3.6)	0.45 [0.08; 2.50] 0.361	0.46 [0.09; 2.45] 0.362	-0.02 [-0.06; 0.02] 0.356
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any AE leading to study drug discontinuation, n (%)	3 (10.0)	4 (10.3)	0.97 [0.20; 4.71] 0.972	0.98 [0.24; 4.03] 0.972	-0.00 [-0.15; 0.14] 0.972
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any AE leading to study drug discontinuation, n (%)	0 (0.0)	1 (2.6)	N.E.	0.33 [0.01; 7.74] 0.487	-0.03 [-0.08; 0.02] 0.311

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.186				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any AE leading to study drug discontinuation, n (%)	7 (8.2)	2 (2.2)	4.04 [0.81; 20.01] 0.087	3.79 [0.81; 17.73] 0.091	0.06 [-0.00; 0.13] 0.070
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any AE leading to study drug discontinuation, n (%)	1 (2.0)	3 (6.1)	0.31 [0.03; 3.05] 0.313	0.32 [0.03; 2.98] 0.317	-0.04 [-0.12; 0.04] 0.290
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any AE leading to study drug discontinuation, n (%)	7 (16.3)	3 (7.5)	2.40 [0.57; 10.00] 0.230	2.17 [0.60; 7.82] 0.236	0.09 [-0.05; 0.23] 0.210
Pooled Analysis					
Interaction Test:	p = 0.318				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any AE leading to study drug discontinuation, n (%)	9 (4.4)	6 (3.0)	1.41 [0.48; 4.13] 0.533	1.51 [0.56; 4.09] 0.415	0.02 [-0.02; 0.05] 0.420
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any AE leading to study drug discontinuation, n (%)	4 (4.9)	7 (8.0)	0.44 [0.12; 1.65] 0.223	0.67 [0.21; 2.14] 0.496	-0.03 [-0.10; 0.05] 0.493

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any AE leading to study drug discontinuation, n (%)	7 (8.5)	4 (5.1)	1.43 [0.39; 5.29] 0.588	1.56 [0.51; 4.79] 0.428	0.03 [-0.04; 0.11] 0.400

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE, Week 100 / KESTREL: logit(proportion) = treatment [by duration of DME].

Table 15-1.9 Any adverse event leading to study drug discontinuation by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.298**					
KESTREL					
Interaction Test:	N.E.				
focal					
N'/N	59 / 59	48 / 48			
Any AE leading to study drug discontinuation, n (%)	1 (1.7)	0 (0.0)	N.E.	2.45 [0.10; 58.81] 0.581	0.02 [-0.02; 0.05] 0.313
diffuse					
N'/N	127 / 127	134 / 134			
Any AE leading to study drug discontinuation, n (%)	3 (2.4)	6 (4.5)	0.52 [0.13; 2.11] 0.357	0.53 [0.13; 2.06] 0.358	-0.02 [-0.07; 0.02] 0.345
KITE					
Interaction Test:	p = 0.877				
focal					
N'/N	63 / 63	66 / 66			
Any AE leading to study drug discontinuation, n (%)	3 (4.8)	2 (3.0)	1.60 [0.26; 9.91] 0.613	1.57 [0.27; 9.09] 0.614	0.02 [-0.05; 0.08] 0.612
diffuse					
N'/N	115 / 115	109 / 109			
Any AE leading to study drug discontinuation, n (%)	7 (6.1)	5 (4.6)	1.35 [0.41; 4.38] 0.619	1.33 [0.43; 4.06] 0.620	0.01 [-0.04; 0.07] 0.617
Pooled Analysis					
Interaction Test:	p = 0.458				
focal					
N'/N	122 / 122	114 / 114			
Any AE leading to study drug discontinuation, n (%)	4 (3.3)	2 (1.8)	1.71 [0.30; 9.86] 0.548	1.76 [0.38; 8.17] 0.463	0.02 [-0.02; 0.06] 0.396

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any AE leading to study drug discontinuation, n (%)	10 (4.1)	11 (4.5)	0.82 [0.33; 2.04] 0.672	0.90 [0.39; 2.09] 0.810	-0.00 [-0.04; 0.03] 0.809
Any AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.072**					
KESTREL					
Interaction Test:	p = 0.690				
focal					
N'/N	59 / 59	48 / 48			
Any AE leading to study drug discontinuation, n (%)	1 (1.7)	2 (4.2)	0.40 [0.03; 4.51] 0.456	0.41 [0.04; 4.35] 0.457	-0.02 [-0.09; 0.04] 0.459
diffuse					
N'/N	127 / 127	134 / 134			
Any AE leading to study drug discontinuation, n (%)	4 (3.1)	6 (4.5)	0.69 [0.19; 2.52] 0.578	0.70 [0.20; 2.43] 0.579	-0.01 [-0.06; 0.03] 0.574
KITE					
Interaction Test:	p = 0.318				
focal					
N'/N	63 / 63	66 / 66			
Any AE leading to study drug discontinuation, n (%)	5 (7.9)	1 (1.5)	5.60 [0.64; 49.37] 0.121	5.24 [0.63; 43.60] 0.126	0.06 [-0.01; 0.14] 0.085
diffuse					
N'/N	115 / 115	109 / 109			
Any AE leading to study drug discontinuation, n (%)	10 (8.7)	6 (5.5)	1.63 [0.57; 4.66] 0.358	1.58 [0.59; 4.20] 0.359	0.03 [-0.04; 0.10] 0.350
Pooled Analysis					
Interaction Test:	p = 0.606				
focal					
N'/N	122 / 122	114 / 114			
Any AE leading to study drug discontinuation, n (%)	6 (4.9)	3 (2.6)	1.58 [0.37; 6.69] 0.535	1.89 [0.50; 7.10] 0.336	0.02 [-0.03; 0.07] 0.340

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any AE leading to study drug discontinuation, n (%)	14 (5.8)	12 (4.9)	1.03 [0.45; 2.37] 0.946	1.15 [0.54; 2.45] 0.710	0.01 [-0.03; 0.05] 0.710

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL: logit(proportion) = treatment [by DME type].

Table 15-1.10 Any adverse event leading to study drug discontinuation by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.298**					
KESTREL					
Interaction Test:	N.E.				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any AE leading to study drug discontinuation, n (%)	2 (1.9)	3 (3.1)	0.59 [0.10; 3.61] 0.569	0.60 [0.10; 3.50] 0.569	-0.01 [-0.06; 0.03] 0.569
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any AE leading to study drug discontinuation, n (%)	2 (2.9)	4 (5.6)	0.49 [0.09; 2.78] 0.423	0.51 [0.10; 2.68] 0.424	-0.03 [-0.09; 0.04] 0.412
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE					
Interaction Test:	p = 0.938				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any AE leading to study drug discontinuation, n (%)	6 (7.1)	5 (6.1)	1.17 [0.34; 3.99] 0.802	1.16 [0.37; 3.65] 0.803	0.01 [-0.07; 0.08] 0.802
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any AE leading to study drug discontinuation, n (%)	3 (4.1)	2 (2.5)	1.63 [0.26; 10.02] 0.600	1.60 [0.28; 9.32] 0.600	0.02 [-0.04; 0.07] 0.599
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any AE leading to study drug discontinuation, n (%)	1 (5.0)	1 (5.3)	0.95 [0.06; 16.31] 0.970	0.95 [0.06; 14.13] 0.970	-0.00 [-0.14; 0.14] 0.970

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.981				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any AE leading to study drug discontinuation, n (%)	8 (4.2)	8 (4.5)	0.86 [0.31; 2.40] 0.770	0.94 [0.36; 2.44] 0.904	-0.00 [-0.04; 0.04] 0.904
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any AE leading to study drug discontinuation, n (%)	5 (3.5)	6 (4.0)	0.75 [0.22; 2.63] 0.659	0.87 [0.27; 2.77] 0.808	-0.01 [-0.05; 0.04] 0.807
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any AE leading to study drug discontinuation, n (%)	1 (3.1)	1 (2.6)	0.96 [0.06; 16.49] 0.978	0.95 [0.06; 14.13] 0.971	-0.00 [-0.08; 0.08] 0.970
Any AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.072**					
KESTREL					
Interaction Test:	N.E.				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any AE leading to study drug discontinuation, n (%)	3 (2.8)	4 (4.2)	0.66 [0.14; 3.04] 0.597	0.67 [0.15; 2.93] 0.598	-0.01 [-0.06; 0.04] 0.599
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any AE leading to study drug discontinuation, n (%)	2 (2.9)	5 (7.0)	0.39 [0.07; 2.07] 0.268	0.41 [0.08; 2.02] 0.271	-0.04 [-0.11; 0.03] 0.249
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.984				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any AE leading to study drug discontinuation, n (%)	9 (10.6)	5 (6.1)	1.82 [0.58; 5.69] 0.301	1.74 [0.61; 4.96] 0.303	0.04 [-0.04; 0.13] 0.291
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any AE leading to study drug discontinuation, n (%)	4 (5.4)	2 (2.5)	2.20 [0.39; 12.38] 0.371	2.14 [0.40; 11.31] 0.373	0.03 [-0.03; 0.09] 0.364
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any AE leading to study drug discontinuation, n (%)	2 (10.0)	1 (5.3)	2.00 [0.17; 24.07] 0.585	1.90 [0.19; 19.27] 0.587	0.05 [-0.12; 0.21] 0.575
Pooled Analysis					
Interaction Test:	p = 0.732				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any AE leading to study drug discontinuation, n (%)	12 (6.3)	9 (5.1)	1.13 [0.45; 2.83] 0.799	1.25 [0.55; 2.89] 0.593	0.01 [-0.03; 0.06] 0.592
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any AE leading to study drug discontinuation, n (%)	6 (4.2)	7 (4.7)	0.73 [0.23; 2.31] 0.589	0.89 [0.31; 2.58] 0.831	-0.01 [-0.05; 0.04] 0.831

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any AE leading to study drug discontinuation, n (%)	2 (6.3)	1 (2.6)	1.86 [0.16; 22.18] 0.625	1.90 [0.19; 19.27] 0.584	0.03 [-0.07; 0.12] 0.583

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 100 / KESTREL: logit(proportion) = treatment [by CSFT].

Table 15-1.11 Any adverse event leading to study drug discontinuation by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.298**					
KESTREL					
Interaction Test:	p = 0.547				
presence					
N'/N	62 / 62	61 / 61			
Any AE leading to study drug discontinuation, n (%)	1 (1.6)	3 (4.9)	0.32 [0.03; 3.13] 0.326	0.33 [0.04; 3.07] 0.328	-0.03 [-0.10; 0.03] 0.301
absence					
N'/N	127 / 127	126 / 126			
Any AE leading to study drug discontinuation, n (%)	3 (2.4)	4 (3.2)	0.74 [0.16; 3.37] 0.695	0.74 [0.17; 3.26] 0.695	-0.01 [-0.05; 0.03] 0.694
KITE					
Interaction Test:	p = 0.274				
presence					
N'/N	56 / 56	67 / 67			
Any AE leading to study drug discontinuation, n (%)	2 (3.6)	4 (6.0)	0.58 [0.10; 3.31] 0.543	0.60 [0.11; 3.15] 0.544	-0.02 [-0.10; 0.05] 0.529
absence					
N'/N	123 / 123	114 / 114			
Any AE leading to study drug discontinuation, n (%)	8 (6.5)	4 (3.5)	1.91 [0.56; 6.53] 0.301	1.85 [0.57; 5.99] 0.302	0.03 [-0.03; 0.09] 0.287
Pooled Analysis					
Interaction Test:	p = 0.210				
presence					
N'/N	118 / 118	128 / 128			
Any AE leading to study drug discontinuation, n (%)	3 (2.5)	7 (5.5)	0.41 [0.10; 1.67] 0.214	0.48 [0.13; 1.78] 0.259	-0.03 [-0.08; 0.02] 0.250

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any AE leading to study drug discontinuation, n (%)	11 (4.4)	8 (3.3)	1.19 [0.45; 3.13] 0.721	1.31 [0.53; 3.21] 0.556	0.01 [-0.02; 0.04] 0.554
Any AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.072**					
KESTREL					
Interaction Test:	p = 0.359				
presence					
N'/N	62 / 62	61 / 61			
Any AE leading to study drug discontinuation, n (%)	1 (1.6)	4 (6.6)	0.23 [0.03; 2.15] 0.199	0.25 [0.03; 2.14] 0.204	-0.05 [-0.12; 0.02] 0.164
absence					
N'/N	127 / 127	126 / 126			
Any AE leading to study drug discontinuation, n (%)	4 (3.1)	5 (4.0)	0.79 [0.21; 3.00] 0.726	0.79 [0.22; 2.89] 0.726	-0.01 [-0.05; 0.04] 0.725
KITE					
Interaction Test:	p = 0.221				
presence					
N'/N	56 / 56	67 / 67			
Any AE leading to study drug discontinuation, n (%)	3 (5.4)	4 (6.0)	0.89 [0.19; 4.16] 0.884	0.90 [0.21; 3.84] 0.884	-0.01 [-0.09; 0.08] 0.883
absence					
N'/N	123 / 123	114 / 114			
Any AE leading to study drug discontinuation, n (%)	12 (9.8)	4 (3.5)	2.97 [0.93; 9.50] 0.066	2.78 [0.92; 8.37] 0.069	0.06 [0.00; 0.12] 0.050 *
Pooled Analysis					
Interaction Test:	p = 0.115				
presence					
N'/N	118 / 118	128 / 128			
Any AE leading to study drug discontinuation, n (%)	4 (3.4)	8 (6.3)	0.45 [0.13; 1.60] 0.218	0.56 [0.17; 1.77] 0.313	-0.03 [-0.08; 0.03] 0.308

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any AE leading to study drug discontinuation, n (%)	16 (6.4)	9 (3.8)	1.51 [0.63; 3.63] 0.361	1.69 [0.76; 3.78] 0.191	0.03 [-0.01; 0.06] 0.188

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 15-1.12 Any adverse event leading to study drug discontinuation by exposure (week 52) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.298**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed					
N'/N	71 / 71	75 / 75			
Any AE leading to study drug discontinuation, n (%)	0 (0.0)	4 (5.3)	N.E.	0.12 [0.01; 2.14] 0.148	-0.05 [-0.10; -0.00] 0.040 *
Exposed					
N'/N	118 / 118	112 / 112			
Any AE leading to study drug discontinuation, n (%)	4 (3.4)	3 (2.7)	1.27 [0.28; 5.83] 0.754	1.27 [0.29; 5.53] 0.754	0.01 [-0.04; 0.05] 0.753
KITE					
Interaction Test:	p = 0.358				
Non-exposed					
N'/N	85 / 85	90 / 90			
Any AE leading to study drug discontinuation, n (%)	9 (10.6)	6 (6.7)	1.66 [0.56; 4.88] 0.358	1.59 [0.59; 4.27] 0.360	0.04 [-0.04; 0.12] 0.356
Exposed					
N'/N	94 / 94	91 / 91			
Any AE leading to study drug discontinuation, n (%)	1 (1.1)	2 (2.2)	0.48 [0.04; 5.37] 0.550	0.48 [0.04; 5.25] 0.551	-0.01 [-0.05; 0.03] 0.543
Pooled Analysis					
Interaction Test:	p = 0.918				
Non-exposed					
N'/N	156 / 156	165 / 165			
Any AE leading to study drug discontinuation, n (%)	9 (5.8)	10 (6.1)	0.83 [0.31; 2.20] 0.706	0.96 [0.41; 2.24] 0.920	-0.00 [-0.05; 0.05] 0.913

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	212 / 212	203 / 203			
Any AE leading to study drug discontinuation, n (%)	5 (2.4)	5 (2.5)	0.90 [0.25; 3.21] 0.871	0.95 [0.28; 3.25] 0.941	-0.00 [-0.03; 0.03] 0.941

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL: logit(proportion) = treatment [by exposure (week 52)].

Table 15-1.13 Any adverse event leading to study drug discontinuation by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.072**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any AE leading to study drug discontinuation, n (%)	0 (0.0)	3 (23.1)	N.E.	0.15 [0.01; 2.70] 0.200	-0.23 [-0.46; -0.00] 0.048 *
Exposed					
N'/N	177 / 177	174 / 174			
Any AE leading to study drug discontinuation, n (%)	5 (2.8)	6 (3.4)	0.81 [0.24; 2.72] 0.738	0.82 [0.25; 2.63] 0.738	-0.01 [-0.04; 0.03] 0.738
KITE					
Interaction Test:	p = 0.295				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any AE leading to study drug discontinuation, n (%)	7 (41.2)	5 (41.7)	0.98 [0.22; 4.39] 0.979	0.99 [0.41; 2.38] 0.979	-0.00 [-0.37; 0.36] 0.979
Exposed					
N'/N	162 / 162	169 / 169			
Any AE leading to study drug discontinuation, n (%)	8 (4.9)	3 (1.8)	2.87 [0.75; 11.03] 0.124	2.78 [0.75; 10.30] 0.126	0.03 [-0.01; 0.07] 0.111
Pooled Analysis					
Interaction Test:	p = 0.267				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any AE leading to study drug discontinuation, n (%)	7 (24.1)	8 (32.0)	0.56 [0.16; 1.92] 0.354	0.68 [0.30; 1.57] 0.370	-0.11 [-0.34; 0.12] 0.336

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any AE leading to study drug discontinuation, n (%)	13 (3.8)	9 (2.6)	1.29 [0.53; 3.19] 0.574	1.46 [0.63; 3.36] 0.370	0.01 [-0.01; 0.04] 0.372

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL: logit(proportion) = treatment [by exposure (week 100)].

Table 15-2.1 Any ocular adverse event leading to study drug discontinuation (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event leading to study drug discontinuation (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE leading to study drug discontinuation, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular AE leading to study drug discontinuation, n (%)	3 (1.6)	2 (1.1)	1.49 [0.25; 9.03] 0.663	1.48 [0.25; 8.78] 0.663	0.01 [-0.02; 0.03] 0.661
KITE, N'/N	179 / 179	181 / 181			
Any ocular AE leading to study drug discontinuation, n (%)	3 (1.7)	4 (2.2)	0.75 [0.17; 3.42] 0.715	0.76 [0.17; 3.34] 0.715	-0.01 [-0.03; 0.02] 0.713
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular AE leading to study drug discontinuation, n (%)	6 (1.6)	6 (1.6)	1.07 [0.33; 3.48] 0.913	1.00 [0.33; 3.08] 0.997	0.00 [-0.02; 0.02] 0.997
p_H=0.570					
Any ocular AE leading to study drug discontinuation, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular AE leading to study drug discontinuation, n (%)	3 (1.6)	2 (1.1)	1.49 [0.25; 9.03] 0.663	1.48 [0.25; 8.78] 0.663	0.01 [-0.02; 0.03] 0.661
KITE, N'/N	179 / 179	181 / 181			
Any ocular AE leading to study drug discontinuation, n (%)	5 (2.8)	4 (2.2)	1.27 [0.34; 4.81] 0.724	1.26 [0.35; 4.63] 0.724	0.01 [-0.03; 0.04] 0.723

	Treatment Groups		Comparison		
Any ocular adverse event leading to study drug discontinuation (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular AE leading to study drug discontinuation, n (%)	8 (2.2)	6 (1.6)	1.38 [0.45; 4.26] 0.576	1.34 [0.47; 3.82] 0.585	0.01 [-0.01; 0.03] 0.585
p_H=0.889					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 15-2.2 Any ocular adverse event leading to study drug discontinuation by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event leading to study drug discontinuation by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.889**					
KESTREL					
Interaction Test:	p = 0.625				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular AE leading to study drug discontinuation, n (%)	1 (1.0)	1 (1.1)	0.89 [0.06; 14.48] 0.937	0.89 [0.06; 14.10] 0.937	-0.00 [-0.03; 0.03] 0.937
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular AE leading to study drug discontinuation, n (%)	2 (2.4)	1 (1.1)	2.24 [0.20; 25.17] 0.513	2.21 [0.20; 23.96] 0.514	0.01 [-0.03; 0.05] 0.510
KITE					
Interaction Test:	p = 0.862				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular AE leading to study drug discontinuation, n (%)	1 (1.0)	1 (1.0)	1.02 [0.06; 16.54] 0.989	1.02 [0.06; 16.08] 0.989	0.00 [-0.03; 0.03] 0.989
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular AE leading to study drug discontinuation, n (%)	4 (5.1)	3 (3.8)	1.35 [0.29; 6.24] 0.700	1.33 [0.31; 5.76] 0.700	0.01 [-0.05; 0.08] 0.699
Pooled Analysis					
Interaction Test:	p = 0.694				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular AE leading to study drug discontinuation, n (%)	2 (1.0)	2 (1.0)	1.01 [0.13; 7.60] 0.990	0.96 [0.14; 6.71] 0.963	-0.00 [-0.02; 0.02] 0.963

	Treatment Groups		Comparison		
Any ocular adverse event leading to study drug discontinuation by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular AE leading to study drug discontinuation, n (%)	6 (3.7)	4 (2.3)	1.62 [0.43; 6.11] 0.473	1.54 [0.45; 5.34] 0.490	0.01 [-0.02; 0.05] 0.490

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 15-2.3 Any ocular adverse event leading to study drug discontinuation by gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-2.4 Any ocular adverse event leading to study drug discontinuation by BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-2.5 Any ocular adverse event leading to study drug discontinuation by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-2.6 Any ocular adverse event leading to study drug discontinuation by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event leading to study drug discontinuation by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.570**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular AE leading to study drug discontinuation, n (%)	3 (1.7)	2 (1.1)	1.54 [0.25; 9.35] 0.637	1.53 [0.26; 9.07] 0.637	0.01 [-0.02; 0.03] 0.635
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular AE leading to study drug discontinuation, n (%)	3 (1.9)	4 (2.3)	0.81 [0.18; 3.69] 0.787	0.82 [0.19; 3.59] 0.787	-0.00 [-0.03; 0.03] 0.786
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any ocular adverse event leading to study drug discontinuation by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular AE leading to study drug discontinuation, n (%)	6 (1.8)	6 (1.7)	1.13 [0.35; 3.67] 0.843	1.06 [0.34; 3.26] 0.919	0.00 [-0.02; 0.02] 0.919
Any ocular AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.889**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular AE leading to study drug discontinuation, n (%)	3 (1.7)	2 (1.1)	1.54 [0.25; 9.35] 0.637	1.53 [0.26; 9.07] 0.637	0.01 [-0.02; 0.03] 0.635
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular AE leading to study drug discontinuation, n (%)	5 (3.1)	4 (2.3)	1.37 [0.36; 5.20] 0.643	1.36 [0.37; 4.97] 0.643	0.01 [-0.03; 0.04] 0.643
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any ocular adverse event leading to study drug discontinuation by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular AE leading to study drug discontinuation, n (%)	8 (2.4)	6 (1.7)	1.46 [0.47; 4.49] 0.513	1.42 [0.50; 4.04] 0.511	0.01 [-0.01; 0.03] 0.512

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE, Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by diabetes type].
Week 52 / Pooled Analysis, Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 15-2.7 Any ocular adverse event leading to study drug discontinuation by HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-2.8 Any ocular adverse event leading to study drug discontinuation by duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-2.9 Any ocular adverse event leading to study drug discontinuation by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event leading to study drug discontinuation by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.889**					
KESTREL					
Interaction Test:	N.E.				
focal					
N'/N	59 / 59	48 / 48			
Any ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular AE leading to study drug discontinuation, n (%)	3 (2.4)	2 (1.5)	1.60 [0.26; 9.72] 0.612	1.58 [0.27; 9.32] 0.612	0.01 [-0.02; 0.04] 0.610
KITE					
Interaction Test:	N.E.				
focal					
N'/N	63 / 63	66 / 66			
Any ocular AE leading to study drug discontinuation, n (%)	2 (3.2)	0 (0.0)	N.E.	5.23 [0.26; 106.94] 0.282	0.03 [-0.01; 0.08] 0.151
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular AE leading to study drug discontinuation, n (%)	3 (2.6)	3 (2.8)	0.95 [0.19; 4.79] 0.947	0.95 [0.20; 4.60] 0.947	-0.00 [-0.04; 0.04] 0.947
Pooled Analysis					
Interaction Test:	N.E.				
focal					
N'/N	122 / 122	114 / 114			
Any ocular AE leading to study drug discontinuation, n (%)	2 (1.6)	0 (0.0)	N.E.	5.23 [0.26; 106.94] 0.229	0.02 [-0.01; 0.04] 0.142

	Treatment Groups		Comparison		
Any ocular adverse event leading to study drug discontinuation by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular AE leading to study drug discontinuation, n (%)	6 (2.5)	5 (2.1)	1.24 [0.37; 4.17] 0.733	1.19 [0.37; 3.84] 0.767	0.00 [-0.02; 0.03] 0.767

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by DME type].
Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by DME type].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 15-2.10 Any ocular adverse event leading to study drug discontinuation by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-2.11 Any ocular adverse event leading to study drug discontinuation by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event leading to study drug discontinuation by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.570**					
KESTREL					
Interaction Test:	N.E.				
presence					
N'/N	62 / 62	61 / 61			
Any ocular AE leading to study drug discontinuation, n (%)	1 (1.6)	0 (0.0)	N.E.	2.95 [0.12; 71.09] 0.505	0.02 [-0.02; 0.05] 0.313
absence					
N'/N	127 / 127	126 / 126			
Any ocular AE leading to study drug discontinuation, n (%)	2 (1.6)	2 (1.6)	0.99 [0.14; 7.15] 0.994	0.99 [0.14; 6.93] 0.994	-0.00 [-0.03; 0.03] 0.994
KITE					
Interaction Test:	N.E.				
presence					
N'/N	56 / 56	67 / 67			
Any ocular AE leading to study drug discontinuation, n (%)	1 (1.8)	0 (0.0)	N.E.	3.58 [0.15; 86.17] 0.432	0.02 [-0.02; 0.05] 0.313
absence					
N'/N	123 / 123	114 / 114			
Any ocular AE leading to study drug discontinuation, n (%)	2 (1.6)	4 (3.5)	0.45 [0.08; 2.53] 0.368	0.46 [0.09; 2.48] 0.369	-0.02 [-0.06; 0.02] 0.362
Pooled Analysis					
Interaction Test:	N.E.				
presence					
N'/N	118 / 118	128 / 128			
Any ocular AE leading to study drug discontinuation, n (%)	2 (1.7)	0 (0.0)	N.E.	3.25 [0.34; 30.74] 0.277	0.02 [-0.01; 0.04] 0.154

	Treatment Groups		Comparison		
Any ocular adverse event leading to study drug discontinuation by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular AE leading to study drug discontinuation, n (%)	4 (1.6)	6 (2.5)	0.68 [0.18; 2.51] 0.560	0.64 [0.18; 2.22] 0.474	-0.01 [-0.03; 0.02] 0.476
Any ocular AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.889**					
KESTREL					
Interaction Test:	N.E.				
presence					
N'/N	62 / 62	61 / 61			
Any ocular AE leading to study drug discontinuation, n (%)	1 (1.6)	0 (0.0)	N.E.	2.95 [0.12; 71.09] 0.505	0.02 [-0.02; 0.05] 0.313
absence					
N'/N	127 / 127	126 / 126			
Any ocular AE leading to study drug discontinuation, n (%)	2 (1.6)	2 (1.6)	0.99 [0.14; 7.15] 0.994	0.99 [0.14; 6.93] 0.994	-0.00 [-0.03; 0.03] 0.994
KITE					
Interaction Test:	N.E.				
presence					
N'/N	56 / 56	67 / 67			
Any ocular AE leading to study drug discontinuation, n (%)	1 (1.8)	0 (0.0)	N.E.	3.58 [0.15; 86.17] 0.432	0.02 [-0.02; 0.05] 0.313
absence					
N'/N	123 / 123	114 / 114			
Any ocular AE leading to study drug discontinuation, n (%)	4 (3.3)	4 (3.5)	0.92 [0.23; 3.79] 0.913	0.93 [0.24; 3.62] 0.913	-0.00 [-0.05; 0.04] 0.913
Pooled Analysis					
Interaction Test:	N.E.				
presence					
N'/N	118 / 118	128 / 128			
Any ocular AE leading to study drug discontinuation, n (%)	2 (1.7)	0 (0.0)	N.E.	3.25 [0.34; 30.74] 0.277	0.02 [-0.01; 0.04] 0.154

	Treatment Groups		Comparison		
Any ocular adverse event leading to study drug discontinuation by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular AE leading to study drug discontinuation, n (%)	6 (2.4)	6 (2.5)	0.96 [0.28; 3.25] 0.945	0.95 [0.31; 2.89] 0.926	-0.00 [-0.03; 0.03] 0.925

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE, Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by status of SRF].
Week 52 / Pooled Analysis, Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by status of SRF].

Table 15-2.12 Any ocular adverse event leading to study drug discontinuation by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-2.13 Any ocular adverse event leading to study drug discontinuation by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event leading to study drug discontinuation by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.889**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	1 (7.7)	N.E.	0.36 [0.02; 8.05] 0.519	-0.08 [-0.22; 0.07] 0.298
Exposed					
N'/N	177 / 177	174 / 174			
Any ocular AE leading to study drug discontinuation, n (%)	3 (1.7)	1 (0.6)	2.98 [0.31; 28.95] 0.346	2.95 [0.31; 28.08] 0.347	0.01 [-0.01; 0.03] 0.320
KITE					
Interaction Test:	p = 0.824				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any ocular AE leading to study drug discontinuation, n (%)	2 (11.8)	1 (8.3)	1.47 [0.12; 18.29] 0.766	1.41 [0.14; 13.86] 0.767	0.03 [-0.18; 0.25] 0.759
Exposed					
N'/N	162 / 162	169 / 169			
Any ocular AE leading to study drug discontinuation, n (%)	3 (1.9)	3 (1.8)	1.04 [0.21; 5.25] 0.958	1.04 [0.21; 5.09] 0.958	0.00 [-0.03; 0.03] 0.958
Pooled Analysis					
Interaction Test:	p = 0.596				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any ocular AE leading to study drug discontinuation, n (%)	2 (6.9)	2 (8.0)	0.83 [0.10; 6.67] 0.864	0.83 [0.14; 4.77] 0.837	-0.02 [-0.16; 0.12] 0.799

	Treatment Groups		Comparison		
Any ocular adverse event leading to study drug discontinuation by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any ocular AE leading to study drug discontinuation, n (%)	6 (1.8)	4 (1.2)	1.60 [0.43; 6.01] 0.486	1.53 [0.43; 5.40] 0.505	0.01 [-0.01; 0.02] 0.505

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL: logit(proportion) = treatment [by exposure (week 100)].

Table 15-3.1 Any ocular adverse event at the study eye leading to study drug discontinuation (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye leading to study drug discontinuation (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE leading to study drug discontinuation at the study eye, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	3 (1.6)	2 (1.1)	1.49 [0.25; 9.03] 0.663	1.48 [0.25; 8.78] 0.663	0.01 [-0.02; 0.03] 0.661
KITE, N'/N	179 / 179	181 / 181			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	3 (1.7)	4 (2.2)	0.75 [0.17; 3.42] 0.715	0.76 [0.17; 3.34] 0.715	-0.01 [-0.03; 0.02] 0.713
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	6 (1.6)	6 (1.6)	1.07 [0.33; 3.48] 0.913	1.00 [0.33; 3.08] 0.997	0.00 [-0.02; 0.02] 0.997
p_H=0.570					
Any ocular AE leading to study drug discontinuation at the study eye, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	3 (1.6)	2 (1.1)	1.49 [0.25; 9.03] 0.663	1.48 [0.25; 8.78] 0.663	0.01 [-0.02; 0.03] 0.661
KITE, N'/N	179 / 179	181 / 181			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	5 (2.8)	4 (2.2)	1.27 [0.34; 4.81] 0.724	1.26 [0.35; 4.63] 0.724	0.01 [-0.03; 0.04] 0.723

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye leading to study drug discontinuation (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	8 (2.2)	6 (1.6)	1.38 [0.45; 4.26] 0.576	1.34 [0.47; 3.82] 0.585	0.01 [-0.01; 0.03] 0.585
p_H=0.889					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 15-3.2 Any ocular adverse event at the study eye leading to study drug discontinuation by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye leading to study drug discontinuation by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE leading to study drug discontinuation at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.889**					
KESTREL					
Interaction Test:	p = 0.625				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	1 (1.0)	1 (1.1)	0.89 [0.06; 14.48] 0.937	0.89 [0.06; 14.10] 0.937	-0.00 [-0.03; 0.03] 0.937
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	2 (2.4)	1 (1.1)	2.24 [0.20; 25.17] 0.513	2.21 [0.20; 23.96] 0.514	0.01 [-0.03; 0.05] 0.510
KITE					
Interaction Test:	p = 0.862				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	1 (1.0)	1 (1.0)	1.02 [0.06; 16.54] 0.989	1.02 [0.06; 16.08] 0.989	0.00 [-0.03; 0.03] 0.989
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	4 (5.1)	3 (3.8)	1.35 [0.29; 6.24] 0.700	1.33 [0.31; 5.76] 0.700	0.01 [-0.05; 0.08] 0.699
Pooled Analysis					
Interaction Test:	p = 0.694				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	2 (1.0)	2 (1.0)	1.01 [0.13; 7.60] 0.990	0.96 [0.14; 6.71] 0.963	-0.00 [-0.02; 0.02] 0.963

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye leading to study drug discontinuation by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	6 (3.7)	4 (2.3)	1.62 [0.43; 6.11] 0.473	1.54 [0.45; 5.34] 0.490	0.01 [-0.02; 0.05] 0.490

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 15-3.3 Any ocular adverse event at the study eye leading to study drug discontinuation by gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-3.4 Any ocular adverse event at the study eye leading to study drug discontinuation by BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-3.5 Any ocular adverse event at the study eye leading to study drug discontinuation by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-3.6 Any ocular adverse event at the study eye leading to study drug discontinuation by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye leading to study drug discontinuation by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE leading to study drug discontinuation at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.570**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	3 (1.7)	2 (1.1)	1.54 [0.25; 9.35] 0.637	1.53 [0.26; 9.07] 0.637	0.01 [-0.02; 0.03] 0.635
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	3 (1.9)	4 (2.3)	0.81 [0.18; 3.69] 0.787	0.82 [0.19; 3.59] 0.787	-0.00 [-0.03; 0.03] 0.786
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye leading to study drug discontinuation by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	6 (1.8)	6 (1.7)	1.13 [0.35; 3.67] 0.843	1.06 [0.34; 3.26] 0.919	0.00 [-0.02; 0.02] 0.919
Any ocular AE leading to study drug discontinuation at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.889**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	3 (1.7)	2 (1.1)	1.54 [0.25; 9.35] 0.637	1.53 [0.26; 9.07] 0.637	0.01 [-0.02; 0.03] 0.635
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	5 (3.1)	4 (2.3)	1.37 [0.36; 5.20] 0.643	1.36 [0.37; 4.97] 0.643	0.01 [-0.03; 0.04] 0.643
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye leading to study drug discontinuation by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	8 (2.4)	6 (1.7)	1.46 [0.47; 4.49] 0.513	1.42 [0.50; 4.04] 0.511	0.01 [-0.01; 0.03] 0.512

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE, Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by diabetes type].
Week 52 / Pooled Analysis, Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 15-3.7 Any ocular adverse event at the study eye leading to study drug discontinuation by HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-3.8 Any ocular adverse event at the study eye leading to study drug discontinuation by duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-3.9 Any ocular adverse event at the study eye leading to study drug discontinuation by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye leading to study drug discontinuation by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE leading to study drug discontinuation at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.889**					
KESTREL					
Interaction Test:	N.E.				
focal					
N'/N	59 / 59	48 / 48			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	3 (2.4)	2 (1.5)	1.60 [0.26; 9.72] 0.612	1.58 [0.27; 9.32] 0.612	0.01 [-0.02; 0.04] 0.610
KITE					
Interaction Test:	N.E.				
focal					
N'/N	63 / 63	66 / 66			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	2 (3.2)	0 (0.0)	N.E.	5.23 [0.26; 106.94] 0.282	0.03 [-0.01; 0.08] 0.151
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	3 (2.6)	3 (2.8)	0.95 [0.19; 4.79] 0.947	0.95 [0.20; 4.60] 0.947	-0.00 [-0.04; 0.04] 0.947
Pooled Analysis					
Interaction Test:	N.E.				
focal					
N'/N	122 / 122	114 / 114			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	2 (1.6)	0 (0.0)	N.E.	5.23 [0.26; 106.94] 0.229	0.02 [-0.01; 0.04] 0.142

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye leading to study drug discontinuation by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	6 (2.5)	5 (2.1)	1.24 [0.37; 4.17] 0.733	1.19 [0.37; 3.84] 0.767	0.00 [-0.02; 0.03] 0.767

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by DME type].
Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by DME type].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 15-3.10 Any ocular adverse event at the study eye leading to study drug discontinuation by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-3.11 Any ocular adverse event at the study eye leading to study drug discontinuation by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye leading to study drug discontinuation by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE leading to study drug discontinuation at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.570**					
KESTREL					
Interaction Test:	N.E.				
presence					
N'/N	62 / 62	61 / 61			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	1 (1.6)	0 (0.0)	N.E.	2.95 [0.12; 71.09] 0.505	0.02 [-0.02; 0.05] 0.313
absence					
N'/N	127 / 127	126 / 126			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	2 (1.6)	2 (1.6)	0.99 [0.14; 7.15] 0.994	0.99 [0.14; 6.93] 0.994	-0.00 [-0.03; 0.03] 0.994
KITE					
Interaction Test:	N.E.				
presence					
N'/N	56 / 56	67 / 67			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	1 (1.8)	0 (0.0)	N.E.	3.58 [0.15; 86.17] 0.432	0.02 [-0.02; 0.05] 0.313
absence					
N'/N	123 / 123	114 / 114			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	2 (1.6)	4 (3.5)	0.45 [0.08; 2.53] 0.368	0.46 [0.09; 2.48] 0.369	-0.02 [-0.06; 0.02] 0.362
Pooled Analysis					
Interaction Test:	N.E.				
presence					
N'/N	118 / 118	128 / 128			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	2 (1.7)	0 (0.0)	N.E.	3.25 [0.34; 30.74] 0.277	0.02 [-0.01; 0.04] 0.154

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye leading to study drug discontinuation by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	4 (1.6)	6 (2.5)	0.68 [0.18; 2.51] 0.560	0.64 [0.18; 2.22] 0.474	-0.01 [-0.03; 0.02] 0.476
Any ocular AE leading to study drug discontinuation at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.889**					
KESTREL					
Interaction Test:	N.E.				
presence					
N'/N	62 / 62	61 / 61			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	1 (1.6)	0 (0.0)	N.E.	2.95 [0.12; 71.09] 0.505	0.02 [-0.02; 0.05] 0.313
absence					
N'/N	127 / 127	126 / 126			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	2 (1.6)	2 (1.6)	0.99 [0.14; 7.15] 0.994	0.99 [0.14; 6.93] 0.994	-0.00 [-0.03; 0.03] 0.994
KITE					
Interaction Test:	N.E.				
presence					
N'/N	56 / 56	67 / 67			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	1 (1.8)	0 (0.0)	N.E.	3.58 [0.15; 86.17] 0.432	0.02 [-0.02; 0.05] 0.313
absence					
N'/N	123 / 123	114 / 114			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	4 (3.3)	4 (3.5)	0.92 [0.23; 3.79] 0.913	0.93 [0.24; 3.62] 0.913	-0.00 [-0.05; 0.04] 0.913
Pooled Analysis					
Interaction Test:	N.E.				
presence					
N'/N	118 / 118	128 / 128			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	2 (1.7)	0 (0.0)	N.E.	3.25 [0.34; 30.74] 0.277	0.02 [-0.01; 0.04] 0.154

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye leading to study drug discontinuation by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	6 (2.4)	6 (2.5)	0.96 [0.28; 3.25] 0.945	0.95 [0.31; 2.89] 0.926	-0.00 [-0.03; 0.03] 0.925

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE, Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by status of SRF].
Week 52 / Pooled Analysis, Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by status of SRF].

Table 15-3.12 Any ocular adverse event at the study eye leading to study drug discontinuation by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-3.13 Any ocular adverse event at the study eye leading to study drug discontinuation by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye leading to study drug discontinuation by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE leading to study drug discontinuation at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.889**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	0 (0.0)	1 (7.7)	N.E.	0.36 [0.02; 8.05] 0.519	-0.08 [-0.22; 0.07] 0.298
Exposed					
N'/N	177 / 177	174 / 174			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	3 (1.7)	1 (0.6)	2.98 [0.31; 28.95] 0.346	2.95 [0.31; 28.08] 0.347	0.01 [-0.01; 0.03] 0.320
KITE					
Interaction Test:	p = 0.824				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	2 (11.8)	1 (8.3)	1.47 [0.12; 18.29] 0.766	1.41 [0.14; 13.86] 0.767	0.03 [-0.18; 0.25] 0.759
Exposed					
N'/N	162 / 162	169 / 169			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	3 (1.9)	3 (1.8)	1.04 [0.21; 5.25] 0.958	1.04 [0.21; 5.09] 0.958	0.00 [-0.03; 0.03] 0.958
Pooled Analysis					
Interaction Test:	p = 0.596				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	2 (6.9)	2 (8.0)	0.83 [0.10; 6.67] 0.864	0.83 [0.14; 4.77] 0.837	-0.02 [-0.16; 0.12] 0.799

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye leading to study drug discontinuation by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any ocular AE leading to study drug discontinuation at the study eye, n (%)	6 (1.8)	4 (1.2)	1.60 [0.43; 6.01] 0.486	1.53 [0.43; 5.40] 0.505	0.01 [-0.01; 0.02] 0.505

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL: logit(proportion) = treatment [by exposure (week 100)].

Table 15-4.1 Any ocular adverse event at the fellow eye leading to study drug discontinuation (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye leading to study drug discontinuation (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE leading to study drug discontinuation at the fellow eye, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular AE leading to study drug discontinuation at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, N'/N	179 / 179	181 / 181			
Any ocular AE leading to study drug discontinuation at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular AE leading to study drug discontinuation at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
p_H=N.E.					
Any ocular AE leading to study drug discontinuation at the fellow eye, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular AE leading to study drug discontinuation at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, N'/N	179 / 179	181 / 181			
Any ocular AE leading to study drug discontinuation at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye leading to study drug discontinuation (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular AE leading to study drug discontinuation at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
p_H=N.E.					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 15-4.2 Any ocular adverse event at the fellow eye leading to study drug discontinuation by age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-4.3 Any ocular adverse event at the fellow eye leading to study drug discontinuation by gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-4.4 Any ocular adverse event at the fellow eye leading to study drug discontinuation by BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-4.5 Any ocular adverse event at the fellow eye leading to study drug discontinuation by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-4.6 Any ocular adverse event at the fellow eye leading to study drug discontinuation by diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-4.7 Any ocular adverse event at the fellow eye leading to study drug discontinuation by HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-4.8 Any ocular adverse event at the fellow eye leading to study drug discontinuation by duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-4.9 Any ocular adverse event at the fellow eye leading to study drug discontinuation by DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-4.10 Any ocular adverse event at the fellow eye leading to study drug discontinuation by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-4.11 Any ocular adverse event at the fellow eye leading to study drug discontinuation by status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-4.12 Any ocular adverse event at the fellow eye leading to study drug discontinuation by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-4.13 Any ocular adverse event at the fellow eye leading to study drug discontinuation by exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 15-5.1 Any non-ocular adverse event leading to study drug discontinuation (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE leading to study drug discontinuation, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (0.5)	5 (2.7)	0.19 [0.02; 1.67] 0.136	0.20 [0.02; 1.68] 0.137	-0.02 [-0.05; 0.00] 0.097
KITE, N'/N	179 / 179	181 / 181			
Any non-ocular AE leading to study drug discontinuation, n (%)	7 (3.9)	4 (2.2)	1.80 [0.52; 6.26] 0.355	1.77 [0.53; 5.94] 0.356	0.02 [-0.02; 0.05] 0.349
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any non-ocular AE leading to study drug discontinuation, n (%)	8 (2.2)	9 (2.4)	0.58 [0.16; 2.03] 0.392	0.89 [0.35; 2.28] 0.812	-0.00 [-0.02; 0.02] 0.812
p_H=0.079					
Any non-ocular AE leading to study drug discontinuation, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any non-ocular AE leading to study drug discontinuation, n (%)	2 (1.1)	7 (3.7)	0.28 [0.06; 1.34] 0.110	0.28 [0.06; 1.34] 0.112	-0.03 [-0.06; 0.00] 0.088
KITE, N'/N	179 / 179	181 / 181			
Any non-ocular AE leading to study drug discontinuation, n (%)	10 (5.6)	4 (2.2)	2.62 [0.81; 8.51] 0.109	2.53 [0.81; 7.91] 0.111	0.03 [-0.01; 0.07] 0.097

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any non-ocular AE leading to study drug discontinuation, n (%)	12 (3.3)	11 (3.0)	0.83 [0.31; 2.24] 0.713	1.09 [0.49; 2.45] 0.827	0.00 [-0.02; 0.03] 0.828
p_H=0.025 *					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 15-5.2 Any non-ocular adverse event leading to study drug discontinuation by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.079**					
KESTREL					
Interaction Test:	N.E.				
< 65 years					
N'/N	104 / 104	93 / 93			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	3 (3.2)	N.E.	0.13 [0.01; 2.44] 0.172	-0.03 [-0.07; 0.00] 0.078
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (1.2)	2 (2.1)	0.55 [0.05; 6.15] 0.626	0.55 [0.05; 5.99] 0.626	-0.01 [-0.05; 0.03] 0.615
KITE					
Interaction Test:	p = 0.210				
< 65 years					
N'/N	100 / 100	102 / 102			
Any non-ocular AE leading to study drug discontinuation, n (%)	6 (6.0)	2 (2.0)	3.19 [0.63; 16.21] 0.162	3.06 [0.63; 14.80] 0.164	0.04 [-0.01; 0.09] 0.141
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (1.3)	2 (2.5)	0.49 [0.04; 5.56] 0.568	0.50 [0.05; 5.40] 0.568	-0.01 [-0.06; 0.03] 0.560
Pooled Analysis					
Interaction Test:	p = 0.469				
< 65 years					
N'/N	204 / 204	195 / 195			
Any non-ocular AE leading to study drug discontinuation, n (%)	6 (2.9)	5 (2.6)	0.75 [0.17; 3.18] 0.691	1.15 [0.38; 3.47] 0.801	0.00 [-0.03; 0.04] 0.783

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any non-ocular AE leading to study drug discontinuation, n (%)	2 (1.2)	4 (2.3)	0.34 [0.05; 2.29] 0.269	0.53 [0.10; 2.83] 0.447	-0.01 [-0.04; 0.02] 0.442
Any non-ocular AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.025 ***					
KESTREL					
Interaction Test:	p = 0.751				
< 65 years					
N'/N	104 / 104	93 / 93			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (1.0)	4 (4.3)	0.22 [0.02; 1.97] 0.174	0.22 [0.03; 1.96] 0.177	-0.03 [-0.08; 0.01] 0.148
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (1.2)	3 (3.2)	0.36 [0.04; 3.54] 0.382	0.37 [0.04; 3.48] 0.383	-0.02 [-0.06; 0.02] 0.350
KITE					
Interaction Test:	p = 0.462				
< 65 years					
N'/N	100 / 100	102 / 102			
Any non-ocular AE leading to study drug discontinuation, n (%)	7 (7.0)	2 (2.0)	3.76 [0.76; 18.58] 0.104	3.57 [0.76; 16.77] 0.107	0.05 [-0.01; 0.11] 0.082
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any non-ocular AE leading to study drug discontinuation, n (%)	3 (3.8)	2 (2.5)	1.52 [0.25; 9.35] 0.652	1.50 [0.26; 8.73] 0.652	0.01 [-0.04; 0.07] 0.649
Pooled Analysis					
Interaction Test:	p = 0.661				
< 65 years					
N'/N	204 / 204	195 / 195			
Any non-ocular AE leading to study drug discontinuation, n (%)	8 (3.9)	6 (3.1)	0.96 [0.29; 3.20] 0.944	1.29 [0.46; 3.60] 0.623	0.01 [-0.03; 0.05] 0.626

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any non-ocular AE leading to study drug discontinuation, n (%)	4 (2.4)	5 (2.9)	0.65 [0.15; 2.77] 0.562	0.84 [0.23; 3.09] 0.788	-0.00 [-0.04; 0.03] 0.786

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL: logit(proportion) = treatment [by age].

Table 15-5.3 Any non-ocular adverse event leading to study drug discontinuation by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.079**					
KESTREL					
Interaction Test:	N.E.				
Male					
N'/N	110 / 110	126 / 126			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	4 (3.2)	N.E.	0.13 [0.01; 2.34] 0.165	-0.03 [-0.06; -0.00] 0.042 *
Female					
N'/N	79 / 79	61 / 61			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (1.3)	1 (1.6)	0.77 [0.05; 12.55] 0.854	0.77 [0.05; 12.10] 0.854	-0.00 [-0.04; 0.04] 0.856
KITE					
Interaction Test:	p = 0.255				
Male					
N'/N	120 / 120	115 / 115			
Any non-ocular AE leading to study drug discontinuation, n (%)	3 (2.5)	3 (2.6)	0.96 [0.19; 4.84] 0.958	0.96 [0.20; 4.65] 0.958	-0.00 [-0.04; 0.04] 0.958
Female					
N'/N	59 / 59	66 / 66			
Any non-ocular AE leading to study drug discontinuation, n (%)	4 (6.8)	1 (1.5)	4.73 [0.51; 43.55] 0.170	4.47 [0.51; 38.92] 0.175	0.05 [-0.02; 0.12] 0.144
Pooled Analysis					
Interaction Test:	p = 0.094				
Male					
N'/N	230 / 230	241 / 241			
Any non-ocular AE leading to study drug discontinuation, n (%)	3 (1.3)	7 (2.9)	0.26 [0.05; 1.31] 0.102	0.48 [0.13; 1.72] 0.248	-0.02 [-0.04; 0.01] 0.209

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any non-ocular AE leading to study drug discontinuation, n (%)	5 (3.6)	2 (1.6)	1.63 [0.26; 10.15] 0.602	2.46 [0.51; 11.84] 0.246	0.02 [-0.02; 0.06] 0.247
Any non-ocular AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.025 ***					
KESTREL					
Interaction Test:	p = 0.424				
Male					
N'/N	110 / 110	126 / 126			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (0.9)	6 (4.8)	0.18 [0.02; 1.55] 0.119	0.19 [0.02; 1.56] 0.122	-0.04 [-0.08; 0.00] 0.067
Female					
N'/N	79 / 79	61 / 61			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (1.3)	1 (1.6)	0.77 [0.05; 12.55] 0.854	0.77 [0.05; 12.10] 0.854	-0.00 [-0.04; 0.04] 0.856
KITE					
Interaction Test:	p = 0.327				
Male					
N'/N	120 / 120	115 / 115			
Any non-ocular AE leading to study drug discontinuation, n (%)	5 (4.2)	3 (2.6)	1.62 [0.38; 6.95] 0.514	1.60 [0.39; 6.53] 0.515	0.02 [-0.03; 0.06] 0.508
Female					
N'/N	59 / 59	66 / 66			
Any non-ocular AE leading to study drug discontinuation, n (%)	5 (8.5)	1 (1.5)	6.02 [0.68; 53.09] 0.106	5.59 [0.67; 46.51] 0.111	0.07 [-0.01; 0.15] 0.076
Pooled Analysis					
Interaction Test:	p = 0.118				
Male					
N'/N	230 / 230	241 / 241			
Any non-ocular AE leading to study drug discontinuation, n (%)	6 (2.6)	9 (3.7)	0.49 [0.15; 1.62] 0.241	0.69 [0.24; 1.95] 0.480	-0.01 [-0.04; 0.02] 0.474

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any non-ocular AE leading to study drug discontinuation, n (%)	6 (4.3)	2 (1.6)	2.29 [0.42; 12.45] 0.339	2.97 [0.64; 13.69] 0.141	0.03 [-0.01; 0.07] 0.143

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL: logit(proportion) = treatment [by gender].

Table 15-5.4 Any non-ocular adverse event leading to study drug discontinuation by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.025 ***					
KESTREL					
Interaction Test:	p = 0.968				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (1.4)	3 (4.7)	0.28 [0.03; 2.75] 0.274	0.29 [0.03; 2.70] 0.276	-0.03 [-0.09; 0.02] 0.260
> 65 letters					
N'/N	115 / 115	123 / 123			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (0.9)	4 (3.3)	0.26 [0.03; 2.37] 0.233	0.27 [0.03; 2.36] 0.235	-0.02 [-0.06; 0.01] 0.190
KITE					
Interaction Test:	N.E.				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any non-ocular AE leading to study drug discontinuation, n (%)	2 (3.1)	4 (4.4)	0.69 [0.12; 3.89] 0.675	0.70 [0.13; 3.71] 0.675	-0.01 [-0.07; 0.05] 0.664
> 65 letters					
N'/N	114 / 114	90 / 90			
Any non-ocular AE leading to study drug discontinuation, n (%)	8 (7.0)	0 (0.0)	N.E.	13.45 [0.79; 229.99] 0.073	0.07 [0.02; 0.12] 0.003 *
Pooled Analysis					
Interaction Test:	p = 0.087				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any non-ocular AE leading to study drug discontinuation, n (%)	3 (2.2)	7 (4.5)	0.35 [0.08; 1.51] 0.158	0.50 [0.13; 1.84] 0.287	-0.02 [-0.06; 0.02] 0.280

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any non-ocular AE leading to study drug discontinuation, n (%)	9 (3.9)	4 (1.9)	1.73 [0.45; 6.56] 0.423	1.93 [0.59; 6.29] 0.261	0.02 [-0.01; 0.05] 0.216

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KITE: logit(proportion) = treatment [by BCVA].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 15-5.5 Any non-ocular adverse event leading to study drug discontinuation by region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.079**					
KESTREL					
Interaction Test:	N.E.				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (1.1)	1 (1.2)	0.92 [0.06; 14.97] 0.954	0.92 [0.06; 14.51] 0.954	-0.00 [-0.03; 0.03] 0.954
European Region					
N'/N	69 / 69	75 / 75			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	4 (5.3)	N.E.	0.12 [0.01; 2.20] 0.153	-0.05 [-0.10; -0.00] 0.040 *
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE					
Interaction Test:	N.E.				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
European Region					
N'/N	135 / 135	132 / 132			
Any non-ocular AE leading to study drug discontinuation, n (%)	4 (3.0)	2 (1.5)	1.98 [0.36; 11.02] 0.433	1.96 [0.36; 10.50] 0.434	0.01 [-0.02; 0.05] 0.423
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any non-ocular AE leading to study drug discontinuation, n (%)	3 (16.7)	2 (7.1)	2.60 [0.39; 17.36] 0.324	2.33 [0.43; 12.62] 0.325	0.10 [-0.10; 0.29] 0.343

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	N.E.				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (1.1)	1 (1.2)	N.E.	0.92 [0.06; 14.51] 0.954	-0.00 [-0.03; 0.03] 0.954
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
European Region					
N'/N	204 / 204	207 / 207			
Any non-ocular AE leading to study drug discontinuation, n (%)	4 (2.0)	6 (2.9)	N.E.	0.71 [0.21; 2.37] 0.570	-0.01 [-0.04; 0.02] 0.541
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any non-ocular AE leading to study drug discontinuation, n (%)	3 (6.3)	2 (3.5)	N.E.	2.33 [0.43; 12.62] 0.316	0.04 [-0.04; 0.12] 0.338
Any non-ocular AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.025 ***					
KESTREL					
Interaction Test:	N.E.				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (1.1)	1 (1.2)	0.92 [0.06; 14.97] 0.954	0.92 [0.06; 14.51] 0.954	-0.00 [-0.03; 0.03] 0.954
European Region					
N'/N	69 / 69	75 / 75			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (1.4)	6 (8.0)	0.17 [0.02; 1.44] 0.104	0.18 [0.02; 1.47] 0.109	-0.07 [-0.13; 0.00] 0.057
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	N.E.				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
European Region					
N'/N	135 / 135	132 / 132			
Any non-ocular AE leading to study drug discontinuation, n (%)	7 (5.2)	2 (1.5)	3.55 [0.72; 17.43] 0.118	3.42 [0.72; 16.17] 0.121	0.04 [-0.01; 0.08] 0.093
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any non-ocular AE leading to study drug discontinuation, n (%)	3 (16.7)	2 (7.1)	2.60 [0.39; 17.36] 0.324	2.33 [0.43; 12.62] 0.325	0.10 [-0.10; 0.29] 0.343
Pooled Analysis					
Interaction Test:	N.E.				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (1.1)	1 (1.2)	N.E.	0.92 [0.06; 14.51] 0.954	-0.00 [-0.03; 0.03] 0.954
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
European Region					
N'/N	204 / 204	207 / 207			
Any non-ocular AE leading to study drug discontinuation, n (%)	8 (3.9)	8 (3.9)	0.75 [0.20; 2.88] 0.677	1.02 [0.38; 2.74] 0.961	0.00 [-0.04; 0.04] 0.961

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any non-ocular AE leading to study drug discontinuation, n (%)	3 (6.3)	2 (3.5)	N.E.	2.33 [0.43; 12.62] 0.316	0.04 [-0.04; 0.12] 0.338

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE, Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by region].
Week 52 / Pooled Analysis, Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by region].

Table 15-5.6 Any non-ocular adverse event leading to study drug discontinuation by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.079**					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	177 / 177	181 / 181			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (0.6)	5 (2.8)	0.20 [0.02; 1.73] 0.144	0.20 [0.02; 1.73] 0.146	-0.02 [-0.05; 0.00] 0.102
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	160 / 160	174 / 174			
Any non-ocular AE leading to study drug discontinuation, n (%)	7 (4.4)	4 (2.3)	1.94 [0.56; 6.77] 0.296	1.90 [0.57; 6.38] 0.297	0.02 [-0.02; 0.06] 0.293
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any non-ocular AE leading to study drug discontinuation, n (%)	8 (2.4)	9 (2.5)	0.61 [0.17; 2.15] 0.441	0.95 [0.37; 2.41] 0.908	-0.00 [-0.02; 0.02] 0.908
Any non-ocular AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.025 ***					
KESTREL					
Interaction Test:	N.E.				
Type 1					
N'/N	12 / 12	6 / 6			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2					
N'/N	177 / 177	181 / 181			
Any non-ocular AE leading to study drug discontinuation, n (%)	2 (1.1)	7 (3.9)	0.28 [0.06; 1.39] 0.120	0.29 [0.06; 1.39] 0.122	-0.03 [-0.06; 0.00] 0.095
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (5.3)	0 (0.0)	N.E.	1.20 [0.05; 26.47] 0.908	0.05 [-0.05; 0.15] 0.304
Type 2					
N'/N	160 / 160	174 / 174			
Any non-ocular AE leading to study drug discontinuation, n (%)	9 (5.6)	4 (2.3)	2.53 [0.76; 8.39] 0.128	2.45 [0.77; 7.79] 0.130	0.03 [-0.01; 0.08] 0.121
Pooled Analysis					
Interaction Test:	N.E.				
Type 1					
N'/N	31 / 31	13 / 13			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (3.2)	0 (0.0)	N.E.	1.20 [0.05; 26.47] 0.909	0.03 [-0.03; 0.09] 0.335

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any non-ocular AE leading to study drug discontinuation, n (%)	11 (3.3)	11 (3.1)	0.83 [0.31; 2.25] 0.715	1.06 [0.47; 2.40] 0.889	0.00 [-0.02; 0.03] 0.889

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE, Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by diabetes type].
Week 52 / Pooled Analysis, Week 100 / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 15-5.7 Any non-ocular adverse event leading to study drug discontinuation by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.025 ***					
KESTREL					
Interaction Test:	p = 0.807				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (1.3)	4 (3.7)	0.34 [0.04; 3.13] 0.343	0.35 [0.04; 3.09] 0.346	-0.02 [-0.07; 0.02] 0.282
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (0.9)	3 (3.8)	0.23 [0.02; 2.26] 0.208	0.24 [0.03; 2.25] 0.210	-0.03 [-0.07; 0.02] 0.215
KITE					
Interaction Test:	p = 0.108				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any non-ocular AE leading to study drug discontinuation, n (%)	2 (2.4)	3 (3.1)	0.78 [0.13; 4.75] 0.783	0.78 [0.13; 4.56] 0.783	-0.01 [-0.06; 0.04] 0.780
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any non-ocular AE leading to study drug discontinuation, n (%)	8 (8.2)	1 (1.2)	7.55 [0.92; 61.67] 0.059	7.01 [0.89; 54.91] 0.064	0.07 [0.01; 0.13] 0.020 *
Pooled Analysis					
Interaction Test:	p = 0.170				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any non-ocular AE leading to study drug discontinuation, n (%)	3 (1.9)	7 (3.4)	0.39 [0.09; 1.72] 0.212	0.55 [0.14; 2.11] 0.373	-0.02 [-0.05; 0.02] 0.353

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any non-ocular AE leading to study drug discontinuation, n (%)	9 (4.3)	4 (2.4)	1.39 [0.38; 5.13] 0.623	1.82 [0.59; 5.63] 0.288	0.02 [-0.02; 0.06] 0.283

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 15-5.8 Any non-ocular adverse event leading to study drug discontinuation by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.025 ***					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (0.8)	3 (2.7)	0.30 [0.03; 2.92] 0.300	0.31 [0.03; 2.89] 0.301	-0.02 [-0.05; 0.02] 0.282
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (3.3)	3 (7.7)	0.41 [0.04; 4.19] 0.455	0.43 [0.05; 3.96] 0.459	-0.04 [-0.15; 0.06] 0.418
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	1 (2.6)	N.E.	0.33 [0.01; 7.74] 0.487	-0.03 [-0.08; 0.02] 0.311
KITE					
Interaction Test:	N.E.				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any non-ocular AE leading to study drug discontinuation, n (%)	5 (5.9)	1 (1.1)	5.69 [0.65; 49.71] 0.116	5.41 [0.65; 45.39] 0.120	0.05 [-0.01; 0.10] 0.084
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	1 (2.0)	N.E.	0.32 [0.01; 7.68] 0.483	-0.02 [-0.06; 0.02] 0.312
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any non-ocular AE leading to study drug discontinuation, n (%)	5 (11.6)	2 (5.0)	2.50 [0.46; 13.69] 0.291	2.33 [0.48; 11.32] 0.296	0.07 [-0.05; 0.18] 0.268

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.246				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any non-ocular AE leading to study drug discontinuation, n (%)	6 (2.9)	4 (2.0)	1.27 [0.32; 5.09] 0.731	1.50 [0.44; 5.12] 0.509	0.01 [-0.02; 0.04] 0.515
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (1.2)	4 (4.5)	0.15 [0.02; 1.55] 0.112	0.39 [0.06; 2.40] 0.293	-0.03 [-0.08; 0.02] 0.235
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any non-ocular AE leading to study drug discontinuation, n (%)	5 (6.1)	3 (3.8)	1.15 [0.24; 5.59] 0.864	1.48 [0.40; 5.46] 0.554	0.02 [-0.04; 0.09] 0.522

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by duration of DME].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 15-5.9 Any non-ocular adverse event leading to study drug discontinuation by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.079**					
KESTREL					
Interaction Test:	N.E.				
focal					
N'/N	59 / 59	48 / 48			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (1.7)	0 (0.0)	N.E.	2.45 [0.10; 58.81] 0.581	0.02 [-0.02; 0.05] 0.313
diffuse					
N'/N	127 / 127	134 / 134			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	4 (3.0)	N.E.	0.12 [0.01; 2.15] 0.149	-0.03 [-0.06; -0.00] 0.042 *
KITE					
Interaction Test:	p = 0.845				
focal					
N'/N	63 / 63	66 / 66			
Any non-ocular AE leading to study drug discontinuation, n (%)	2 (3.2)	1 (1.5)	2.13 [0.19; 24.10] 0.541	2.10 [0.19; 22.54] 0.542	0.02 [-0.04; 0.07] 0.535
diffuse					
N'/N	115 / 115	109 / 109			
Any non-ocular AE leading to study drug discontinuation, n (%)	5 (4.3)	3 (2.8)	1.61 [0.37; 6.89] 0.524	1.58 [0.39; 6.45] 0.524	0.02 [-0.03; 0.06] 0.517
Pooled Analysis					
Interaction Test:	p = 0.305				
focal					
N'/N	122 / 122	114 / 114			
Any non-ocular AE leading to study drug discontinuation, n (%)	3 (2.5)	1 (0.9)	1.80 [0.16; 20.55] 0.635	2.22 [0.33; 14.91] 0.399	0.02 [-0.02; 0.05] 0.310

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any non-ocular AE leading to study drug discontinuation, n (%)	5 (2.1)	7 (2.9)	0.47 [0.12; 1.92] 0.294	0.72 [0.24; 2.17] 0.559	-0.01 [-0.04; 0.02] 0.535
Any non-ocular AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.025 ***					
KESTREL					
Interaction Test:	p = 0.797				
focal					
N'/N	59 / 59	48 / 48			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (1.7)	2 (4.2)	0.40 [0.03; 4.51] 0.456	0.41 [0.04; 4.35] 0.457	-0.02 [-0.09; 0.04] 0.459
diffuse					
N'/N	127 / 127	134 / 134			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (0.8)	4 (3.0)	0.26 [0.03; 2.34] 0.228	0.26 [0.03; 2.33] 0.230	-0.02 [-0.05; 0.01] 0.187
KITE					
Interaction Test:	p = 0.797				
focal					
N'/N	63 / 63	66 / 66			
Any non-ocular AE leading to study drug discontinuation, n (%)	3 (4.8)	1 (1.5)	3.25 [0.33; 32.10] 0.313	3.14 [0.34; 29.42] 0.316	0.03 [-0.03; 0.09] 0.291
diffuse					
N'/N	115 / 115	109 / 109			
Any non-ocular AE leading to study drug discontinuation, n (%)	7 (6.1)	3 (2.8)	2.29 [0.58; 9.09] 0.239	2.21 [0.59; 8.34] 0.241	0.03 [-0.02; 0.09] 0.221
Pooled Analysis					
Interaction Test:	p = 0.981				
focal					
N'/N	122 / 122	114 / 114			
Any non-ocular AE leading to study drug discontinuation, n (%)	4 (3.3)	3 (2.6)	0.87 [0.17; 4.38] 0.865	1.25 [0.30; 5.25] 0.764	0.01 [-0.04; 0.05] 0.766

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any non-ocular AE leading to study drug discontinuation, n (%)	8 (3.3)	7 (2.9)	0.89 [0.28; 2.84] 0.843	1.12 [0.41; 3.09] 0.820	0.00 [-0.03; 0.03] 0.819

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 15-5.10 Any non-ocular adverse event leading to study drug discontinuation by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.025 ***					
KESTREL					
Interaction Test:	N.E.				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (0.9)	3 (3.1)	0.29 [0.03; 2.86] 0.291	0.30 [0.03; 2.83] 0.292	-0.02 [-0.06; 0.02] 0.275
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (1.4)	4 (5.6)	0.24 [0.03; 2.23] 0.211	0.25 [0.03; 2.21] 0.214	-0.04 [-0.10; 0.02] 0.172
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE					
Interaction Test:	p = 0.757				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any non-ocular AE leading to study drug discontinuation, n (%)	6 (7.1)	2 (2.4)	3.04 [0.60; 15.51] 0.182	2.89 [0.60; 13.93] 0.185	0.05 [-0.02; 0.11] 0.156
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any non-ocular AE leading to study drug discontinuation, n (%)	3 (4.1)	1 (1.3)	3.30 [0.34; 32.41] 0.307	3.20 [0.34; 30.11] 0.309	0.03 [-0.02; 0.08] 0.286
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (5.0)	1 (5.3)	0.95 [0.06; 16.31] 0.970	0.95 [0.06; 14.13] 0.970	-0.00 [-0.14; 0.14] 0.970

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.801				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any non-ocular AE leading to study drug discontinuation, n (%)	7 (3.6)	5 (2.8)	1.07 [0.30; 3.85] 0.919	1.32 [0.43; 4.04] 0.630	0.01 [-0.03; 0.05] 0.630
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any non-ocular AE leading to study drug discontinuation, n (%)	4 (2.8)	5 (3.3)	0.58 [0.14; 2.50] 0.468	0.83 [0.23; 3.02] 0.778	-0.01 [-0.05; 0.03] 0.779
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (3.1)	1 (2.6)	0.76 [0.04; 13.80] 0.855	0.95 [0.06; 14.13] 0.971	-0.00 [-0.08; 0.08] 0.970

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL: logit(proportion) = treatment [by CSFT].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 15-5.11 Any non-ocular adverse event leading to study drug discontinuation by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.025 ***					
KESTREL					
Interaction Test:	N.E.				
presence					
N'/N	62 / 62	61 / 61			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	4 (6.6)	N.E.	0.11 [0.01; 1.99] 0.135	-0.07 [-0.13; -0.00] 0.039 *
absence					
N'/N	127 / 127	126 / 126			
Any non-ocular AE leading to study drug discontinuation, n (%)	2 (1.6)	3 (2.4)	0.66 [0.11; 3.99] 0.647	0.66 [0.11; 3.89] 0.648	-0.01 [-0.04; 0.03] 0.645
KITE					
Interaction Test:	N.E.				
presence					
N'/N	56 / 56	67 / 67			
Any non-ocular AE leading to study drug discontinuation, n (%)	2 (3.6)	4 (6.0)	0.58 [0.10; 3.31] 0.543	0.60 [0.11; 3.15] 0.544	-0.02 [-0.10; 0.05] 0.529
absence					
N'/N	123 / 123	114 / 114			
Any non-ocular AE leading to study drug discontinuation, n (%)	8 (6.5)	0 (0.0)	N.E.	15.77 [0.92; 270.08] 0.057	0.07 [0.02; 0.11] 0.003 *
Pooled Analysis					
Interaction Test:	p = 0.014 *				
presence					
N'/N	118 / 118	128 / 128			
Any non-ocular AE leading to study drug discontinuation, n (%)	2 (1.7)	8 (6.3)	0.20 [0.04; 1.04] 0.055	0.33 [0.08; 1.28] 0.090	-0.04 [-0.09; 0.00] 0.069

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any non-ocular AE leading to study drug discontinuation, n (%)	10 (4.0)	3 (1.3)	2.55 [0.62; 10.54] 0.196	2.88 [0.85; 9.72] 0.072	0.03 [-0.00; 0.06] 0.057

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by status of SRF].

In case no subgroup analysis for Week 52 / 100 is presented, there is no data meeting the display criteria.

Table 15-5.12 Any non-ocular adverse event leading to study drug discontinuation by exposure (week 52) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE leading to study drug discontinuation, Week 52					
Test of heterogeneity in main analysis: **p_H=0.079**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed					
N'/N	71 / 71	75 / 75			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	2 (2.7)	N.E.	0.21 [0.01; 4.32] 0.313	-0.03 [-0.06; 0.01] 0.152
Exposed					
N'/N	118 / 118	112 / 112			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (0.8)	3 (2.7)	0.31 [0.03; 3.03] 0.314	0.32 [0.03; 3.00] 0.316	-0.02 [-0.05; 0.02] 0.294
KITE					
Interaction Test:	N.E.				
Non-exposed					
N'/N	85 / 85	90 / 90			
Any non-ocular AE leading to study drug discontinuation, n (%)	6 (7.1)	4 (4.4)	1.63 [0.44; 6.00] 0.460	1.59 [0.46; 5.43] 0.461	0.03 [-0.04; 0.10] 0.458
Exposed					
N'/N	94 / 94	91 / 91			
Any non-ocular AE leading to study drug discontinuation, n (%)	1 (1.1)	0 (0.0)	N.E.	2.91 [0.12; 70.41] 0.512	0.01 [-0.01; 0.03] 0.315
Pooled Analysis					
Interaction Test:	p = 0.753				
Non-exposed					
N'/N	156 / 156	165 / 165			
Any non-ocular AE leading to study drug discontinuation, n (%)	6 (3.8)	6 (3.6)	0.66 [0.16; 2.73] 0.565	1.06 [0.37; 3.06] 0.917	0.00 [-0.04; 0.04] 0.920

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	212 / 212	203 / 203			
Any non-ocular AE leading to study drug discontinuation, n (%)	2 (0.9)	3 (1.5)	0.47 [0.07; 3.30] 0.445	0.68 [0.14; 3.42] 0.641	-0.01 [-0.03; 0.02] 0.616

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KESTREL, Week 52 / KITE: logit(proportion) = treatment [by exposure (week 52)].

Table 15-5.13 Any non-ocular adverse event leading to study drug discontinuation by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE leading to study drug discontinuation, Week 100					
Test of heterogeneity in main analysis: **p_H=0.025 ***					
KESTREL					
Interaction Test:	N.E.				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any non-ocular AE leading to study drug discontinuation, n (%)	0 (0.0)	2 (15.4)	N.E.	0.22 [0.01; 4.08] 0.306	-0.15 [-0.35; 0.04] 0.124
Exposed					
N'/N	177 / 177	174 / 174			
Any non-ocular AE leading to study drug discontinuation, n (%)	2 (1.1)	5 (2.9)	0.39 [0.07; 2.02] 0.260	0.39 [0.08; 2.00] 0.261	-0.02 [-0.05; 0.01] 0.244
KITE					
Interaction Test:	N.E.				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any non-ocular AE leading to study drug discontinuation, n (%)	5 (29.4)	4 (33.3)	0.83 [0.17; 4.09] 0.822	0.88 [0.30; 2.62] 0.822	-0.04 [-0.38; 0.30] 0.823
Exposed					
N'/N	162 / 162	169 / 169			
Any non-ocular AE leading to study drug discontinuation, n (%)	5 (3.1)	0 (0.0)	N.E.	11.47 [0.64; 205.82] 0.098	0.03 [0.00; 0.06] 0.023 *
Pooled Analysis					
Interaction Test:	p = 0.344				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any non-ocular AE leading to study drug discontinuation, n (%)	5 (17.2)	6 (24.0)	0.47 [0.11; 2.04] 0.315	0.66 [0.24; 1.80] 0.416	-0.09 [-0.30; 0.11] 0.376

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any non-ocular AE leading to study drug discontinuation, n (%)	7 (2.1)	5 (1.5)	1.12 [0.31; 4.03] 0.859	1.37 [0.46; 4.06] 0.563	0.01 [-0.01; 0.03] 0.555

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / KESTREL, Week 100 / KITE: logit(proportion) = treatment [by exposure (week 100)].

16 Safety analysis: Any adverse event by SOC and PT

Table 16-1.1 Any adverse event by SOC and PT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any adverse event by SOC and PT, week 100					
Eye disorders					
KESTREL, n (%)	115 (60.8)	108 (57.8)	1.14 [0.75; 1.72] 0.542	1.05 [0.89; 1.25] 0.542	0.03 [-0.07; 0.13] 0.541
KITE, n (%)	93 (52.0)	93 (51.4)	1.02 [0.68; 1.55] 0.913	1.01 [0.83; 1.23] 0.913	0.01 [-0.10; 0.11] 0.913
Pooled Analysis, n (%) p_H=0.724	208 (56.5)	201 (54.6)	1.08 [0.81; 1.45] 0.607	1.03 [0.91; 1.18] 0.611	0.02 [-0.05; 0.09] 0.610
Cataract					
KESTREL, n (%)	24 (12.7)	17 (9.1)	1.45 [0.75; 2.81] 0.264	1.40 [0.78; 2.51] 0.265	0.04 [-0.03; 0.10] 0.261
KITE, n (%)	16 (8.9)	25 (13.8)	0.61 [0.32; 1.19] 0.148	0.65 [0.36; 1.17] 0.150	-0.05 [-0.11; 0.02] 0.144
Pooled Analysis, n (%) p_H=0.070	40 (10.9)	42 (11.4)	0.95 [0.60; 1.52] 0.837	0.95 [0.63; 1.43] 0.816	-0.01 [-0.05; 0.04] 0.816
Diabetic retinal oedema					
KESTREL, n (%)	20 (10.6)	15 (8.0)	1.36 [0.67; 2.74] 0.394	1.32 [0.70; 2.50] 0.395	0.03 [-0.03; 0.08] 0.392
KITE, n (%)	20 (11.2)	19 (10.5)	1.07 [0.55; 2.09] 0.837	1.06 [0.59; 1.93] 0.837	0.01 [-0.06; 0.07] 0.837
Pooled Analysis, n (%) p_H=0.634	40 (10.9)	34 (9.2)	1.21 [0.75; 1.96] 0.442	1.18 [0.76; 1.82] 0.460	0.02 [-0.03; 0.06] 0.459
Conjunctival haemorrhage					
KESTREL, n (%)	19 (10.1)	22 (11.8)	0.84 [0.44; 1.61] 0.595	0.85 [0.48; 1.53] 0.595	-0.02 [-0.08; 0.05] 0.594

	Treatment Groups		Comparison		
Any adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE, n (%)	10 (5.6)	12 (6.6)	0.83 [0.35; 1.98] 0.680	0.84 [0.37; 1.90] 0.680	-0.01 [-0.06; 0.04] 0.679
Pooled Analysis, n (%) p_H=0.992	29 (7.9)	34 (9.2)	0.84 [0.49; 1.43] 0.514	0.85 [0.53; 1.36] 0.501	-0.01 [-0.05; 0.03] 0.500
Dry eye					
KESTREL, n (%)	7 (3.7)	6 (3.2)	1.16 [0.38; 3.52] 0.793	1.15 [0.40; 3.37] 0.793	0.00 [-0.03; 0.04] 0.793
KITE, n (%)	11 (6.1)	10 (5.5)	1.12 [0.46; 2.71] 0.802	1.11 [0.48; 2.55] 0.802	0.01 [-0.04; 0.05] 0.802
Pooled Analysis, n (%) p_H=0.961	18 (4.9)	16 (4.3)	1.14 [0.56; 2.32] 0.718	1.13 [0.58; 2.18] 0.719	0.01 [-0.02; 0.04] 0.719
Vitreous haemorrhage					
KESTREL, n (%)	9 (4.8)	8 (4.3)	1.12 [0.42; 2.96] 0.821	1.11 [0.44; 2.82] 0.821	0.00 [-0.04; 0.05] 0.821
KITE, n (%)	7 (3.9)	9 (5.0)	0.78 [0.28; 2.14] 0.626	0.79 [0.30; 2.07] 0.626	-0.01 [-0.05; 0.03] 0.625
Pooled Analysis, n (%) p_H=0.612	16 (4.3)	17 (4.6)	0.94 [0.46; 1.89] 0.854	0.94 [0.48; 1.83] 0.859	-0.00 [-0.03; 0.03] 0.858
Visual acuity reduced					
KESTREL, n (%)	5 (2.6)	9 (4.8)	0.54 [0.18; 1.63] 0.274	0.55 [0.19; 1.61] 0.275	-0.02 [-0.06; 0.02] 0.267
KITE, n (%)	9 (5.0)	6 (3.3)	1.54 [0.54; 4.43] 0.419	1.52 [0.55; 4.17] 0.420	0.02 [-0.02; 0.06] 0.416
Pooled Analysis, n (%) p_H=0.177	14 (3.8)	15 (4.1)	0.90 [0.42; 1.94] 0.791	0.93 [0.46; 1.91] 0.851	-0.00 [-0.03; 0.03] 0.851
Vitreous floaters					
KESTREL, n (%)	11 (5.8)	9 (4.8)	1.22 [0.49; 3.02] 0.664	1.21 [0.51; 2.85] 0.664	0.01 [-0.04; 0.06] 0.663
KITE, n (%)	4 (2.2)	6 (3.3)	0.67 [0.18; 2.40] 0.536	0.67 [0.19; 2.35] 0.536	-0.01 [-0.04; 0.02] 0.532
Pooled Analysis, n (%) p_H=0.449	15 (4.1)	15 (4.1)	0.91 [0.42; 1.98] 0.809	1.00 [0.49; 2.01] 0.992	-0.00 [-0.03; 0.03] 0.992

	Treatment Groups		Comparison		
Any adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Diabetic retinopathy					
KESTREL, n (%)	8 (4.2)	10 (5.3)	0.78 [0.30; 2.03] 0.613	0.79 [0.32; 1.96] 0.614	-0.01 [-0.05; 0.03] 0.613
KITE, n (%)	5 (2.8)	2 (1.1)	2.57 [0.49; 13.43] 0.263	2.53 [0.50; 12.86] 0.264	0.02 [-0.01; 0.05] 0.246
Pooled Analysis, n (%) p_H=0.221	13 (3.5)	12 (3.3)	1.40 [0.55; 3.60] 0.483	1.08 [0.50; 2.33] 0.848	0.00 [-0.02; 0.03] 0.848
Eye pain					
KESTREL, n (%)	7 (3.7)	8 (4.3)	0.86 [0.31; 2.42] 0.776	0.87 [0.32; 2.34] 0.776	-0.01 [-0.05; 0.03] 0.776
KITE, n (%)	6 (3.4)	4 (2.2)	1.53 [0.43; 5.53] 0.513	1.52 [0.44; 5.28] 0.513	0.01 [-0.02; 0.05] 0.510
Pooled Analysis, n (%) p_H=0.491	13 (3.5)	12 (3.3)	1.14 [0.50; 2.60] 0.750	1.08 [0.50; 2.34] 0.843	0.00 [-0.02; 0.03] 0.843
Macular oedema					
KESTREL, n (%)	7 (3.7)	2 (1.1)	3.56 [0.73; 17.34] 0.117	3.46 [0.73; 16.45] 0.118	0.03 [-0.00; 0.06] 0.093
KITE, n (%)	6 (3.4)	5 (2.8)	1.22 [0.37; 4.07] 0.746	1.21 [0.38; 3.90] 0.746	0.01 [-0.03; 0.04] 0.745
Pooled Analysis, n (%) p_H=0.292	13 (3.5)	7 (1.9)	2.11 [0.77; 5.73] 0.145	1.86 [0.75; 4.62] 0.173	0.02 [-0.01; 0.04] 0.172
Vitreous detachment					
KESTREL, n (%)	13 (6.9)	7 (3.7)	1.90 [0.74; 4.87] 0.182	1.84 [0.75; 4.50] 0.183	0.03 [-0.01; 0.08] 0.174
KITE, n (%)	0 (0.0)	1 (0.6)	N.E.	0.34 [0.01; 8.22] 0.505	-0.01 [-0.02; 0.01] 0.316
Pooled Analysis, n (%) p_H=N.E.	13 (3.5)	8 (2.2)	N.E.	1.58 [0.68; 3.65] 0.284	0.01 [-0.01; 0.04] 0.272
Infections and infestations					
KESTREL, n (%)	87 (46.0)	79 (42.2)	1.17 [0.78; 1.75] 0.460	1.09 [0.87; 1.37] 0.460	0.04 [-0.06; 0.14] 0.459

	Treatment Groups		Comparison		
Any adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE, n (%)	75 (41.9)	72 (39.8)	1.09 [0.72; 1.66] 0.682	1.05 [0.82; 1.35] 0.682	0.02 [-0.08; 0.12] 0.682
Pooled Analysis, n (%) p_H=0.826	162 (44.0)	151 (41.0)	1.13 [0.84; 1.51] 0.416	1.07 [0.91; 1.27] 0.415	0.03 [-0.04; 0.10] 0.414
Nasopharyngitis					
KESTREL, n (%)	18 (9.5)	16 (8.6)	1.12 [0.56; 2.28] 0.744	1.11 [0.59; 2.12] 0.744	0.01 [-0.05; 0.07] 0.743
KITE, n (%)	16 (8.9)	17 (9.4)	0.95 [0.46; 1.94] 0.881	0.95 [0.50; 1.82] 0.881	-0.00 [-0.06; 0.06] 0.881
Pooled Analysis, n (%) p_H=0.737	34 (9.2)	33 (9.0)	1.03 [0.63; 1.71] 0.897	1.03 [0.65; 1.63] 0.898	0.00 [-0.04; 0.04] 0.898
Urinary tract infection					
KESTREL, n (%)	21 (11.1)	8 (4.3)	2.80 [1.21; 6.49] 0.017 *	2.60 [1.18; 5.72] 0.018 *	0.07 [0.01; 0.12] 0.012 *
KITE, n (%)	5 (2.8)	6 (3.3)	0.84 [0.25; 2.80] 0.774	0.84 [0.26; 2.71] 0.774	-0.01 [-0.04; 0.03] 0.774
Pooled Analysis, n (%) p_H=0.108	26 (7.1)	14 (3.8)	1.55 [0.75; 3.22] 0.240	1.85 [0.98; 3.48] 0.052	0.03 [-0.00; 0.06] 0.052
COVID-19					
KESTREL, n (%)	10 (5.3)	8 (4.3)	1.25 [0.48; 3.24] 0.646	1.24 [0.50; 3.06] 0.646	0.01 [-0.03; 0.05] 0.645
KITE, n (%)	7 (3.9)	6 (3.3)	1.19 [0.39; 3.60] 0.762	1.18 [0.40; 3.44] 0.762	0.01 [-0.03; 0.04] 0.762
Pooled Analysis, n (%) p_H=0.945	17 (4.6)	14 (3.8)	1.22 [0.59; 2.53] 0.595	1.21 [0.61; 2.42] 0.585	0.01 [-0.02; 0.04] 0.585
Influenza					
KESTREL, n (%)	8 (4.2)	7 (3.7)	1.14 [0.40; 3.20] 0.809	1.13 [0.42; 3.06] 0.809	0.00 [-0.03; 0.04] 0.808
KITE, n (%)	7 (3.9)	4 (2.2)	1.80 [0.52; 6.26] 0.355	1.77 [0.53; 5.94] 0.356	0.02 [-0.02; 0.05] 0.349
Pooled Analysis, n (%) p_H=0.578	15 (4.1)	11 (3.0)	1.42 [0.64; 3.19] 0.391	1.36 [0.63; 2.92] 0.427	0.01 [-0.02; 0.04] 0.426

	Treatment Groups		Comparison		
Any adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Conjunctivitis					
KESTREL, n (%)	7 (3.7)	4 (2.1)	1.76 [0.51; 6.11] 0.374	1.73 [0.52; 5.82] 0.375	0.02 [-0.02; 0.05] 0.367
KITE, n (%)	6 (3.4)	2 (1.1)	3.10 [0.62; 15.59] 0.169	3.03 [0.62; 14.83] 0.171	0.02 [-0.01; 0.05] 0.148
Pooled Analysis, n (%) p_H=0.586	13 (3.5)	6 (1.6)	2.32 [0.84; 6.41] 0.103	2.16 [0.83; 5.62] 0.105	0.02 [-0.00; 0.04] 0.104
Bronchitis					
KESTREL, n (%)	5 (2.6)	4 (2.1)	1.24 [0.33; 4.70] 0.748	1.24 [0.34; 4.53] 0.749	0.01 [-0.03; 0.04] 0.748
KITE, n (%)	7 (3.9)	5 (2.8)	1.43 [0.45; 4.60] 0.546	1.42 [0.46; 4.38] 0.546	0.01 [-0.03; 0.05] 0.544
Pooled Analysis, n (%) p_H=0.875	12 (3.3)	9 (2.4)	1.33 [0.55; 3.24] 0.526	1.34 [0.57; 3.13] 0.504	0.01 [-0.02; 0.03] 0.504
Pneumonia					
KESTREL, n (%)	6 (3.2)	5 (2.7)	1.19 [0.36; 3.98] 0.774	1.19 [0.37; 3.82] 0.774	0.01 [-0.03; 0.04] 0.773
KITE, n (%)	6 (3.4)	5 (2.8)	1.22 [0.37; 4.07] 0.746	1.21 [0.38; 3.90] 0.746	0.01 [-0.03; 0.04] 0.745
Pooled Analysis, n (%) p_H=0.979	12 (3.3)	10 (2.7)	1.21 [0.51; 2.83] 0.666	1.20 [0.53; 2.74] 0.665	0.01 [-0.02; 0.03] 0.665
Upper respiratory tract infection					
KESTREL, n (%)	5 (2.6)	5 (2.7)	0.99 [0.28; 3.47] 0.986	0.99 [0.29; 3.36] 0.986	-0.00 [-0.03; 0.03] 0.986
KITE, n (%)	5 (2.8)	3 (1.7)	1.70 [0.40; 7.24] 0.470	1.69 [0.41; 6.95] 0.470	0.01 [-0.02; 0.04] 0.465
Pooled Analysis, n (%) p_H=0.578	10 (2.7)	8 (2.2)	1.29 [0.50; 3.36] 0.600	1.25 [0.50; 3.13] 0.635	0.01 [-0.02; 0.03] 0.635
Metabolism and nutrition disorders					
KESTREL, n (%)	47 (24.9)	36 (19.3)	1.39 [0.85; 2.27] 0.190	1.29 [0.88; 1.90] 0.192	0.06 [-0.03; 0.14] 0.188

	Treatment Groups		Comparison		
Any adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE, n (%)	29 (16.2)	25 (13.8)	1.21 [0.68; 2.15] 0.526	1.17 [0.72; 1.92] 0.526	0.02 [-0.05; 0.10] 0.526
Pooled Analysis, n (%) p_H=0.717	76 (20.7)	61 (16.6)	1.30 [0.89; 1.89] 0.180	1.24 [0.92; 1.68] 0.158	0.04 [-0.02; 0.10] 0.157
Investigations					
KESTREL, n (%)	29 (15.3)	29 (15.5)	0.99 [0.56; 1.73] 0.965	0.99 [0.62; 1.59] 0.965	-0.00 [-0.07; 0.07] 0.965
KITE, n (%)	35 (19.6)	33 (18.2)	1.09 [0.64; 1.85] 0.749	1.07 [0.70; 1.65] 0.749	0.01 [-0.07; 0.09] 0.749
Pooled Analysis, n (%) p_H=0.801	64 (17.4)	62 (16.8)	1.04 [0.71; 1.52] 0.855	1.03 [0.75; 1.42] 0.840	0.01 [-0.05; 0.06] 0.839
Intraocular pressure increased					
KESTREL, n (%)	11 (5.8)	6 (3.2)	1.86 [0.67; 5.15] 0.230	1.81 [0.68; 4.80] 0.231	0.03 [-0.02; 0.07] 0.221
KITE, n (%)	6 (3.4)	7 (3.9)	0.86 [0.28; 2.62] 0.793	0.87 [0.30; 2.53] 0.793	-0.01 [-0.04; 0.03] 0.793
Pooled Analysis, n (%) p_H=0.315	17 (4.6)	13 (3.5)	1.28 [0.60; 2.71] 0.523	1.31 [0.64; 2.65] 0.458	0.01 [-0.02; 0.04] 0.458
Gastrointestinal disorders					
KESTREL, n (%)	32 (16.9)	29 (15.5)	1.11 [0.64; 1.92] 0.708	1.09 [0.69; 1.73] 0.708	0.01 [-0.06; 0.09] 0.708
KITE, n (%)	31 (17.3)	31 (17.1)	1.01 [0.59; 1.75] 0.962	1.01 [0.64; 1.59] 0.962	0.00 [-0.08; 0.08] 0.962
Pooled Analysis, n (%) p_H=0.817	63 (17.1)	60 (16.3)	1.06 [0.72; 1.56] 0.762	1.05 [0.76; 1.45] 0.766	0.01 [-0.05; 0.06] 0.765
Diarrhoea					
KESTREL, n (%)	10 (5.3)	6 (3.2)	1.69 [0.60; 4.73] 0.322	1.65 [0.61; 4.45] 0.323	0.02 [-0.02; 0.06] 0.316
KITE, n (%)	3 (1.7)	8 (4.4)	0.37 [0.10; 1.41] 0.145	0.38 [0.10; 1.41] 0.147	-0.03 [-0.06; 0.01] 0.128
Pooled Analysis, n (%) p_H=0.079	13 (3.5)	14 (3.8)	0.80 [0.34; 1.86] 0.605	0.93 [0.44; 1.95] 0.841	-0.00 [-0.03; 0.02] 0.841

	Treatment Groups		Comparison		
Any adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Nausea					
KESTREL, n (%)	5 (2.6)	3 (1.6)	1.67 [0.39; 7.08] 0.489	1.65 [0.40; 6.80] 0.489	0.01 [-0.02; 0.04] 0.483
KITE, n (%)	5 (2.8)	5 (2.8)	1.01 [0.29; 3.56] 0.986	1.01 [0.30; 3.43] 0.986	0.00 [-0.03; 0.03] 0.986
Pooled Analysis, n (%) p_H=0.609	10 (2.7)	8 (2.2)	1.30 [0.50; 3.41] 0.587	1.25 [0.50; 3.14] 0.631	0.01 [-0.02; 0.03] 0.631
Vascular disorders					
KESTREL, n (%)	28 (14.8)	33 (17.6)	0.81 [0.47; 1.41] 0.457	0.84 [0.53; 1.33] 0.457	-0.03 [-0.10; 0.05] 0.456
KITE, n (%)	28 (15.6)	30 (16.6)	0.93 [0.53; 1.64] 0.810	0.94 [0.59; 1.51] 0.810	-0.01 [-0.09; 0.07] 0.810
Pooled Analysis, n (%) p_H=0.728	56 (15.2)	63 (17.1)	0.87 [0.59; 1.29] 0.484	0.89 [0.64; 1.24] 0.484	-0.02 [-0.07; 0.03] 0.483
Hypertension					
KESTREL, n (%)	21 (11.1)	24 (12.8)	0.85 [0.45; 1.58] 0.607	0.87 [0.50; 1.50] 0.607	-0.02 [-0.08; 0.05] 0.607
KITE, n (%)	15 (8.4)	17 (9.4)	0.88 [0.43; 1.83] 0.736	0.89 [0.46; 1.73] 0.736	-0.01 [-0.07; 0.05] 0.736
Pooled Analysis, n (%) p_H=0.936	36 (9.8)	41 (11.1)	0.87 [0.54; 1.40] 0.552	0.88 [0.57; 1.34] 0.542	-0.01 [-0.06; 0.03] 0.542
Renal and urinary disorders					
KESTREL, n (%)	26 (13.8)	26 (13.9)	0.99 [0.55; 1.77] 0.967	0.99 [0.60; 1.64] 0.967	-0.00 [-0.07; 0.07] 0.967
KITE, n (%)	22 (12.3)	34 (18.8)	0.61 [0.34; 1.08] 0.091	0.65 [0.40; 1.07] 0.093	-0.06 [-0.14; 0.01] 0.088
Pooled Analysis, n (%) p_H=0.245	48 (13.0)	60 (16.3)	0.78 [0.51; 1.17] 0.232	0.80 [0.56; 1.14] 0.213	-0.03 [-0.08; 0.02] 0.212
Proteinuria					
KESTREL, n (%)	2 (1.1)	0 (0.0)	N.E.	4.95 [0.24; 102.36] 0.301	0.01 [-0.00; 0.03] 0.155

	Treatment Groups		Comparison		
Any adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE, n (%)	6 (3.4)	13 (7.2)	0.45 [0.17; 1.21] 0.112	0.47 [0.18; 1.20] 0.114	-0.04 [-0.08; 0.01] 0.102
Pooled Analysis, n (%) p_H=N.E.	8 (2.2)	13 (3.5)	N.E.	0.63 [0.27; 1.47] 0.284	-0.01 [-0.04; 0.01] 0.273
Chronic kidney disease					
KESTREL, n (%)	7 (3.7)	7 (3.7)	0.99 [0.34; 2.88] 0.984	0.99 [0.35; 2.77] 0.984	-0.00 [-0.04; 0.04] 0.984
KITE, n (%)	4 (2.2)	6 (3.3)	0.67 [0.18; 2.40] 0.536	0.67 [0.19; 2.35] 0.536	-0.01 [-0.04; 0.02] 0.532
Pooled Analysis, n (%) p_H=0.643	11 (3.0)	13 (3.5)	0.82 [0.35; 1.87] 0.630	0.84 [0.38; 1.86] 0.676	-0.01 [-0.03; 0.02] 0.675
Diabetic nephropathy					
KESTREL, n (%)	3 (1.6)	2 (1.1)	1.49 [0.25; 9.03] 0.663	1.48 [0.25; 8.78] 0.663	0.01 [-0.02; 0.03] 0.661
KITE, n (%)	6 (3.4)	9 (5.0)	0.66 [0.23; 1.90] 0.445	0.67 [0.25; 1.85] 0.445	-0.02 [-0.06; 0.03] 0.441
Pooled Analysis, n (%) p_H=0.446	9 (2.4)	11 (3.0)	1.00 [0.35; 2.88] 0.996	0.82 [0.35; 1.96] 0.659	-0.01 [-0.03; 0.02] 0.658
Nervous system disorders					
KESTREL, n (%)	24 (12.7)	30 (16.0)	0.76 [0.43; 1.36] 0.356	0.79 [0.48; 1.30] 0.357	-0.03 [-0.10; 0.04] 0.355
KITE, n (%)	29 (16.2)	29 (16.0)	1.01 [0.58; 1.78] 0.963	1.01 [0.63; 1.62] 0.963	0.00 [-0.07; 0.08] 0.963
Pooled Analysis, n (%) p_H=0.487	53 (14.4)	59 (16.0)	0.88 [0.58; 1.31] 0.520	0.90 [0.64; 1.26] 0.541	-0.02 [-0.07; 0.04] 0.540
Headache					
KESTREL, n (%)	10 (5.3)	3 (1.6)	3.43 [0.93; 12.65] 0.065	3.30 [0.92; 11.79] 0.066	0.04 [0.00; 0.07] 0.049 *
KITE, n (%)	8 (4.5)	5 (2.8)	1.65 [0.53; 5.13] 0.390	1.62 [0.54; 4.85] 0.390	0.02 [-0.02; 0.06] 0.386
Pooled Analysis, n (%) p_H=0.407	18 (4.9)	8 (2.2)	2.39 [1.00; 5.70] 0.049 *	2.25 [0.99; 5.12] 0.046 *	0.03 [0.00; 0.05] 0.045 *

	Treatment Groups		Comparison		
Any adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Injury, poisoning and procedural complications					
KESTREL, n (%)	31 (16.4)	34 (18.2)	0.88 [0.52; 1.51] 0.648	0.90 [0.58; 1.40] 0.648	-0.02 [-0.09; 0.06] 0.648
KITE, n (%)	18 (10.1)	24 (13.3)	0.73 [0.38; 1.40] 0.345	0.76 [0.43; 1.35] 0.346	-0.03 [-0.10; 0.03] 0.343
Pooled Analysis, n (%) p_H=0.661	49 (13.3)	58 (15.8)	0.81 [0.53; 1.22] 0.311	0.84 [0.59; 1.20] 0.340	-0.02 [-0.08; 0.03] 0.339
Respiratory, thoracic and mediastinal disorders					
KESTREL, n (%)	30 (15.9)	28 (15.0)	1.07 [0.61; 1.88] 0.809	1.06 [0.66; 1.70] 0.809	0.01 [-0.06; 0.08] 0.809
KITE, n (%)	16 (8.9)	26 (14.4)	0.59 [0.30; 1.13] 0.112	0.62 [0.35; 1.12] 0.114	-0.05 [-0.12; 0.01] 0.107
Pooled Analysis, n (%) p_H=0.171	46 (12.5)	54 (14.7)	0.80 [0.52; 1.23] 0.302	0.85 [0.59; 1.23] 0.385	-0.02 [-0.07; 0.03] 0.384
Cough					
KESTREL, n (%)	11 (5.8)	10 (5.3)	1.09 [0.45; 2.64] 0.842	1.09 [0.47; 2.50] 0.842	0.00 [-0.04; 0.05] 0.842
KITE, n (%)	5 (2.8)	10 (5.5)	0.49 [0.16; 1.47] 0.203	0.51 [0.18; 1.45] 0.204	-0.03 [-0.07; 0.01] 0.193
Pooled Analysis, n (%) p_H=0.264	16 (4.3)	20 (5.4)	0.74 [0.37; 1.49] 0.397	0.80 [0.42; 1.52] 0.492	-0.01 [-0.04; 0.02] 0.491
Musculoskeletal and connective tissue disorders					
KESTREL, n (%)	28 (14.8)	23 (12.3)	1.24 [0.69; 2.24] 0.477	1.20 [0.72; 2.01] 0.477	0.03 [-0.04; 0.09] 0.476
KITE, n (%)	25 (14.0)	25 (13.8)	1.01 [0.56; 1.84] 0.966	1.01 [0.60; 1.69] 0.966	0.00 [-0.07; 0.07] 0.966
Pooled Analysis, n (%) p_H=0.638	53 (14.4)	48 (13.0)	1.12 [0.74; 1.71] 0.589	1.10 [0.77; 1.59] 0.592	0.01 [-0.04; 0.06] 0.592
Arthralgia					
KESTREL, n (%)	6 (3.2)	5 (2.7)	1.19 [0.36; 3.98] 0.774	1.19 [0.37; 3.82] 0.774	0.01 [-0.03; 0.04] 0.773

	Treatment Groups		Comparison		
Any adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE, n (%)	5 (2.8)	7 (3.9)	0.71 [0.22; 2.29] 0.572	0.72 [0.23; 2.23] 0.572	-0.01 [-0.05; 0.03] 0.570
Pooled Analysis, n (%) p_H=0.548	11 (3.0)	12 (3.3)	0.93 [0.40; 2.15] 0.861	0.92 [0.41; 2.05] 0.834	-0.00 [-0.03; 0.02] 0.834
Back pain					
KESTREL, n (%)	5 (2.6)	6 (3.2)	0.82 [0.25; 2.73] 0.746	0.82 [0.26; 2.66] 0.746	-0.01 [-0.04; 0.03] 0.746
KITE, n (%)	7 (3.9)	2 (1.1)	3.64 [0.75; 17.77] 0.110	3.54 [0.75; 16.81] 0.112	0.03 [-0.00; 0.06] 0.088
Pooled Analysis, n (%) p_H=0.142	12 (3.3)	8 (2.2)	1.70 [0.63; 4.58] 0.292	1.50 [0.62; 3.62] 0.366	0.01 [-0.01; 0.03] 0.366
General disorders and administration site conditions					
KESTREL, n (%)	23 (12.2)	22 (11.8)	1.04 [0.56; 1.94] 0.904	1.03 [0.60; 1.79] 0.904	0.00 [-0.06; 0.07] 0.904
KITE, n (%)	27 (15.1)	26 (14.4)	1.06 [0.59; 1.90] 0.847	1.05 [0.64; 1.73] 0.847	0.01 [-0.07; 0.08] 0.847
Pooled Analysis, n (%) p_H=0.965	50 (13.6)	48 (13.0)	1.05 [0.68; 1.61] 0.827	1.04 [0.72; 1.51] 0.824	0.01 [-0.04; 0.05] 0.823
Pyrexia					
KESTREL, n (%)	8 (4.2)	4 (2.1)	2.02 [0.60; 6.83] 0.257	1.98 [0.61; 6.46] 0.258	0.02 [-0.01; 0.06] 0.247
KITE, n (%)	8 (4.5)	5 (2.8)	1.65 [0.53; 5.13] 0.390	1.62 [0.54; 4.85] 0.390	0.02 [-0.02; 0.06] 0.386
Pooled Analysis, n (%) p_H=0.809	16 (4.3)	9 (2.4)	1.83 [0.79; 4.21] 0.156	1.78 [0.80; 3.98] 0.154	0.02 [-0.01; 0.05] 0.153
Oedema peripheral					
KESTREL, n (%)	5 (2.6)	5 (2.7)	0.99 [0.28; 3.47] 0.986	0.99 [0.29; 3.36] 0.986	-0.00 [-0.03; 0.03] 0.986
KITE, n (%)	5 (2.8)	2 (1.1)	2.57 [0.49; 13.43] 0.263	2.53 [0.50; 12.86] 0.264	0.02 [-0.01; 0.05] 0.246
Pooled Analysis, n (%) p_H=0.367	10 (2.7)	7 (1.9)	1.58 [0.56; 4.44] 0.386	1.43 [0.55; 3.70] 0.464	0.01 [-0.01; 0.03] 0.464

	Treatment Groups		Comparison		
Any adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Cardiac disorders					
KESTREL, n (%)	16 (8.5)	27 (14.4)	0.55 [0.28; 1.05] 0.072	0.59 [0.33; 1.05] 0.073	-0.06 [-0.12; 0.00] 0.068
KITE, n (%)	16 (8.9)	21 (11.6)	0.75 [0.38; 1.49] 0.407	0.77 [0.42; 1.43] 0.407	-0.03 [-0.09; 0.04] 0.405
Pooled Analysis, n (%) p_H=0.521	32 (8.7)	48 (13.0)	0.64 [0.40; 1.03] 0.063	0.67 [0.44; 1.02] 0.058	-0.04 [-0.09; 0.00] 0.057
Skin and subcutaneous tissue disorders					
KESTREL, n (%)	19 (10.1)	14 (7.5)	1.38 [0.67; 2.84] 0.381	1.34 [0.69; 2.60] 0.381	0.03 [-0.03; 0.08] 0.378
KITE, n (%)	11 (6.1)	16 (8.8)	0.68 [0.30; 1.50] 0.334	0.70 [0.33; 1.46] 0.335	-0.03 [-0.08; 0.03] 0.331
Pooled Analysis, n (%) p_H=0.192	30 (8.2)	30 (8.2)	0.97 [0.57; 1.66] 0.919	1.00 [0.61; 1.62] 0.997	-0.00 [-0.04; 0.04] 0.997
Blood and lymphatic system disorders					
KESTREL, n (%)	15 (7.9)	14 (7.5)	1.07 [0.50; 2.27] 0.870	1.06 [0.53; 2.13] 0.870	0.00 [-0.05; 0.06] 0.870
KITE, n (%)	10 (5.6)	13 (7.2)	0.76 [0.33; 1.79] 0.537	0.78 [0.35; 1.73] 0.537	-0.02 [-0.07; 0.03] 0.535
Pooled Analysis, n (%) p_H=0.569	25 (6.8)	27 (7.3)	0.91 [0.51; 1.60] 0.733	0.92 [0.55; 1.56] 0.771	-0.01 [-0.04; 0.03] 0.771
Anaemia					
KESTREL, n (%)	9 (4.8)	9 (4.8)	0.99 [0.38; 2.55] 0.982	0.99 [0.40; 2.44] 0.982	-0.00 [-0.04; 0.04] 0.982
KITE, n (%)	9 (5.0)	9 (5.0)	1.01 [0.39; 2.61] 0.981	1.01 [0.41; 2.49] 0.981	0.00 [-0.04; 0.05] 0.981
Pooled Analysis, n (%) p_H=0.973	18 (4.9)	18 (4.9)	1.00 [0.51; 1.95] 1.000	1.00 [0.53; 1.89] 0.999	0.00 [-0.03; 0.03] 0.999
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
KESTREL, n (%)	9 (4.8)	10 (5.3)	0.89 [0.35; 2.23] 0.796	0.89 [0.37; 2.14] 0.796	-0.01 [-0.05; 0.04] 0.795

	Treatment Groups		Comparison		
Any adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE, n (%)	8 (4.5)	11 (6.1)	0.72 [0.28; 1.84] 0.497	0.74 [0.30; 1.79] 0.497	-0.02 [-0.06; 0.03] 0.494
Pooled Analysis, n (%) p_H=0.763	17 (4.6)	21 (5.7)	0.80 [0.42; 1.55] 0.509	0.81 [0.43; 1.51] 0.506	-0.01 [-0.04; 0.02] 0.506
Psychiatric disorders					
KESTREL, n (%)	10 (5.3)	9 (4.8)	1.10 [0.44; 2.78] 0.832	1.10 [0.46; 2.64] 0.832	0.00 [-0.04; 0.05] 0.832
KITE, n (%)	7 (3.9)	7 (3.9)	1.01 [0.35; 2.95] 0.983	1.01 [0.36; 2.82] 0.983	0.00 [-0.04; 0.04] 0.983
Pooled Analysis, n (%) p_H=0.903	17 (4.6)	16 (4.3)	1.06 [0.52; 2.14] 0.875	1.06 [0.54; 2.07] 0.862	0.00 [-0.03; 0.03] 0.862
Ear and labyrinth disorders					
KESTREL, n (%)	7 (3.7)	7 (3.7)	0.99 [0.34; 2.88] 0.984	0.99 [0.35; 2.77] 0.984	-0.00 [-0.04; 0.04] 0.984
KITE, n (%)	7 (3.9)	6 (3.3)	1.19 [0.39; 3.60] 0.762	1.18 [0.40; 3.44] 0.762	0.01 [-0.03; 0.04] 0.762
Pooled Analysis, n (%) p_H=0.816	14 (3.8)	13 (3.5)	1.08 [0.50; 2.34] 0.842	1.08 [0.51; 2.26] 0.845	0.00 [-0.02; 0.03] 0.845
Reproductive system and breast disorders					
KESTREL, n (%)	5 (2.6)	5 (2.7)	0.99 [0.28; 3.47] 0.986	0.99 [0.29; 3.36] 0.986	-0.00 [-0.03; 0.03] 0.986
KITE, n (%)	5 (2.8)	7 (3.9)	0.71 [0.22; 2.29] 0.572	0.72 [0.23; 2.23] 0.572	-0.01 [-0.05; 0.03] 0.570
Pooled Analysis, n (%) p_H=0.710	10 (2.7)	12 (3.3)	0.84 [0.36; 1.99] 0.697	0.83 [0.36; 1.91] 0.668	-0.01 [-0.03; 0.02] 0.667
Hepatobiliary disorders					
KESTREL, n (%)	6 (3.2)	3 (1.6)	2.01 [0.50; 8.16] 0.328	1.98 [0.50; 7.80] 0.329	0.02 [-0.02; 0.05] 0.318
KITE, n (%)	5 (2.8)	5 (2.8)	1.01 [0.29; 3.56] 0.986	1.01 [0.30; 3.43] 0.986	0.00 [-0.03; 0.03] 0.986

	Treatment Groups		Comparison		
Any adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, n (%) p_H=0.474	11 (3.0)	8 (2.2)	1.44 [0.56; 3.69] 0.452	1.38 [0.56; 3.39] 0.485	0.01 [-0.01; 0.03] 0.484

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 16-1.2 Any adverse event by SOC, PT and age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
< 65 years, N'/N	104 / 104	93 / 93			
≥ 65 years, N'/N	85 / 85	94 / 94			
KITE, N'/N	179 / 179	181 / 181			
< 65 years, N'/N	100 / 100	102 / 102			
≥ 65 years, N'/N	79 / 79	79 / 79			
Pooled Analysis, N'/N	368 / 368	368 / 368			
< 65 years, N'/N	204 / 204	195 / 195			
≥ 65 years, N'/N	164 / 164	173 / 173			
Any adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	p = 0.721				
< 65 years, n (%)	6 (5.8)	2 (2.2)	2.79 [0.55; 14.15] 0.217	2.68 [0.55; 12.97] 0.220	0.04 [-0.02; 0.09] 0.186
≥ 65 years, n (%)	4 (4.7)	1 (1.1)	4.59 [0.50; 41.93] 0.177	4.42 [0.50; 38.80] 0.180	0.04 [-0.01; 0.09] 0.150
KITE					
Interaction Test:	p = 0.085				
< 65 years, n (%)	7 (7.0)	2 (2.0)	3.76 [0.76; 18.58] 0.104	3.57 [0.76; 16.77] 0.107	0.05 [-0.01; 0.11] 0.082
≥ 65 years, n (%)	1 (1.3)	3 (3.8)	0.32 [0.03; 3.19] 0.335	0.33 [0.04; 3.14] 0.337	-0.03 [-0.07; 0.02] 0.310
Pooled Analysis					
Interaction Test:	p = 0.297				
< 65 years, n (%)	13 (6.4)	4 (2.1)	3.43 [1.07; 10.97] 0.038 *	3.11 [1.03; 9.36] 0.032 *	0.04 [0.00; 0.08] 0.029 *

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years, n (%)	5 (3.0)	4 (2.3)	1.35 [0.35; 5.15] 0.664	1.32 [0.36; 4.76] 0.673	0.01 [-0.03; 0.04] 0.677

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 16-1.3 Any adverse event by SOC, PT and gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Male, N'/N	110 / 110	126 / 126			
Female, N'/N	79 / 79	61 / 61			
KITE, N'/N	179 / 179	181 / 181			
Male, N'/N	120 / 120	115 / 115			
Female, N'/N	59 / 59	66 / 66			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Male, N'/N	230 / 230	241 / 241			
Female, N'/N	138 / 138	127 / 127			
Any adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	p = 0.433				
Male, n (%)	5 (4.5)	1 (0.8)	5.95 [0.68; 51.74] 0.106	5.73 [0.68; 48.28] 0.109	0.04 [-0.00; 0.08] 0.079
Female, n (%)	5 (6.3)	2 (3.3)	1.99 [0.37; 10.64] 0.420	1.93 [0.39; 9.61] 0.422	0.03 [-0.04; 0.10] 0.392
KITE					
Interaction Test:	p = 0.115				
Male, n (%)	3 (2.5)	4 (3.5)	0.71 [0.16; 3.25] 0.661	0.72 [0.16; 3.14] 0.661	-0.01 [-0.05; 0.03] 0.660
Female, n (%)	5 (8.5)	1 (1.5)	6.02 [0.68; 53.09] 0.106	5.59 [0.67; 46.51] 0.111	0.07 [-0.01; 0.15] 0.076
Pooled Analysis					
Interaction Test:	p = 0.461				
Male, n (%)	8 (3.5)	5 (2.1)	1.75 [0.56; 5.52] 0.336	1.65 [0.56; 4.87] 0.360	0.01 [-0.02; 0.04] 0.367

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female, n (%)	10 (7.2)	3 (2.4)	3.37 [0.89; 12.84] 0.074	3.01 [0.87; 10.44] 0.067	0.05 [-0.00; 0.10] 0.061

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 16-1.4 Any adverse event by SOC, PT and BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
≤ 65 letters, N'/N	74 / 74	64 / 64			
> 65 letters, N'/N	115 / 115	123 / 123			
KITE, N'/N	179 / 179	181 / 181			
≤ 65 letters, N'/N	65 / 65	91 / 91			
> 65 letters, N'/N	114 / 114	90 / 90			
Pooled Analysis, N'/N	368 / 368	368 / 368			
≤ 65 letters, N'/N	139 / 139	155 / 155			
> 65 letters, N'/N	229 / 229	213 / 213			
Any adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	p = 0.956				
≤ 65 letters, n (%)	4 (5.4)	1 (1.6)	3.60 [0.39; 33.05] 0.258	3.46 [0.40; 30.17] 0.261	0.04 [-0.02; 0.10] 0.208
> 65 letters, n (%)	6 (5.2)	2 (1.6)	3.33 [0.66; 16.84] 0.146	3.21 [0.66; 15.58] 0.148	0.04 [-0.01; 0.08] 0.129
KITE					
Interaction Test:	p = 0.534				
≤ 65 letters, n (%)	2 (3.1)	1 (1.1)	2.86 [0.25; 32.19] 0.396	2.80 [0.26; 30.23] 0.396	0.02 [-0.03; 0.07] 0.411
> 65 letters, n (%)	6 (5.3)	4 (4.4)	1.19 [0.33; 4.37] 0.788	1.18 [0.34; 4.07] 0.788	0.01 [-0.05; 0.07] 0.786
Pooled Analysis					
Interaction Test:	p = 0.475				
≤ 65 letters, n (%)	6 (4.3)	2 (1.3)	3.86 [0.73; 20.26] 0.111	3.17 [0.64; 15.78] 0.136	0.03 [-0.01; 0.07] 0.140

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters, n (%)	12 (5.2)	6 (2.8)	1.92 [0.70; 5.27] 0.205	1.80 [0.70; 4.63] 0.219	0.02 [-0.01; 0.06] 0.216

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 16-1.5 Any adverse event by SOC, PT and region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Region of the Americas, N'/N	90 / 90	83 / 83			
European Region, N'/N	69 / 69	75 / 75			
Western Pacific Region, N'/N	30 / 30	29 / 29			
KITE, N'/N	179 / 179	181 / 181			
South-East Asia Region and Eastern Mediterranean Region, N'/N	26 / 26	21 / 21			
European Region, N'/N	135 / 135	132 / 132			
Western Pacific Region, N'/N	18 / 18	28 / 28			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Region of the Americas, N'/N	90 / 90	83 / 83			
South-East Asia Region and Eastern Mediterranean Region, N'/N	26 / 26	21 / 21			
European Region, N'/N	204 / 204	207 / 207			
Western Pacific Region, N'/N	48 / 48	57 / 57			
Any adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	N.E.				
Region of the Americas, n (%)	5 (5.6)	0 (0.0)	N.E.	10.15 [0.57; 180.85] 0.115	0.06 [0.01; 0.10] 0.021 *
European Region, n (%)	2 (2.9)	2 (2.7)	1.09 [0.15; 7.95] 0.933	1.09 [0.16; 7.51] 0.933	0.00 [-0.05; 0.06] 0.933
Western Pacific Region, n (%)	3 (10.0)	1 (3.4)	3.11 [0.30; 31.78] 0.339	2.90 [0.32; 26.30] 0.344	0.07 [-0.06; 0.19] 0.309

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	N.E.				
South-East Asia Region and Eastern Mediterranean Region, n (%)	2 (7.7)	0 (0.0)	N.E.	4.07 [0.21; 80.51] 0.356	0.08 [-0.03; 0.18] 0.141
European Region, n (%)	6 (4.4)	5 (3.8)	1.18 [0.35; 3.97] 0.787	1.17 [0.37; 3.75] 0.788	0.01 [-0.04; 0.05] 0.787
Western Pacific Region, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Pooled Analysis					
Interaction Test:	N.E.				
Region of the Americas, n (%)	5 (5.6)	0 (0.0)	N.E.	10.15 [0.57; 180.85] 0.048 *	0.06 [0.01; 0.10] 0.021 *
South-East Asia Region and Eastern Mediterranean Region, n (%)	2 (7.7)	0 (0.0)	N.E.	4.07 [0.21; 80.51] 0.315	0.08 [-0.03; 0.18] 0.141
European Region, n (%)	8 (3.9)	7 (3.4)	1.13 [0.35; 3.67] 0.834	1.15 [0.42; 3.11] 0.784	0.01 [-0.03; 0.04] 0.784
Western Pacific Region, n (%)	3 (6.3)	1 (1.8)	N.E.	2.90 [0.32; 26.30] 0.321	0.04 [-0.04; 0.11] 0.325

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Headache / KESTREL, Week 100 / Headache / KITE: logit(proportion) = treatment [by region].
Week 100 / Headache / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by region].

Table 16-1.6 Any adverse event by SOC, PT and diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Type 1, N'/N	12 / 12	6 / 6			
Type 2, N'/N	177 / 177	181 / 181			
KITE, N'/N	179 / 179	181 / 181			
Type 1, N'/N	19 / 19	7 / 7			
Type 2, N'/N	160 / 160	174 / 174			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Type 1, N'/N	31 / 31	13 / 13			
Type 2, N'/N	337 / 337	355 / 355			
Any adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	N.E.				
Type 1, n (%)	2 (16.7)	0 (0.0)	N.E.	2.69 [0.15; 48.64] 0.502	0.17 [-0.04; 0.38] 0.121
Type 2, n (%)	8 (4.5)	3 (1.7)	2.81 [0.73; 10.76] 0.132	2.73 [0.74; 10.11] 0.134	0.03 [-0.01; 0.06] 0.117
KITE					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2, n (%)	8 (5.0)	5 (2.9)	1.78 [0.57; 5.55] 0.321	1.74 [0.58; 5.21] 0.322	0.02 [-0.02; 0.06] 0.320
Pooled Analysis					
Interaction Test:	N.E.				
Type 1, n (%)	2 (6.5)	0 (0.0)	N.E.	2.69 [0.15; 48.64] 0.482	0.07 [-0.02; 0.16] 0.118

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2, n (%)	16 (4.7)	8 (2.3)	2.25 [0.93; 5.43] 0.073	2.12 [0.92; 4.89] 0.072	0.03 [-0.00; 0.05] 0.073

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Headache / KESTREL, Week 100 / Headache / KITE: logit(proportion) = treatment [by diabetes type].
Week 100 / Headache / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 16-1.7 Any adverse event by SOC, PT and HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	188 / 188	187 / 187			
< 7.5 %, N'/N	76 / 76	107 / 107			
≥ 7.5 %, N'/N	112 / 112	80 / 80			
KITE, N'/N	179 / 179	181 / 181			
< 7.5 %, N'/N	82 / 82	96 / 96			
≥ 7.5 %, N'/N	97 / 97	85 / 85			
Pooled Analysis, N'/N	367 / 367	368 / 368			
< 7.5 %, N'/N	158 / 158	203 / 203			
≥ 7.5 %, N'/N	209 / 209	165 / 165			
Any adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	p = 0.484				
< 7.5 %, n (%)	4 (5.3)	1 (0.9)	5.89 [0.64; 53.77] 0.116	5.63 [0.64; 49.40] 0.119	0.04 [-0.01; 0.10] 0.112
≥ 7.5 %, n (%)	6 (5.4)	2 (2.5)	2.21 [0.43; 11.23] 0.340	2.14 [0.44; 10.35] 0.343	0.03 [-0.03; 0.08] 0.299
KITE					
Interaction Test:	p = 0.731				
< 7.5 %, n (%)	2 (2.4)	2 (2.1)	1.17 [0.16; 8.53] 0.873	1.17 [0.17; 8.13] 0.873	0.00 [-0.04; 0.05] 0.874
≥ 7.5 %, n (%)	6 (6.2)	3 (3.5)	1.80 [0.44; 7.44] 0.415	1.75 [0.45; 6.79] 0.417	0.03 [-0.04; 0.09] 0.401
Pooled Analysis					
Interaction Test:	p = 0.749				
< 7.5 %, n (%)	6 (3.8)	3 (1.5)	2.70 [0.66; 11.08] 0.168	2.56 [0.66; 9.85] 0.157	0.02 [-0.01; 0.06] 0.182

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %, n (%)	12 (5.7)	5 (3.0)	2.03 [0.68; 6.01] 0.203	1.92 [0.69; 5.35] 0.205	0.03 [-0.01; 0.07] 0.187

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 16-1.8 Any adverse event by SOC, PT and duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
≤ 3 months, N'/N	120 / 120	110 / 110			
> 3 - < 12 months, N'/N	30 / 30	39 / 39			
≥ 12 months, N'/N	39 / 39	38 / 38			
KITE, N'/N	179 / 179	181 / 181			
≤ 3 months, N'/N	85 / 85	92 / 92			
> 3 - < 12 months, N'/N	51 / 51	49 / 49			
≥ 12 months, N'/N	43 / 43	40 / 40			
Pooled Analysis, N'/N	368 / 368	368 / 368			
≤ 3 months, N'/N	205 / 205	202 / 202			
> 3 - < 12 months, N'/N	81 / 81	88 / 88			
≥ 12 months, N'/N	82 / 82	78 / 78			
Any adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months, n (%)	6 (5.0)	1 (0.9)	5.74 [0.68; 48.43] 0.108	5.50 [0.67; 44.96] 0.112	0.04 [-0.00; 0.08] 0.061
> 3 - < 12 months, n (%)	3 (10.0)	0 (0.0)	N.E.	9.03 [0.48; 168.45] 0.140	0.10 [-0.01; 0.21] 0.068
≥ 12 months, n (%)	1 (2.6)	2 (5.3)	0.47 [0.04; 5.45] 0.549	0.49 [0.05; 5.15] 0.550	-0.03 [-0.11; 0.06] 0.541
KITE					
Interaction Test:	N.E.				
≤ 3 months, n (%)	4 (4.7)	3 (3.3)	1.46 [0.32; 6.74] 0.624	1.44 [0.33; 6.26] 0.624	0.01 [-0.04; 0.07] 0.624
> 3 - < 12 months, n (%)	2 (3.9)	0 (0.0)	N.E.	4.81 [0.24; 97.68] 0.307	0.04 [-0.01; 0.09] 0.149
≥ 12 months, n (%)	2 (4.7)	2 (5.0)	0.93 [0.12; 6.91] 0.941	0.93 [0.14; 6.30] 0.941	-0.00 [-0.10; 0.09] 0.941

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	N.E.				
≤ 3 months, n (%)	10 (4.9)	4 (2.0)	2.94 [0.78; 11.01] 0.110	2.52 [0.79; 8.04] 0.105	0.03 [-0.01; 0.06] 0.101
> 3 - < 12 months, n (%)	5 (6.2)	0 (0.0)	N.E.	6.76 [0.85; 53.84] 0.035 *	0.06 [0.01; 0.12] 0.019 *
≥ 12 months, n (%)	3 (3.7)	4 (5.1)	0.66 [0.13; 3.22] 0.606	0.71 [0.16; 3.09] 0.649	-0.01 [-0.08; 0.05] 0.648

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Headache / KESTREL, Week 100 / Headache / KITE: logit(proportion) = treatment [by duration of DME].
Week 100 / Headache / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by duration of DME].

Table 16-1.9 Any adverse event by SOC, PT and DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	186 / 186	182 / 182			
focal, N'/N	59 / 59	48 / 48			
diffuse, N'/N	127 / 127	134 / 134			
KITE, N'/N	178 / 178	175 / 175			
focal, N'/N	63 / 63	66 / 66			
diffuse, N'/N	115 / 115	109 / 109			
Pooled Analysis, N'/N	364 / 364	357 / 357			
focal, N'/N	122 / 122	114 / 114			
diffuse, N'/N	242 / 242	243 / 243			
Any adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	N.E.				
focal, n (%)	2 (3.4)	0 (0.0)	N.E.	4.08 [0.20; 83.07] 0.360	0.03 [-0.01; 0.08] 0.150
diffuse, n (%)	8 (6.3)	3 (2.2)	2.94 [0.76; 11.32] 0.118	2.81 [0.76; 10.37] 0.120	0.04 [-0.01; 0.09] 0.105
KITE					
Interaction Test:	p = 0.797				
focal, n (%)	4 (6.3)	3 (4.5)	1.42 [0.31; 6.63] 0.653	1.40 [0.33; 5.99] 0.653	0.02 [-0.06; 0.10] 0.652
diffuse, n (%)	4 (3.5)	2 (1.8)	1.93 [0.35; 10.74] 0.454	1.90 [0.35; 10.14] 0.455	0.02 [-0.03; 0.06] 0.442
Pooled Analysis					
Interaction Test:	p = 0.838				
focal, n (%)	6 (4.9)	3 (2.6)	2.08 [0.49; 8.79] 0.321	1.82 [0.50; 6.61] 0.356	0.03 [-0.02; 0.07] 0.304

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse, n (%)	12 (5.0)	5 (2.1)	2.50 [0.86; 7.27] 0.093	2.43 [0.87; 6.79] 0.078	0.03 [-0.00; 0.06] 0.078

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Headache / KESTREL: logit(proportion) = treatment [by DME type].

Table 16-1.10 Any adverse event by SOC, PT and CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
< 450 µm, N'/N	107 / 107	96 / 96			
≥ 450 - < 650 µm, N'/N	70 / 70	71 / 71			
≥ 650 µm, N'/N	12 / 12	20 / 20			
KITE, N'/N	179 / 179	180 / 180			
< 450 µm, N'/N	85 / 85	82 / 82			
≥ 450 - < 650 µm, N'/N	74 / 74	79 / 79			
≥ 650 µm, N'/N	20 / 20	19 / 19			
Pooled Analysis, N'/N	368 / 368	367 / 367			
< 450 µm, N'/N	192 / 192	178 / 178			
≥ 450 - < 650 µm, N'/N	144 / 144	150 / 150			
≥ 650 µm, N'/N	32 / 32	39 / 39			
Any adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	N.E.				
< 450 µm, n (%)	6 (5.6)	1 (1.0)	5.64 [0.67; 47.75] 0.112	5.38 [0.66; 43.92] 0.116	0.05 [-0.00; 0.09] 0.063
≥ 450 - < 650 µm, n (%)	4 (5.7)	2 (2.8)	2.09 [0.37; 11.80] 0.404	2.03 [0.38; 10.72] 0.405	0.03 [-0.04; 0.10] 0.394
≥ 650 µm, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE					
Interaction Test:	N.E.				
< 450 µm, n (%)	5 (5.9)	4 (4.9)	1.22 [0.32; 4.71] 0.774	1.21 [0.34; 4.33] 0.774	0.01 [-0.06; 0.08] 0.773
≥ 450 - < 650 µm, n (%)	3 (4.1)	0 (0.0)	N.E.	7.47 [0.39; 142.14] 0.181	0.04 [-0.00; 0.09] 0.077
≥ 650 µm, n (%)	0 (0.0)	1 (5.3)	N.E.	0.32 [0.01; 7.35] 0.474	-0.05 [-0.15; 0.05] 0.304

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	N.E.				
< 450 µm, n (%)	11 (5.7)	5 (2.8)	2.66 [0.74; 9.53] 0.132	2.06 [0.73; 5.86] 0.163	0.03 [-0.01; 0.07] 0.155
≥ 450 - < 650 µm, n (%)	7 (4.9)	2 (1.3)	N.E.	3.09 [0.76; 12.63] 0.097	0.03 [-0.00; 0.07] 0.083
≥ 650 µm, n (%)	0 (0.0)	1 (2.6)	N.E.	0.32 [0.01; 7.35] 0.452	-0.03 [-0.08; 0.02] 0.279

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Headache / KESTREL, Week 100 / Headache / KITE: logit(proportion) = treatment [by CSFT].
Week 100 / Headache / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by CSFT].

Table 16-1.11 Any adverse event by SOC, PT and status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
presence, N'/N	62 / 62	61 / 61			
absence, N'/N	127 / 127	126 / 126			
KITE, N'/N	179 / 179	181 / 181			
presence, N'/N	56 / 56	67 / 67			
absence, N'/N	123 / 123	114 / 114			
Pooled Analysis, N'/N	368 / 368	368 / 368			
presence, N'/N	118 / 118	128 / 128			
absence, N'/N	250 / 250	240 / 240			
Any adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	p = 0.602				
presence, n (%)	5 (8.1)	1 (1.6)	5.26 [0.60; 46.44] 0.135	4.92 [0.59; 40.89] 0.140	0.06 [-0.01; 0.14] 0.093
absence, n (%)	5 (3.9)	2 (1.6)	2.54 [0.48; 13.35] 0.271	2.48 [0.49; 12.55] 0.272	0.02 [-0.02; 0.06] 0.253
KITE					
Interaction Test:	N.E.				
presence, n (%)	0 (0.0)	1 (1.5)	N.E.	0.40 [0.02; 9.57] 0.570	-0.01 [-0.04; 0.01] 0.314
absence, n (%)	8 (6.5)	4 (3.5)	1.91 [0.56; 6.53] 0.301	1.85 [0.57; 5.99] 0.302	0.03 [-0.03; 0.09] 0.287
Pooled Analysis					
Interaction Test:	p = 0.769				
presence, n (%)	5 (4.2)	2 (1.6)	2.94 [0.55; 15.74] 0.208	2.32 [0.51; 10.52] 0.260	0.02 [-0.02; 0.07] 0.242

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence, n (%)	13 (5.2)	6 (2.5)	2.20 [0.81; 5.98] 0.123	2.06 [0.80; 5.31] 0.127	0.03 [-0.01; 0.06] 0.123

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Headache / KITE: logit(proportion) = treatment [by status of SRF].

Table 16-1.13 Any adverse event by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Non-exposed, N'/N	12 / 12	13 / 13			
Exposed, N'/N	177 / 177	174 / 174			
KITE, N'/N	179 / 179	181 / 181			
Non-exposed, N'/N	17 / 17	12 / 12			
Exposed, N'/N	162 / 162	169 / 169			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Non-exposed, N'/N	29 / 29	25 / 25			
Exposed, N'/N	339 / 339	343 / 343			
Any adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Exposed, n (%)	10 (5.6)	3 (1.7)	3.41 [0.92; 12.62] 0.066	3.28 [0.92; 11.70] 0.068	0.04 [0.00; 0.08] 0.049 *
KITE					
Interaction Test:	p = 0.533				
Non-exposed, n (%)	1 (5.9)	1 (8.3)	0.69 [0.04; 12.20] 0.798	0.71 [0.05; 10.21] 0.798	-0.02 [-0.22; 0.17] 0.803
Exposed, n (%)	7 (4.3)	4 (2.4)	1.86 [0.53; 6.49] 0.328	1.83 [0.54; 6.12] 0.329	0.02 [-0.02; 0.06] 0.324
Pooled Analysis					
Interaction Test:	p = 0.478				
Non-exposed, n (%)	1 (3.4)	1 (4.0)	0.89 [0.05; 15.20] 0.939	0.71 [0.05; 10.21] 0.801	-0.01 [-0.11; 0.09] 0.801

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed, n (%)	17 (5.0)	7 (2.0)	2.62 [1.05; 6.55] 0.039 *	2.46 [1.03; 5.87] 0.036 *	0.03 [0.00; 0.06] 0.035 *

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Headache / KESTREL: logit(proportion) = treatment [by exposure (week 100)].

Table 16-2.1 Any ocular adverse event by SOC and PT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular adverse event by SOC and PT, week 100					
Eye disorders					
KESTREL, n (%)	115 (60.8)	108 (57.8)	1.14 [0.75; 1.72] 0.542	1.05 [0.89; 1.25] 0.542	0.03 [-0.07; 0.13] 0.541
KITE, n (%)	93 (52.0)	93 (51.4)	1.02 [0.68; 1.55] 0.913	1.01 [0.83; 1.23] 0.913	0.01 [-0.10; 0.11] 0.913
Pooled Analysis, n (%) p_H=0.724	208 (56.5)	201 (54.6)	1.08 [0.81; 1.45] 0.607	1.03 [0.91; 1.18] 0.611	0.02 [-0.05; 0.09] 0.610
Cataract					
KESTREL, n (%)	24 (12.7)	17 (9.1)	1.45 [0.75; 2.81] 0.264	1.40 [0.78; 2.51] 0.265	0.04 [-0.03; 0.10] 0.261
KITE, n (%)	16 (8.9)	25 (13.8)	0.61 [0.32; 1.19] 0.148	0.65 [0.36; 1.17] 0.150	-0.05 [-0.11; 0.02] 0.144
Pooled Analysis, n (%) p_H=0.070	40 (10.9)	42 (11.4)	0.95 [0.60; 1.52] 0.837	0.95 [0.63; 1.43] 0.816	-0.01 [-0.05; 0.04] 0.816
Diabetic retinal oedema					
KESTREL, n (%)	20 (10.6)	15 (8.0)	1.36 [0.67; 2.74] 0.394	1.32 [0.70; 2.50] 0.395	0.03 [-0.03; 0.08] 0.392
KITE, n (%)	20 (11.2)	19 (10.5)	1.07 [0.55; 2.09] 0.837	1.06 [0.59; 1.93] 0.837	0.01 [-0.06; 0.07] 0.837
Pooled Analysis, n (%) p_H=0.634	40 (10.9)	34 (9.2)	1.21 [0.75; 1.96] 0.442	1.18 [0.76; 1.82] 0.460	0.02 [-0.03; 0.06] 0.459
Conjunctival haemorrhage					
KESTREL, n (%)	19 (10.1)	22 (11.8)	0.84 [0.44; 1.61] 0.595	0.85 [0.48; 1.53] 0.595	-0.02 [-0.08; 0.05] 0.594
KITE, n (%)	10 (5.6)	12 (6.6)	0.83 [0.35; 1.98] 0.680	0.84 [0.37; 1.90] 0.680	-0.01 [-0.06; 0.04] 0.679

	Treatment Groups		Comparison		
Any ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, n (%) p_H=0.992	29 (7.9)	34 (9.2)	0.84 [0.49; 1.43] 0.514	0.85 [0.53; 1.36] 0.501	-0.01 [-0.05; 0.03] 0.500
Dry eye					
KESTREL, n (%)	7 (3.7)	6 (3.2)	1.16 [0.38; 3.52] 0.793	1.15 [0.40; 3.37] 0.793	0.00 [-0.03; 0.04] 0.793
KITE, n (%)	11 (6.1)	10 (5.5)	1.12 [0.46; 2.71] 0.802	1.11 [0.48; 2.55] 0.802	0.01 [-0.04; 0.05] 0.802
Pooled Analysis, n (%) p_H=0.961	18 (4.9)	16 (4.3)	1.14 [0.56; 2.32] 0.718	1.13 [0.58; 2.18] 0.719	0.01 [-0.02; 0.04] 0.719
Vitreous haemorrhage					
KESTREL, n (%)	9 (4.8)	8 (4.3)	1.12 [0.42; 2.96] 0.821	1.11 [0.44; 2.82] 0.821	0.00 [-0.04; 0.05] 0.821
KITE, n (%)	7 (3.9)	9 (5.0)	0.78 [0.28; 2.14] 0.626	0.79 [0.30; 2.07] 0.626	-0.01 [-0.05; 0.03] 0.625
Pooled Analysis, n (%) p_H=0.612	16 (4.3)	17 (4.6)	0.94 [0.46; 1.89] 0.854	0.94 [0.48; 1.83] 0.859	-0.00 [-0.03; 0.03] 0.858
Visual acuity reduced					
KESTREL, n (%)	5 (2.6)	9 (4.8)	0.54 [0.18; 1.63] 0.274	0.55 [0.19; 1.61] 0.275	-0.02 [-0.06; 0.02] 0.267
KITE, n (%)	9 (5.0)	6 (3.3)	1.54 [0.54; 4.43] 0.419	1.52 [0.55; 4.17] 0.420	0.02 [-0.02; 0.06] 0.416
Pooled Analysis, n (%) p_H=0.177	14 (3.8)	15 (4.1)	0.90 [0.42; 1.94] 0.791	0.93 [0.46; 1.91] 0.851	-0.00 [-0.03; 0.03] 0.851
Vitreous floaters					
KESTREL, n (%)	11 (5.8)	9 (4.8)	1.22 [0.49; 3.02] 0.664	1.21 [0.51; 2.85] 0.664	0.01 [-0.04; 0.06] 0.663
KITE, n (%)	4 (2.2)	6 (3.3)	0.67 [0.18; 2.40] 0.536	0.67 [0.19; 2.35] 0.536	-0.01 [-0.04; 0.02] 0.532
Pooled Analysis, n (%) p_H=0.449	15 (4.1)	15 (4.1)	0.91 [0.42; 1.98] 0.809	1.00 [0.49; 2.01] 0.992	-0.00 [-0.03; 0.03] 0.992

	Treatment Groups		Comparison		
Any ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Diabetic retinopathy					
KESTREL, n (%)	8 (4.2)	10 (5.3)	0.78 [0.30; 2.03] 0.613	0.79 [0.32; 1.96] 0.614	-0.01 [-0.05; 0.03] 0.613
KITE, n (%)	5 (2.8)	2 (1.1)	2.57 [0.49; 13.43] 0.263	2.53 [0.50; 12.86] 0.264	0.02 [-0.01; 0.05] 0.246
Pooled Analysis, n (%) p_H=0.221	13 (3.5)	12 (3.3)	1.40 [0.55; 3.60] 0.483	1.08 [0.50; 2.33] 0.848	0.00 [-0.02; 0.03] 0.848
Eye pain					
KESTREL, n (%)	7 (3.7)	8 (4.3)	0.86 [0.31; 2.42] 0.776	0.87 [0.32; 2.34] 0.776	-0.01 [-0.05; 0.03] 0.776
KITE, n (%)	6 (3.4)	4 (2.2)	1.53 [0.43; 5.53] 0.513	1.52 [0.44; 5.28] 0.513	0.01 [-0.02; 0.05] 0.510
Pooled Analysis, n (%) p_H=0.491	13 (3.5)	12 (3.3)	1.14 [0.50; 2.60] 0.750	1.08 [0.50; 2.34] 0.843	0.00 [-0.02; 0.03] 0.843
Macular oedema					
KESTREL, n (%)	7 (3.7)	2 (1.1)	3.56 [0.73; 17.34] 0.117	3.46 [0.73; 16.45] 0.118	0.03 [-0.00; 0.06] 0.093
KITE, n (%)	6 (3.4)	5 (2.8)	1.22 [0.37; 4.07] 0.746	1.21 [0.38; 3.90] 0.746	0.01 [-0.03; 0.04] 0.745
Pooled Analysis, n (%) p_H=0.292	13 (3.5)	7 (1.9)	2.11 [0.77; 5.73] 0.145	1.86 [0.75; 4.62] 0.173	0.02 [-0.01; 0.04] 0.172
Vitreous detachment					
KESTREL, n (%)	13 (6.9)	7 (3.7)	1.90 [0.74; 4.87] 0.182	1.84 [0.75; 4.50] 0.183	0.03 [-0.01; 0.08] 0.174
KITE, n (%)	0 (0.0)	1 (0.6)	N.E.	0.34 [0.01; 8.22] 0.505	-0.01 [-0.02; 0.01] 0.316
Pooled Analysis, n (%) p_H=N.E.	13 (3.5)	8 (2.2)	N.E.	1.58 [0.68; 3.65] 0.284	0.01 [-0.01; 0.04] 0.272
Infections and infestations					
KESTREL, n (%)	11 (5.8)	8 (4.3)	1.38 [0.54; 3.52] 0.497	1.36 [0.56; 3.31] 0.497	0.02 [-0.03; 0.06] 0.494

	Treatment Groups		Comparison		
Any ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE, n (%)	12 (6.7)	5 (2.8)	2.53 [0.87; 7.33] 0.088	2.43 [0.87; 6.75] 0.089	0.04 [-0.00; 0.08] 0.077
Pooled Analysis, n (%) p_H=0.403	23 (6.3)	13 (3.5)	1.86 [0.92; 3.77] 0.085	1.77 [0.91; 3.44] 0.088	0.03 [-0.00; 0.06] 0.087
Conjunctivitis					
KESTREL, n (%)	7 (3.7)	4 (2.1)	1.76 [0.51; 6.11] 0.374	1.73 [0.52; 5.82] 0.375	0.02 [-0.02; 0.05] 0.367
KITE, n (%)	6 (3.4)	2 (1.1)	3.10 [0.62; 15.59] 0.169	3.03 [0.62; 14.83] 0.171	0.02 [-0.01; 0.05] 0.148
Pooled Analysis, n (%) p_H=0.586	13 (3.5)	6 (1.6)	2.32 [0.84; 6.41] 0.103	2.16 [0.83; 5.62] 0.105	0.02 [-0.00; 0.04] 0.104
Investigations					
KESTREL, n (%)	11 (5.8)	6 (3.2)	1.86 [0.67; 5.15] 0.230	1.81 [0.68; 4.80] 0.231	0.03 [-0.02; 0.07] 0.221
KITE, n (%)	6 (3.4)	7 (3.9)	0.86 [0.28; 2.62] 0.793	0.87 [0.30; 2.53] 0.793	-0.01 [-0.04; 0.03] 0.793
Pooled Analysis, n (%) p_H=0.315	17 (4.6)	13 (3.5)	1.28 [0.60; 2.71] 0.523	1.31 [0.64; 2.65] 0.458	0.01 [-0.02; 0.04] 0.458
Intraocular pressure increased					
KESTREL, n (%)	11 (5.8)	6 (3.2)	1.86 [0.67; 5.15] 0.230	1.81 [0.68; 4.80] 0.231	0.03 [-0.02; 0.07] 0.221
KITE, n (%)	6 (3.4)	7 (3.9)	0.86 [0.28; 2.62] 0.793	0.87 [0.30; 2.53] 0.793	-0.01 [-0.04; 0.03] 0.793
Pooled Analysis, n (%) p_H=0.315	17 (4.6)	13 (3.5)	1.28 [0.60; 2.71] 0.523	1.31 [0.64; 2.65] 0.458	0.01 [-0.02; 0.04] 0.458
Injury, poisoning and procedural complications					
KESTREL, n (%)	5 (2.6)	10 (5.3)	0.48 [0.16; 1.44] 0.189	0.49 [0.17; 1.42] 0.191	-0.03 [-0.07; 0.01] 0.180
KITE, n (%)	2 (1.1)	5 (2.8)	0.40 [0.08; 2.08] 0.274	0.40 [0.08; 2.06] 0.275	-0.02 [-0.04; 0.01] 0.256

	Treatment Groups		Comparison		
Any ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, n (%) p_H=0.851	7 (1.9)	15 (4.1)	0.44 [0.16; 1.17] 0.100	0.46 [0.19; 1.13] 0.082	-0.02 [-0.05; 0.00] 0.081

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 16-2.2 Any ocular adverse event by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 16-2.3 Any ocular adverse event by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 16-2.4 Any ocular adverse event by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 16-2.5 Any ocular adverse event by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 16-2.6 Any ocular adverse event by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 16-2.7 Any ocular adverse event by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 16-2.8 Any ocular adverse event by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 16-2.9 Any ocular adverse event by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 16-2.10 Any ocular adverse event by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 16-2.11 Any ocular adverse event by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 16-2.13 Any ocular adverse event by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 16-3.1 Any ocular adverse event at the study eye by SOC and PT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular adverse event at the study eye by SOC and PT, week 100					
Eye disorders					
KESTREL, n (%)	86 (45.5)	86 (46.0)	0.98 [0.65; 1.47] 0.925	0.99 [0.79; 1.23] 0.925	-0.00 [-0.11; 0.10] 0.925
KITE, n (%)	63 (35.2)	67 (37.0)	0.92 [0.60; 1.42] 0.719	0.95 [0.72; 1.25] 0.719	-0.02 [-0.12; 0.08] 0.719
Pooled Analysis, n (%) p_H=0.844	149 (40.5)	153 (41.6)	0.95 [0.71; 1.28] 0.747	0.97 [0.82; 1.16] 0.753	-0.01 [-0.08; 0.06] 0.752
Cataract					
KESTREL, n (%)	16 (8.5)	13 (7.0)	1.24 [0.58; 2.65] 0.583	1.22 [0.60; 2.46] 0.583	0.02 [-0.04; 0.07] 0.582
KITE, n (%)	12 (6.7)	19 (10.5)	0.61 [0.29; 1.30] 0.203	0.64 [0.32; 1.28] 0.204	-0.04 [-0.10; 0.02] 0.198
Pooled Analysis, n (%) p_H=0.198	28 (7.6)	32 (8.7)	0.88 [0.51; 1.50] 0.631	0.88 [0.54; 1.42] 0.592	-0.01 [-0.05; 0.03] 0.592
Conjunctival haemorrhage					
KESTREL, n (%)	16 (8.5)	19 (10.2)	0.82 [0.41; 1.64] 0.572	0.83 [0.44; 1.57] 0.572	-0.02 [-0.08; 0.04] 0.572
KITE, n (%)	9 (5.0)	6 (3.3)	1.54 [0.54; 4.43] 0.419	1.52 [0.55; 4.17] 0.420	0.02 [-0.02; 0.06] 0.416
Pooled Analysis, n (%) p_H=0.325	25 (6.8)	25 (6.8)	1.12 [0.60; 2.09] 0.731	1.00 [0.58; 1.70] 0.988	-0.00 [-0.04; 0.04] 0.988
Dry eye					
KESTREL, n (%)	6 (3.2)	5 (2.7)	1.19 [0.36; 3.98] 0.774	1.19 [0.37; 3.82] 0.774	0.01 [-0.03; 0.04] 0.773
KITE, n (%)	9 (5.0)	9 (5.0)	1.01 [0.39; 2.61] 0.981	1.01 [0.41; 2.49] 0.981	0.00 [-0.04; 0.05] 0.981

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, n (%) p_H=0.833	15 (4.1)	14 (3.8)	1.10 [0.51; 2.38] 0.807	1.07 [0.53; 2.19] 0.844	0.00 [-0.03; 0.03] 0.843
Visual acuity reduced					
KESTREL, n (%)	3 (1.6)	9 (4.8)	0.32 [0.09; 1.20] 0.090	0.33 [0.09; 1.20] 0.092	-0.03 [-0.07; 0.00] 0.075
KITE, n (%)	6 (3.4)	6 (3.3)	1.01 [0.32; 3.20] 0.984	1.01 [0.33; 3.08] 0.984	0.00 [-0.04; 0.04] 0.984
Pooled Analysis, n (%) p_H=0.197	9 (2.4)	15 (4.1)	0.56 [0.23; 1.35] 0.198	0.60 [0.27; 1.35] 0.214	-0.02 [-0.04; 0.01] 0.214
Vitreous floaters					
KESTREL, n (%)	10 (5.3)	6 (3.2)	1.69 [0.60; 4.73] 0.322	1.65 [0.61; 4.45] 0.323	0.02 [-0.02; 0.06] 0.316
KITE, n (%)	4 (2.2)	4 (2.2)	1.01 [0.25; 4.11] 0.987	1.01 [0.26; 3.98] 0.987	0.00 [-0.03; 0.03] 0.987
Pooled Analysis, n (%) p_H=0.565	14 (3.8)	10 (2.7)	1.31 [0.55; 3.12] 0.538	1.40 [0.63; 3.10] 0.411	0.01 [-0.01; 0.04] 0.410
Eye pain					
KESTREL, n (%)	6 (3.2)	5 (2.7)	1.19 [0.36; 3.98] 0.774	1.19 [0.37; 3.82] 0.774	0.01 [-0.03; 0.04] 0.773
KITE, n (%)	6 (3.4)	4 (2.2)	1.53 [0.43; 5.53] 0.513	1.52 [0.44; 5.28] 0.513	0.01 [-0.02; 0.05] 0.510
Pooled Analysis, n (%) p_H=0.780	12 (3.3)	9 (2.4)	1.35 [0.56; 3.25] 0.504	1.33 [0.57; 3.12] 0.508	0.01 [-0.02; 0.03] 0.507
Diabetic retinal oedema					
KESTREL, n (%)	9 (4.8)	4 (2.1)	2.29 [0.69; 7.56] 0.175	2.23 [0.70; 7.10] 0.176	0.03 [-0.01; 0.06] 0.162
KITE, n (%)	2 (1.1)	3 (1.7)	0.67 [0.11; 4.06] 0.664	0.67 [0.11; 3.99] 0.664	-0.01 [-0.03; 0.02] 0.661
Pooled Analysis, n (%) p_H=0.266	11 (3.0)	7 (1.9)	1.25 [0.43; 3.67] 0.680	1.57 [0.61; 3.99] 0.344	0.01 [-0.01; 0.03] 0.344

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Vitreous detachment					
KESTREL, n (%)	10 (5.3)	3 (1.6)	3.43 [0.93; 12.65] 0.065	3.30 [0.92; 11.79] 0.066	0.04 [0.00; 0.07] 0.049 *
KITE, n (%)	0 (0.0)	1 (0.6)	N.E.	0.34 [0.01; 8.22] 0.505	-0.01 [-0.02; 0.01] 0.316
Pooled Analysis, n (%) p_H=N.E.	10 (2.7)	4 (1.1)	N.E.	2.32 [0.78; 6.92] 0.120	0.02 [-0.00; 0.04] 0.107
Infections and infestations					
KESTREL, n (%)	9 (4.8)	4 (2.1)	2.29 [0.69; 7.56] 0.175	2.23 [0.70; 7.10] 0.176	0.03 [-0.01; 0.06] 0.162
KITE, n (%)	11 (6.1)	4 (2.2)	2.90 [0.90; 9.28] 0.073	2.78 [0.90; 8.57] 0.075	0.04 [-0.00; 0.08] 0.061
Pooled Analysis, n (%) p_H=0.781	20 (5.4)	8 (2.2)	2.57 [1.11; 5.92] 0.027 *	2.50 [1.12; 5.61] 0.021 *	0.03 [0.01; 0.06] 0.020 *
Conjunctivitis					
KESTREL, n (%)	6 (3.2)	1 (0.5)	6.10 [0.73; 51.15] 0.096	5.94 [0.72; 48.84] 0.098	0.03 [-0.00; 0.05] 0.056
KITE, n (%)	6 (3.4)	1 (0.6)	6.24 [0.74; 52.39] 0.092	6.07 [0.74; 49.89] 0.094	0.03 [-0.00; 0.06] 0.054
Pooled Analysis, n (%) p_H=0.988	12 (3.3)	2 (0.5)	6.17 [1.37; 27.77] 0.018 *	6.00 [1.35; 26.63] 0.007 *	0.03 [0.01; 0.05] 0.007 *
Investigations					
KESTREL, n (%)	11 (5.8)	3 (1.6)	3.79 [1.04; 13.81] 0.043 *	3.63 [1.03; 12.80] 0.045 *	0.04 [0.00; 0.08] 0.029 *
KITE, n (%)	6 (3.4)	4 (2.2)	1.53 [0.43; 5.53] 0.513	1.52 [0.44; 5.28] 0.513	0.01 [-0.02; 0.05] 0.510
Pooled Analysis, n (%) p_H=0.331	17 (4.6)	7 (1.9)	2.43 [0.98; 6.05] 0.056	2.43 [1.02; 5.79] 0.039 *	0.03 [0.00; 0.05] 0.038 *
Intraocular pressure increased					
KESTREL, n (%)	11 (5.8)	3 (1.6)	3.79 [1.04; 13.81] 0.043 *	3.63 [1.03; 12.80] 0.045 *	0.04 [0.00; 0.08] 0.029 *

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE, n (%)	6 (3.4)	4 (2.2)	1.53 [0.43; 5.53] 0.513	1.52 [0.44; 5.28] 0.513	0.01 [-0.02; 0.05] 0.510
Pooled Analysis, n (%) p_H=0.331	17 (4.6)	7 (1.9)	2.43 [0.98; 6.05] 0.056	2.43 [1.02; 5.79] 0.039 *	0.03 [0.00; 0.05] 0.038 *
Injury, poisoning and procedural complications					
KESTREL, n (%)	3 (1.6)	6 (3.2)	0.49 [0.12; 1.97] 0.314	0.49 [0.13; 1.95] 0.314	-0.02 [-0.05; 0.01] 0.304
KITE, n (%)	2 (1.1)	4 (2.2)	0.50 [0.09; 2.76] 0.427	0.51 [0.09; 2.73] 0.428	-0.01 [-0.04; 0.02] 0.417
Pooled Analysis, n (%) p_H=0.981	5 (1.4)	10 (2.7)	0.49 [0.16; 1.48] 0.208	0.50 [0.17; 1.45] 0.191	-0.01 [-0.03; 0.01] 0.190

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 16-3.2 Any ocular adverse event at the study eye by SOC, PT and age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
< 65 years, N'/N	104 / 104	93 / 93			
≥ 65 years, N'/N	85 / 85	94 / 94			
KITE, N'/N	179 / 179	181 / 181			
< 65 years, N'/N	100 / 100	102 / 102			
≥ 65 years, N'/N	79 / 79	79 / 79			
Pooled Analysis, N'/N	368 / 368	368 / 368			
< 65 years, N'/N	204 / 204	195 / 195			
≥ 65 years, N'/N	164 / 164	173 / 173			
Any ocular adverse event at the study eye by SOC and PT, week 100					
Infections and infestations					
Test of heterogeneity in main analysis: **p_H=0.781**					
KESTREL					
Interaction Test:	p = 0.243				
< 65 years, n (%)	4 (3.8)	3 (3.2)	1.20 [0.26; 5.51] 0.815	1.19 [0.27; 5.19] 0.815	0.01 [-0.05; 0.06] 0.813
≥ 65 years, n (%)	5 (5.9)	1 (1.1)	5.81 [0.67; 50.79] 0.112	5.53 [0.66; 46.39] 0.115	0.05 [-0.01; 0.10] 0.081
KITE					
Interaction Test:	p = 0.316				
< 65 years, n (%)	6 (6.0)	1 (1.0)	6.45 [0.76; 54.54] 0.087	6.12 [0.75; 49.92] 0.091	0.05 [-0.00; 0.10] 0.051
≥ 65 years, n (%)	5 (6.3)	3 (3.8)	1.71 [0.39; 7.42] 0.473	1.67 [0.41; 6.74] 0.474	0.03 [-0.04; 0.09] 0.467
Pooled Analysis					
Interaction Test:	p = 0.899				
< 65 years, n (%)	10 (4.9)	4 (2.1)	2.44 [0.75; 7.95] 0.137	2.37 [0.76; 7.33] 0.123	0.03 [-0.01; 0.06] 0.120
≥ 65 years, n (%)	10 (6.1)	4 (2.3)	2.72 [0.84; 8.88] 0.096	2.60 [0.84; 8.05] 0.086	0.04 [-0.01; 0.08] 0.088

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Investigations					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	p = 0.939				
< 65 years, n (%)	8 (7.7)	2 (2.2)	3.79 [0.78; 18.33] 0.097	3.58 [0.78; 16.42] 0.101	0.06 [-0.00; 0.11] 0.066
≥ 65 years, n (%)	3 (3.5)	1 (1.1)	3.40 [0.35; 33.35] 0.293	3.32 [0.35; 31.29] 0.295	0.02 [-0.02; 0.07] 0.276
KITE					
Interaction Test:	p = 0.440				
< 65 years, n (%)	3 (3.0)	3 (2.9)	1.02 [0.20; 5.18] 0.980	1.02 [0.21; 4.93] 0.980	0.00 [-0.05; 0.05] 0.980
≥ 65 years, n (%)	3 (3.8)	1 (1.3)	3.08 [0.31; 30.24] 0.335	3.00 [0.32; 28.22] 0.337	0.03 [-0.02; 0.07] 0.310
Pooled Analysis					
Interaction Test:	p = 0.701				
< 65 years, n (%)	11 (5.4)	5 (2.6)	2.13 [0.71; 6.35] 0.177	2.08 [0.73; 5.96] 0.160	0.03 [-0.01; 0.07] 0.154
≥ 65 years, n (%)	6 (3.7)	2 (1.2)	3.11 [0.61; 15.75] 0.171	3.15 [0.65; 15.40] 0.134	0.02 [-0.01; 0.06] 0.136
Intraocular pressure increased					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	p = 0.939				
< 65 years, n (%)	8 (7.7)	2 (2.2)	3.79 [0.78; 18.33] 0.097	3.58 [0.78; 16.42] 0.101	0.06 [-0.00; 0.11] 0.066
≥ 65 years, n (%)	3 (3.5)	1 (1.1)	3.40 [0.35; 33.35] 0.293	3.32 [0.35; 31.29] 0.295	0.02 [-0.02; 0.07] 0.276
KITE					
Interaction Test:	p = 0.440				
< 65 years, n (%)	3 (3.0)	3 (2.9)	1.02 [0.20; 5.18] 0.980	1.02 [0.21; 4.93] 0.980	0.00 [-0.05; 0.05] 0.980

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years, n (%)	3 (3.8)	1 (1.3)	3.08 [0.31; 30.24] 0.335	3.00 [0.32; 28.22] 0.337	0.03 [-0.02; 0.07] 0.310
Pooled Analysis					
Interaction Test:	p = 0.701				
< 65 years, n (%)	11 (5.4)	5 (2.6)	2.13 [0.71; 6.35] 0.177	2.08 [0.73; 5.96] 0.160	0.03 [-0.01; 0.07] 0.154
≥ 65 years, n (%)	6 (3.7)	2 (1.2)	3.11 [0.61; 15.75] 0.171	3.15 [0.65; 15.40] 0.134	0.02 [-0.01; 0.06] 0.136

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 16-3.3 Any ocular adverse event at the study eye by SOC, PT and gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Male, N'/N	110 / 110	126 / 126			
Female, N'/N	79 / 79	61 / 61			
KITE, N'/N	179 / 179	181 / 181			
Male, N'/N	120 / 120	115 / 115			
Female, N'/N	59 / 59	66 / 66			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Male, N'/N	230 / 230	241 / 241			
Female, N'/N	138 / 138	127 / 127			
Any ocular adverse event at the study eye by SOC and PT, week 100					
Infections and infestations					
Test of heterogeneity in main analysis: **p_H=0.781**					
KESTREL					
Interaction Test:	p = 0.896				
Male, n (%)	4 (3.6)	2 (1.6)	2.34 [0.42; 13.02] 0.332	2.29 [0.43; 12.27] 0.333	0.02 [-0.02; 0.06] 0.330
Female, n (%)	5 (6.3)	2 (3.3)	1.99 [0.37; 10.64] 0.420	1.93 [0.39; 9.61] 0.422	0.03 [-0.04; 0.10] 0.392
KITE					
Interaction Test:	p = 0.844				
Male, n (%)	8 (6.7)	3 (2.6)	2.67 [0.69; 10.31] 0.155	2.56 [0.70; 9.40] 0.158	0.04 [-0.01; 0.09] 0.136
Female, n (%)	3 (5.1)	1 (1.5)	3.48 [0.35; 34.43] 0.286	3.36 [0.36; 31.39] 0.289	0.04 [-0.03; 0.10] 0.269
Pooled Analysis					
Interaction Test:	p = 0.994				
Male, n (%)	12 (5.2)	5 (2.1)	2.55 [0.88; 7.39] 0.084	2.46 [0.88; 6.87] 0.076	0.03 [-0.00; 0.06] 0.077
Female, n (%)	8 (5.8)	3 (2.4)	2.57 [0.67; 9.92] 0.171	2.35 [0.64; 8.57] 0.182	0.03 [-0.01; 0.08] 0.172

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Investigations					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	N.E.				
Male, n (%)	7 (6.4)	3 (2.4)	2.79 [0.70; 11.05] 0.145	2.67 [0.71; 10.09] 0.147	0.04 [-0.01; 0.09] 0.139
Female, n (%)	4 (5.1)	0 (0.0)	N.E.	6.98 [0.38; 127.13] 0.190	0.05 [0.00; 0.10] 0.040 *
KITE					
Interaction Test:	p = 0.818				
Male, n (%)	5 (4.2)	3 (2.6)	1.62 [0.38; 6.95] 0.514	1.60 [0.39; 6.53] 0.515	0.02 [-0.03; 0.06] 0.508
Female, n (%)	1 (1.7)	1 (1.5)	1.12 [0.07; 18.32] 0.936	1.12 [0.07; 17.49] 0.936	0.00 [-0.04; 0.05] 0.936
Pooled Analysis					
Interaction Test:	p = 0.540				
Male, n (%)	12 (5.2)	6 (2.5)	2.13 [0.78; 5.85] 0.142	2.11 [0.81; 5.50] 0.118	0.03 [-0.01; 0.06] 0.121
Female, n (%)	5 (3.6)	1 (0.8)	4.49 [0.51; 39.65] 0.176	3.31 [0.51; 21.39] 0.181	0.03 [-0.01; 0.06] 0.115
Intraocular pressure increased					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	N.E.				
Male, n (%)	7 (6.4)	3 (2.4)	2.79 [0.70; 11.05] 0.145	2.67 [0.71; 10.09] 0.147	0.04 [-0.01; 0.09] 0.139
Female, n (%)	4 (5.1)	0 (0.0)	N.E.	6.98 [0.38; 127.13] 0.190	0.05 [0.00; 0.10] 0.040 *
KITE					
Interaction Test:	p = 0.818				
Male, n (%)	5 (4.2)	3 (2.6)	1.62 [0.38; 6.95] 0.514	1.60 [0.39; 6.53] 0.515	0.02 [-0.03; 0.06] 0.508

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female, n (%)	1 (1.7)	1 (1.5)	1.12 [0.07; 18.32] 0.936	1.12 [0.07; 17.49] 0.936	0.00 [-0.04; 0.05] 0.936
Pooled Analysis					
Interaction Test:	p = 0.540				
Male, n (%)	12 (5.2)	6 (2.5)	2.13 [0.78; 5.85] 0.142	2.11 [0.81; 5.50] 0.118	0.03 [-0.01; 0.06] 0.121
Female, n (%)	5 (3.6)	1 (0.8)	4.49 [0.51; 39.65] 0.176	3.31 [0.51; 21.39] 0.181	0.03 [-0.01; 0.06] 0.115

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Investigations / KESTREL, Week 100 / Intraocular pressure increased / KESTREL: logit(proportion) = treatment [by gender].

Table 16-3.4 Any ocular adverse event at the study eye by SOC, PT and BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
≤ 65 letters, N'/N	74 / 74	64 / 64			
> 65 letters, N'/N	115 / 115	123 / 123			
KITE, N'/N	179 / 179	181 / 181			
≤ 65 letters, N'/N	65 / 65	91 / 91			
> 65 letters, N'/N	114 / 114	90 / 90			
Pooled Analysis, N'/N	368 / 368	368 / 368			
≤ 65 letters, N'/N	139 / 139	155 / 155			
> 65 letters, N'/N	229 / 229	213 / 213			
Any ocular adverse event at the study eye by SOC and PT, week 100					
Infections and infestations					
Test of heterogeneity in main analysis: **p_H=0.781**					
KESTREL					
Interaction Test:	p = 0.614				
≤ 65 letters, n (%)	4 (5.4)	1 (1.6)	3.60 [0.39; 33.05] 0.258	3.46 [0.40; 30.17] 0.261	0.04 [-0.02; 0.10] 0.208
> 65 letters, n (%)	5 (4.3)	3 (2.4)	1.82 [0.42; 7.79] 0.420	1.78 [0.44; 7.29] 0.421	0.02 [-0.03; 0.07] 0.418
KITE					
Interaction Test:	p = 0.497				
≤ 65 letters, n (%)	6 (9.2)	2 (2.2)	4.53 [0.88; 23.18] 0.070	4.20 [0.88; 20.15] 0.073	0.07 [-0.01; 0.15] 0.072
> 65 letters, n (%)	5 (4.4)	2 (2.2)	2.02 [0.38; 10.65] 0.408	1.97 [0.39; 9.94] 0.410	0.02 [-0.03; 0.07] 0.381
Pooled Analysis					
Interaction Test:	p = 0.395				
≤ 65 letters, n (%)	10 (7.2)	3 (1.9)	3.95 [1.05; 14.80] 0.042 *	3.91 [1.10; 13.93] 0.023 *	0.06 [0.01; 0.10] 0.027 *
> 65 letters, n (%)	10 (4.4)	5 (2.3)	1.87 [0.63; 5.59] 0.262	1.87 [0.65; 5.40] 0.242	0.02 [-0.01; 0.05] 0.235

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Investigations					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	N.E.				
≤ 65 letters, n (%)	4 (5.4)	0 (0.0)	N.E.	7.80 [0.43; 142.16] 0.165	0.05 [0.00; 0.11] 0.040 *
> 65 letters, n (%)	7 (6.1)	3 (2.4)	2.59 [0.65; 10.28] 0.175	2.50 [0.66; 9.42] 0.177	0.04 [-0.02; 0.09] 0.165
KITE					
Interaction Test:	p = 0.231				
≤ 65 letters, n (%)	3 (4.6)	1 (1.1)	4.35 [0.44; 42.84] 0.207	4.20 [0.45; 39.48] 0.209	0.04 [-0.02; 0.09] 0.213
> 65 letters, n (%)	3 (2.6)	3 (3.3)	0.78 [0.15; 3.98] 0.769	0.79 [0.16; 3.82] 0.769	-0.01 [-0.05; 0.04] 0.771
Pooled Analysis					
Interaction Test:	p = 0.154				
≤ 65 letters, n (%)	7 (5.0)	1 (0.6)	8.44 [0.99; 71.68] 0.051	5.61 [0.94; 33.44] 0.032 *	0.04 [0.01; 0.08] 0.024 *
> 65 letters, n (%)	10 (4.4)	6 (2.8)	1.52 [0.54; 4.31] 0.431	1.58 [0.59; 4.20] 0.355	0.02 [-0.02; 0.05] 0.355
Intraocular pressure increased					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	N.E.				
≤ 65 letters, n (%)	4 (5.4)	0 (0.0)	N.E.	7.80 [0.43; 142.16] 0.165	0.05 [0.00; 0.11] 0.040 *
> 65 letters, n (%)	7 (6.1)	3 (2.4)	2.59 [0.65; 10.28] 0.175	2.50 [0.66; 9.42] 0.177	0.04 [-0.02; 0.09] 0.165
KITE					
Interaction Test:	p = 0.231				
≤ 65 letters, n (%)	3 (4.6)	1 (1.1)	4.35 [0.44; 42.84] 0.207	4.20 [0.45; 39.48] 0.209	0.04 [-0.02; 0.09] 0.213

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters, n (%)	3 (2.6)	3 (3.3)	0.78 [0.15; 3.98] 0.769	0.79 [0.16; 3.82] 0.769	-0.01 [-0.05; 0.04] 0.771
Pooled Analysis					
Interaction Test:	p = 0.154				
≤ 65 letters, n (%)	7 (5.0)	1 (0.6)	8.44 [0.99; 71.68] 0.051	5.61 [0.94; 33.44] 0.032 *	0.04 [0.01; 0.08] 0.024 *
> 65 letters, n (%)	10 (4.4)	6 (2.8)	1.52 [0.54; 4.31] 0.431	1.58 [0.59; 4.20] 0.355	0.02 [-0.02; 0.05] 0.355

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Investigations / KESTREL, Week 100 / Intraocular pressure increased / KESTREL: logit(proportion) = treatment [by BCVA].

Table 16-3.5 Any ocular adverse event at the study eye by SOC, PT and region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Region of the Americas, N'/N	90 / 90	83 / 83			
European Region, N'/N	69 / 69	75 / 75			
Western Pacific Region, N'/N	30 / 30	29 / 29			
KITE, N'/N	179 / 179	181 / 181			
South-East Asia Region and Eastern Mediterranean Region, N'/N	26 / 26	21 / 21			
European Region, N'/N	135 / 135	132 / 132			
Western Pacific Region, N'/N	18 / 18	28 / 28			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Region of the Americas, N'/N	90 / 90	83 / 83			
South-East Asia Region and Eastern Mediterranean Region, N'/N	26 / 26	21 / 21			
European Region, N'/N	204 / 204	207 / 207			
Western Pacific Region, N'/N	48 / 48	57 / 57			
Any ocular adverse event at the study eye by SOC and PT, week 100					
Infections and infestations					
Test of heterogeneity in main analysis: p_H=**0.781**					
KESTREL					
Interaction Test:	N.E.				
Region of the Americas, n (%)	5 (5.6)	2 (2.4)	2.38 [0.45; 12.63] 0.308	2.31 [0.46; 11.56] 0.310	0.03 [-0.03; 0.09] 0.285
European Region, n (%)	4 (5.8)	2 (2.7)	2.25 [0.40; 12.67] 0.359	2.17 [0.41; 11.50] 0.361	0.03 [-0.03; 0.10] 0.353
Western Pacific Region, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.745				
South-East Asia Region and Eastern Mediterranean Region, n (%)	4 (15.4)	1 (4.8)	3.64 [0.37; 35.32] 0.266	3.23 [0.39; 26.77] 0.277	0.11 [-0.06; 0.27] 0.210
European Region, n (%)	5 (3.7)	1 (0.8)	5.04 [0.58; 43.72] 0.142	4.89 [0.58; 41.29] 0.145	0.03 [-0.01; 0.06] 0.100
Western Pacific Region, n (%)	2 (11.1)	2 (7.1)	1.63 [0.21; 12.71] 0.644	1.56 [0.24; 10.08] 0.643	0.04 [-0.13; 0.21] 0.654
Pooled Analysis					
Interaction Test:	p = 0.883				
Region of the Americas, n (%)	5 (5.6)	2 (2.4)	2.42 [0.33; 17.84] 0.385	2.31 [0.46; 11.56] 0.296	0.03 [-0.03; 0.09] 0.285
South-East Asia Region and Eastern Mediterranean Region, n (%)	4 (15.4)	1 (4.8)	3.57 [0.28; 45.47] 0.327	3.23 [0.39; 26.77] 0.245	0.11 [-0.06; 0.27] 0.210
European Region, n (%)	9 (4.4)	3 (1.4)	3.11 [0.78; 12.37] 0.107	3.11 [0.85; 11.39] 0.070	0.03 [-0.00; 0.06] 0.069
Western Pacific Region, n (%)	2 (4.2)	2 (3.5)	1.21 [0.16; 8.98] 0.851	1.56 [0.24; 10.08] 0.645	0.02 [-0.06; 0.09] 0.651
Investigations					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	p = 0.713				
Region of the Americas, n (%)	2 (2.2)	1 (1.2)	1.86 [0.17; 20.94] 0.614	1.84 [0.17; 19.97] 0.614	0.01 [-0.03; 0.05] 0.604
European Region, n (%)	6 (8.7)	1 (1.3)	7.05 [0.83; 60.11] 0.074	6.52 [0.81; 52.81] 0.079	0.07 [0.00; 0.14] 0.043 *
Western Pacific Region, n (%)	3 (10.0)	1 (3.4)	3.11 [0.30; 31.79] 0.338	2.90 [0.32; 26.30] 0.344	0.07 [-0.06; 0.19] 0.309

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	N.E.				
South-East Asia Region and Eastern Mediterranean Region, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
European Region, n (%)	5 (3.7)	3 (2.3)	1.65 [0.39; 7.06] 0.497	1.63 [0.40; 6.68] 0.498	0.01 [-0.03; 0.06] 0.491
Western Pacific Region, n (%)	1 (5.6)	1 (3.6)	1.59 [0.09; 27.11] 0.749	1.56 [0.10; 23.33] 0.749	0.02 [-0.11; 0.15] 0.758
Pooled Analysis					
Interaction Test:	N.E.				
Region of the Americas, n (%)	2 (2.2)	1 (1.2)	N.E.	1.84 [0.17; 19.97] 0.610	0.01 [-0.03; 0.05] 0.604
South-East Asia Region and Eastern Mediterranean Region, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
European Region, n (%)	11 (5.4)	4 (1.9)	3.46 [0.94; 12.76] 0.062	2.80 [0.91; 8.60] 0.058	0.04 [-0.00; 0.07] 0.059
Western Pacific Region, n (%)	4 (8.3)	2 (3.5)	2.24 [0.36; 13.91] 0.387	2.32 [0.42; 12.62] 0.320	0.05 [-0.05; 0.14] 0.323
Intraocular pressure increased					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	p = 0.713				
Region of the Americas, n (%)	2 (2.2)	1 (1.2)	1.86 [0.17; 20.94] 0.614	1.84 [0.17; 19.97] 0.614	0.01 [-0.03; 0.05] 0.604
European Region, n (%)	6 (8.7)	1 (1.3)	7.05 [0.83; 60.11] 0.074	6.52 [0.81; 52.81] 0.079	0.07 [0.00; 0.14] 0.043 *
Western Pacific Region, n (%)	3 (10.0)	1 (3.4)	3.11 [0.30; 31.79] 0.338	2.90 [0.32; 26.30] 0.344	0.07 [-0.06; 0.19] 0.309

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	N.E.				
South-East Asia Region and Eastern Mediterranean Region, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
European Region, n (%)	5 (3.7)	3 (2.3)	1.65 [0.39; 7.06] 0.497	1.63 [0.40; 6.68] 0.498	0.01 [-0.03; 0.06] 0.491
Western Pacific Region, n (%)	1 (5.6)	1 (3.6)	1.59 [0.09; 27.11] 0.749	1.56 [0.10; 23.33] 0.749	0.02 [-0.11; 0.15] 0.758
Pooled Analysis					
Interaction Test:	N.E.				
Region of the Americas, n (%)	2 (2.2)	1 (1.2)	N.E.	1.84 [0.17; 19.97] 0.610	0.01 [-0.03; 0.05] 0.604
South-East Asia Region and Eastern Mediterranean Region, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
European Region, n (%)	11 (5.4)	4 (1.9)	3.46 [0.94; 12.76] 0.062	2.80 [0.91; 8.60] 0.058	0.04 [-0.00; 0.07] 0.059

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Western Pacific Region, n (%)	4 (8.3)	2 (3.5)	2.24 [0.36; 13.91] 0.387	2.32 [0.42; 12.62] 0.320	0.05 [-0.05; 0.14] 0.323

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Infections and infestations / KESTREL, Week 100 / Investigations / KITE, Week 100 / Intraocular pressure increased / KITE: logit(proportion) = treatment [by region].
Week 100 / Investigations / Pooled Analysis, Week 100 / Intraocular pressure increased / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by region].

Table 16-3.6 Any ocular adverse event at the study eye by SOC, PT and diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Type 1, N'/N	12 / 12	6 / 6			
Type 2, N'/N	177 / 177	181 / 181			
KITE, N'/N	179 / 179	181 / 181			
Type 1, N'/N	19 / 19	7 / 7			
Type 2, N'/N	160 / 160	174 / 174			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Type 1, N'/N	31 / 31	13 / 13			
Type 2, N'/N	337 / 337	355 / 355			
Any ocular adverse event at the study eye by SOC and PT, week 100					
Infections and infestations					
Test of heterogeneity in main analysis: **p_H=0.781**					
KESTREL					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2, n (%)	9 (5.1)	4 (2.2)	2.37 [0.72; 7.84] 0.157	2.30 [0.72; 7.34] 0.159	0.03 [-0.01; 0.07] 0.147
KITE					
Interaction Test:	N.E.				
Type 1, n (%)	2 (10.5)	0 (0.0)	N.E.	2.00 [0.11; 37.22] 0.642	0.11 [-0.03; 0.24] 0.135
Type 2, n (%)	9 (5.6)	4 (2.3)	2.53 [0.76; 8.39] 0.128	2.45 [0.77; 7.79] 0.130	0.03 [-0.01; 0.08] 0.121
Pooled Analysis					
Interaction Test:	N.E.				
Type 1, n (%)	2 (6.5)	0 (0.0)	N.E.	2.00 [0.11; 37.22] 0.635	0.06 [-0.02; 0.14] 0.167
Type 2, n (%)	18 (5.3)	8 (2.3)	2.45 [1.05; 5.71] 0.038 *	2.37 [1.05; 5.38] 0.033 *	0.03 [0.00; 0.06] 0.034 *
Conjunctivitis					
Test of heterogeneity in main analysis: **p_H=0.988**					

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2, n (%)	6 (3.4)	1 (0.6)	6.32 [0.75; 53.00] 0.089	6.14 [0.75; 50.45] 0.091	0.03 [-0.00; 0.06] 0.053
KITE					
Interaction Test:	N.E.				
Type 1, n (%)	1 (5.3)	0 (0.0)	N.E.	1.20 [0.05; 26.47] 0.908	0.05 [-0.05; 0.15] 0.304
Type 2, n (%)	5 (3.1)	1 (0.6)	5.58 [0.64; 48.29] 0.118	5.44 [0.64; 46.04] 0.120	0.03 [-0.00; 0.05] 0.087
Pooled Analysis					
Interaction Test:	N.E.				
Type 1, n (%)	1 (3.2)	0 (0.0)	N.E.	1.20 [0.05; 26.47] 0.909	0.03 [-0.03; 0.09] 0.335
Type 2, n (%)	11 (3.3)	2 (0.6)	5.94 [1.31; 27.04] 0.021 *	5.79 [1.29; 25.96] 0.009 *	0.03 [0.01; 0.05] 0.010 *
Investigations					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2, n (%)	11 (6.2)	3 (1.7)	3.93 [1.08; 14.34] 0.038 *	3.75 [1.06; 13.21] 0.040 *	0.05 [0.01; 0.09] 0.026 *
KITE					
Interaction Test:	N.E.				
Type 1, n (%)	2 (10.5)	0 (0.0)	N.E.	2.00 [0.11; 37.22] 0.642	0.11 [-0.03; 0.24] 0.135
Type 2, n (%)	4 (2.5)	4 (2.3)	1.09 [0.27; 4.43] 0.904	1.09 [0.28; 4.28] 0.904	0.00 [-0.03; 0.03] 0.905

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	N.E.				
Type 1, n (%)	2 (6.5)	0 (0.0)	N.E.	2.00 [0.11; 37.22] 0.635	0.06 [-0.02; 0.14] 0.167
Type 2, n (%)	15 (4.5)	7 (2.0)	2.10 [0.81; 5.44] 0.128	2.25 [0.92; 5.48] 0.066	0.02 [-0.00; 0.05] 0.067
Intraocular pressure increased					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2, n (%)	11 (6.2)	3 (1.7)	3.93 [1.08; 14.34] 0.038 *	3.75 [1.06; 13.21] 0.040 *	0.05 [0.01; 0.09] 0.026 *
KITE					
Interaction Test:	N.E.				
Type 1, n (%)	2 (10.5)	0 (0.0)	N.E.	2.00 [0.11; 37.22] 0.642	0.11 [-0.03; 0.24] 0.135
Type 2, n (%)	4 (2.5)	4 (2.3)	1.09 [0.27; 4.43] 0.904	1.09 [0.28; 4.28] 0.904	0.00 [-0.03; 0.03] 0.905
Pooled Analysis					
Interaction Test:	N.E.				
Type 1, n (%)	2 (6.5)	0 (0.0)	N.E.	2.00 [0.11; 37.22] 0.635	0.06 [-0.02; 0.14] 0.167

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2, n (%)	15 (4.5)	7 (2.0)	2.10 [0.81; 5.44] 0.128	2.25 [0.92; 5.48] 0.066	0.02 [-0.00; 0.05] 0.067

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Infections and infestations / KESTREL, Week 100 / Infections and infestations / KITE, Week 100 / Conjunctivitis / KESTREL, Week 100 / Conjunctivitis / KITE, Week 100 / Investigations / KESTREL, Week 100 / Investigations / KITE, Week 100 / Intraocular pressure increased / KESTREL, Week 100 / Intraocular pressure increased / KITE: logit(proportion) = treatment [by diabetes type].
Week 100 / Infections and infestations / Pooled Analysis, Week 100 / Conjunctivitis / Pooled Analysis, Week 100 / Investigations / Pooled Analysis, Week 100 / Intraocular pressure increased / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 16-3.7 Any ocular adverse event at the study eye by SOC, PT and HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	188 / 188	187 / 187			
< 7.5 %, N'/N	76 / 76	107 / 107			
≥ 7.5 %, N'/N	112 / 112	80 / 80			
KITE, N'/N	179 / 179	181 / 181			
< 7.5 %, N'/N	82 / 82	96 / 96			
≥ 7.5 %, N'/N	97 / 97	85 / 85			
Pooled Analysis, N'/N	367 / 367	368 / 368			
< 7.5 %, N'/N	158 / 158	203 / 203			
≥ 7.5 %, N'/N	209 / 209	165 / 165			
Any ocular adverse event at the study eye by SOC and PT, week 100					
Infections and infestations					
Test of heterogeneity in main analysis: **p_H=0.781**					
KESTREL					
Interaction Test:	p = 0.701				
< 7.5 %, n (%)	4 (5.3)	2 (1.9)	2.92 [0.52; 16.35] 0.224	2.82 [0.53; 14.98] 0.225	0.03 [-0.02; 0.09] 0.238
≥ 7.5 %, n (%)	5 (4.5)	2 (2.5)	1.82 [0.34; 9.64] 0.480	1.79 [0.36; 8.97] 0.482	0.02 [-0.03; 0.07] 0.453
KITE					
Interaction Test:	p = 0.352				
< 7.5 %, n (%)	5 (6.1)	1 (1.0)	6.17 [0.71; 53.91] 0.100	5.85 [0.70; 49.10] 0.103	0.05 [-0.01; 0.11] 0.075
≥ 7.5 %, n (%)	6 (6.2)	3 (3.5)	1.80 [0.44; 7.44] 0.415	1.75 [0.45; 6.79] 0.417	0.03 [-0.04; 0.09] 0.401
Pooled Analysis					
Interaction Test:	p = 0.357				
< 7.5 %, n (%)	9 (5.7)	3 (1.5)	3.97 [1.05; 14.94] 0.042 *	3.90 [1.06; 14.36] 0.027 *	0.04 [0.00; 0.08] 0.037 *
≥ 7.5 %, n (%)	11 (5.3)	5 (3.0)	1.78 [0.60; 5.22] 0.296	1.77 [0.63; 4.99] 0.276	0.02 [-0.02; 0.06] 0.260

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Investigations					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	p = 0.667				
< 7.5 %, n (%)	7 (9.2)	2 (1.9)	5.33 [1.07; 26.40] 0.041 *	4.93 [1.05; 23.07] 0.043 *	0.07 [0.00; 0.14] 0.040 *
≥ 7.5 %, n (%)	4 (3.6)	1 (1.3)	2.93 [0.32; 26.68] 0.341	2.86 [0.33; 25.08] 0.344	0.02 [-0.02; 0.07] 0.280
KITE					
Interaction Test:	p = 0.630				
< 7.5 %, n (%)	2 (2.4)	1 (1.0)	2.37 [0.21; 26.68] 0.483	2.34 [0.22; 25.36] 0.484	0.01 [-0.03; 0.05] 0.483
≥ 7.5 %, n (%)	4 (4.1)	3 (3.5)	1.18 [0.26; 5.41] 0.835	1.17 [0.27; 5.07] 0.835	0.01 [-0.05; 0.06] 0.834
Pooled Analysis					
Interaction Test:	p = 0.305				
< 7.5 %, n (%)	9 (5.7)	3 (1.5)	3.96 [1.05; 14.99] 0.043 *	4.00 [1.11; 14.39] 0.021 *	0.04 [0.00; 0.08] 0.032 *
≥ 7.5 %, n (%)	8 (3.8)	4 (2.4)	1.54 [0.45; 5.32] 0.494	1.62 [0.49; 5.35] 0.425	0.01 [-0.02; 0.05] 0.409
Intraocular pressure increased					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	p = 0.667				
< 7.5 %, n (%)	7 (9.2)	2 (1.9)	5.33 [1.07; 26.40] 0.041 *	4.93 [1.05; 23.07] 0.043 *	0.07 [0.00; 0.14] 0.040 *
≥ 7.5 %, n (%)	4 (3.6)	1 (1.3)	2.93 [0.32; 26.68] 0.341	2.86 [0.33; 25.08] 0.344	0.02 [-0.02; 0.07] 0.280
KITE					
Interaction Test:	p = 0.630				
< 7.5 %, n (%)	2 (2.4)	1 (1.0)	2.37 [0.21; 26.68] 0.483	2.34 [0.22; 25.36] 0.484	0.01 [-0.03; 0.05] 0.483

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %, n (%)	4 (4.1)	3 (3.5)	1.18 [0.26; 5.41] 0.835	1.17 [0.27; 5.07] 0.835	0.01 [-0.05; 0.06] 0.834
Pooled Analysis					
Interaction Test:	p = 0.305				
< 7.5 %, n (%)	9 (5.7)	3 (1.5)	3.96 [1.05; 14.99] 0.043 *	4.00 [1.11; 14.39] 0.021 *	0.04 [0.00; 0.08] 0.032 *
≥ 7.5 %, n (%)	8 (3.8)	4 (2.4)	1.54 [0.45; 5.32] 0.494	1.62 [0.49; 5.35] 0.425	0.01 [-0.02; 0.05] 0.409

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 16-3.8 Any ocular adverse event at the study eye by SOC, PT and duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
≤ 3 months, N'/N	120 / 120	110 / 110			
> 3 - < 12 months, N'/N	30 / 30	39 / 39			
≥ 12 months, N'/N	39 / 39	38 / 38			
KITE, N'/N	179 / 179	181 / 181			
≤ 3 months, N'/N	85 / 85	92 / 92			
> 3 - < 12 months, N'/N	51 / 51	49 / 49			
≥ 12 months, N'/N	43 / 43	40 / 40			
Pooled Analysis, N'/N	368 / 368	368 / 368			
≤ 3 months, N'/N	205 / 205	202 / 202			
> 3 - < 12 months, N'/N	81 / 81	88 / 88			
≥ 12 months, N'/N	82 / 82	78 / 78			
Any ocular adverse event at the study eye by SOC and PT, week 100					
Infections and infestations					
Test of heterogeneity in main analysis: **p_H=0.781**					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months, n (%)	7 (5.8)	0 (0.0)	N.E.	13.76 [0.80; 238.15] 0.071	0.06 [0.02; 0.10] 0.006 *
> 3 - < 12 months, n (%)	1 (3.3)	3 (7.7)	0.41 [0.04; 4.19] 0.455	0.43 [0.05; 3.96] 0.459	-0.04 [-0.15; 0.06] 0.418
≥ 12 months, n (%)	1 (2.6)	1 (2.6)	0.97 [0.06; 16.15] 0.985	0.97 [0.06; 15.02] 0.985	-0.00 [-0.07; 0.07] 0.985
KITE					
Interaction Test:	N.E.				
≤ 3 months, n (%)	4 (4.7)	1 (1.1)	4.49 [0.49; 41.03] 0.183	4.33 [0.49; 37.97] 0.186	0.04 [-0.01; 0.09] 0.154
> 3 - < 12 months, n (%)	4 (7.8)	3 (6.1)	1.30 [0.28; 6.16] 0.737	1.28 [0.30; 5.43] 0.737	0.02 [-0.08; 0.12] 0.735
≥ 12 months, n (%)	3 (7.0)	0 (0.0)	N.E.	6.52 [0.35; 122.46] 0.210	0.07 [-0.01; 0.15] 0.073

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.084				
≤ 3 months, n (%)	11 (5.4)	1 (0.5)	11.64 [1.48; 91.29] 0.019 *	7.65 [1.38; 42.39] 0.006 *	0.05 [0.02; 0.08] 0.003 *
> 3 - < 12 months, n (%)	5 (6.2)	6 (6.8)	0.85 [0.25; 2.95] 0.803	0.89 [0.28; 2.88] 0.847	-0.01 [-0.08; 0.07] 0.845
≥ 12 months, n (%)	4 (4.9)	1 (1.3)	3.88 [0.42; 35.59] 0.230	2.85 [0.45; 17.88] 0.241	0.04 [-0.02; 0.09] 0.185
Investigations					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months, n (%)	7 (5.8)	3 (2.7)	2.21 [0.56; 8.77] 0.260	2.14 [0.57; 8.07] 0.262	0.03 [-0.02; 0.08] 0.240
> 3 - < 12 months, n (%)	2 (6.7)	0 (0.0)	N.E.	6.45 [0.32; 129.57] 0.223	0.07 [-0.02; 0.16] 0.143
≥ 12 months, n (%)	2 (5.1)	0 (0.0)	N.E.	4.88 [0.24; 98.32] 0.301	0.05 [-0.02; 0.12] 0.147
KITE					
Interaction Test:	p = 0.920				
≤ 3 months, n (%)	3 (3.5)	2 (2.2)	1.65 [0.27; 10.10] 0.590	1.62 [0.28; 9.48] 0.590	0.01 [-0.04; 0.06] 0.590
> 3 - < 12 months, n (%)	2 (3.9)	1 (2.0)	1.96 [0.17; 22.33] 0.588	1.92 [0.18; 20.52] 0.589	0.02 [-0.05; 0.09] 0.579
≥ 12 months, n (%)	1 (2.3)	1 (2.5)	0.93 [0.06; 15.36] 0.959	0.93 [0.06; 14.38] 0.959	-0.00 [-0.07; 0.06] 0.959
Pooled Analysis					
Interaction Test:	p = 0.730				
≤ 3 months, n (%)	10 (4.9)	5 (2.5)	1.87 [0.61; 5.70] 0.271	1.94 [0.67; 5.60] 0.210	0.02 [-0.01; 0.06] 0.207
> 3 - < 12 months, n (%)	4 (4.9)	1 (1.1)	4.94 [0.53; 45.75] 0.160	3.28 [0.55; 19.63] 0.168	0.04 [-0.01; 0.09] 0.159

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months, n (%)	3 (3.7)	1 (1.3)	2.94 [0.30; 29.23] 0.356	2.23 [0.34; 14.62] 0.393	0.02 [-0.02; 0.07] 0.332
Intraocular pressure increased					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months, n (%)	7 (5.8)	3 (2.7)	2.21 [0.56; 8.77] 0.260	2.14 [0.57; 8.07] 0.262	0.03 [-0.02; 0.08] 0.240
> 3 - < 12 months, n (%)	2 (6.7)	0 (0.0)	N.E.	6.45 [0.32; 129.57] 0.223	0.07 [-0.02; 0.16] 0.143
≥ 12 months, n (%)	2 (5.1)	0 (0.0)	N.E.	4.88 [0.24; 98.32] 0.301	0.05 [-0.02; 0.12] 0.147
KITE					
Interaction Test:	p = 0.920				
≤ 3 months, n (%)	3 (3.5)	2 (2.2)	1.65 [0.27; 10.10] 0.590	1.62 [0.28; 9.48] 0.590	0.01 [-0.04; 0.06] 0.590
> 3 - < 12 months, n (%)	2 (3.9)	1 (2.0)	1.96 [0.17; 22.33] 0.588	1.92 [0.18; 20.52] 0.589	0.02 [-0.05; 0.09] 0.579
≥ 12 months, n (%)	1 (2.3)	1 (2.5)	0.93 [0.06; 15.36] 0.959	0.93 [0.06; 14.38] 0.959	-0.00 [-0.07; 0.06] 0.959
Pooled Analysis					
Interaction Test:	p = 0.730				
≤ 3 months, n (%)	10 (4.9)	5 (2.5)	1.87 [0.61; 5.70] 0.271	1.94 [0.67; 5.60] 0.210	0.02 [-0.01; 0.06] 0.207
> 3 - < 12 months, n (%)	4 (4.9)	1 (1.1)	4.94 [0.53; 45.75] 0.160	3.28 [0.55; 19.63] 0.168	0.04 [-0.01; 0.09] 0.159

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months, n (%)	3 (3.7)	1 (1.3)	2.94 [0.30; 29.23] 0.356	2.23 [0.34; 14.62] 0.393	0.02 [-0.02; 0.07] 0.332

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Infections and infestations / KESTREL, Week 100 / Infections and infestations / KITE, Week 100 / Investigations / KESTREL, Week 100 / Intraocular pressure increased / KESTREL: logit(proportion) = treatment [by duration of DME].

Table 16-3.9 Any ocular adverse event at the study eye by SOC, PT and DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	186 / 186	182 / 182			
focal, N'/N	59 / 59	48 / 48			
diffuse, N'/N	127 / 127	134 / 134			
KITE, N'/N	178 / 178	175 / 175			
focal, N'/N	63 / 63	66 / 66			
diffuse, N'/N	115 / 115	109 / 109			
Pooled Analysis, N'/N	364 / 364	357 / 357			
focal, N'/N	122 / 122	114 / 114			
diffuse, N'/N	242 / 242	243 / 243			
Any ocular adverse event at the study eye by SOC and PT, week 100					
Infections and infestations					
Test of heterogeneity in main analysis: **p_H=0.781**					
KESTREL					
Interaction Test:	p = 0.286				
focal, n (%)	2 (3.4)	2 (4.2)	0.81 [0.11; 5.95] 0.833	0.81 [0.12; 5.56] 0.833	-0.01 [-0.08; 0.07] 0.835
diffuse, n (%)	6 (4.7)	2 (1.5)	3.27 [0.65; 16.52] 0.151	3.17 [0.65; 15.40] 0.153	0.03 [-0.01; 0.07] 0.134
KITE					
Interaction Test:	p = 0.884				
focal, n (%)	3 (4.8)	1 (1.5)	3.25 [0.33; 32.10] 0.313	3.14 [0.34; 29.42] 0.316	0.03 [-0.03; 0.09] 0.291
diffuse, n (%)	8 (7.0)	2 (1.8)	4.00 [0.83; 19.27] 0.084	3.79 [0.82; 17.46] 0.087	0.05 [-0.00; 0.10] 0.058
Pooled Analysis					
Interaction Test:	p = 0.341				
focal, n (%)	5 (4.1)	3 (2.6)	1.51 [0.35; 6.51] 0.579	1.53 [0.38; 6.10] 0.546	0.01 [-0.03; 0.06] 0.545
diffuse, n (%)	14 (5.8)	4 (1.6)	3.72 [1.19; 11.65] 0.024 *	3.49 [1.16; 10.46] 0.017 *	0.04 [0.01; 0.07] 0.016 *

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Conjunctivitis					
Test of heterogeneity in main analysis: **p_H=0.988**					
KESTREL					
Interaction Test:	N.E.				
focal, n (%)	1 (1.7)	1 (2.1)	0.81 [0.05; 13.30] 0.883	0.81 [0.05; 12.67] 0.883	-0.00 [-0.06; 0.05] 0.884
diffuse, n (%)	4 (3.1)	0 (0.0)	N.E.	9.49 [0.52; 174.55] 0.130	0.03 [0.00; 0.06] 0.042 *
KITE					
Interaction Test:	N.E.				
focal, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
diffuse, n (%)	6 (5.2)	1 (0.9)	5.94 [0.70; 50.21] 0.102	5.69 [0.70; 46.47] 0.105	0.04 [-0.00; 0.09] 0.058
Pooled Analysis					
Interaction Test:	p = 0.171				
focal, n (%)	1 (0.8)	1 (0.9)	0.91 [0.06; 14.94] 0.950	0.81 [0.05; 12.67] 0.883	-0.00 [-0.03; 0.02] 0.883
diffuse, n (%)	10 (4.1)	1 (0.4)	10.41 [1.31; 82.49] 0.027 *	6.91 [1.27; 37.67] 0.009 *	0.04 [0.01; 0.06] 0.006 *
Investigations					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	N.E.				
focal, n (%)	3 (5.1)	0 (0.0)	N.E.	5.72 [0.30; 108.03] 0.245	0.05 [-0.01; 0.11] 0.075
diffuse, n (%)	8 (6.3)	2 (1.5)	4.44 [0.92; 21.31] 0.063	4.22 [0.91; 19.50] 0.065	0.05 [0.00; 0.10] 0.045 *
KITE					
Interaction Test:	N.E.				
focal, n (%)	0 (0.0)	2 (3.0)	N.E.	0.21 [0.01; 4.28] 0.310	-0.03 [-0.07; 0.01] 0.151
diffuse, n (%)	6 (5.2)	2 (1.8)	2.94 [0.58; 14.91] 0.192	2.84 [0.59; 13.79] 0.194	0.03 [-0.01; 0.08] 0.166

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.441				
focal, n (%)	3 (2.5)	2 (1.8)	1.57 [0.24; 10.11] 0.635	1.22 [0.26; 5.76] 0.799	0.01 [-0.03; 0.04] 0.731
diffuse, n (%)	14 (5.8)	4 (1.6)	3.64 [1.14; 11.62] 0.029 *	3.51 [1.18; 10.50] 0.016 *	0.04 [0.01; 0.08] 0.015 *
Intraocular pressure increased					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	N.E.				
focal, n (%)	3 (5.1)	0 (0.0)	N.E.	5.72 [0.30; 108.03] 0.245	0.05 [-0.01; 0.11] 0.075
diffuse, n (%)	8 (6.3)	2 (1.5)	4.44 [0.92; 21.31] 0.063	4.22 [0.91; 19.50] 0.065	0.05 [0.00; 0.10] 0.045 *
KITE					
Interaction Test:	N.E.				
focal, n (%)	0 (0.0)	2 (3.0)	N.E.	0.21 [0.01; 4.28] 0.310	-0.03 [-0.07; 0.01] 0.151
diffuse, n (%)	6 (5.2)	2 (1.8)	2.94 [0.58; 14.91] 0.192	2.84 [0.59; 13.79] 0.194	0.03 [-0.01; 0.08] 0.166
Pooled Analysis					
Interaction Test:	p = 0.441				
focal, n (%)	3 (2.5)	2 (1.8)	1.57 [0.24; 10.11] 0.635	1.22 [0.26; 5.76] 0.799	0.01 [-0.03; 0.04] 0.731

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse, n (%)	14 (5.8)	4 (1.6)	3.64 [1.14; 11.62] 0.029 *	3.51 [1.18; 10.50] 0.016 *	0.04 [0.01; 0.08] 0.015 *

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Conjunctivitis / KESTREL, Week 100 / Conjunctivitis / KITE, Week 100 / Investigations / KESTREL, Week 100 / Investigations / KITE, Week 100 / Intraocular pressure increased / KESTREL, Week 100 / Intraocular pressure increased / KITE: logit(proportion) = treatment [by DME type].

Table 16-3.10 Any ocular adverse event at the study eye by SOC, PT and CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
< 450 µm, N'/N	107 / 107	96 / 96			
≥ 450 - < 650 µm, N'/N	70 / 70	71 / 71			
≥ 650 µm, N'/N	12 / 12	20 / 20			
KITE, N'/N	179 / 179	180 / 180			
< 450 µm, N'/N	85 / 85	82 / 82			
≥ 450 - < 650 µm, N'/N	74 / 74	79 / 79			
≥ 650 µm, N'/N	20 / 20	19 / 19			
Pooled Analysis, N'/N	368 / 368	367 / 367			
< 450 µm, N'/N	192 / 192	178 / 178			
≥ 450 - < 650 µm, N'/N	144 / 144	150 / 150			
≥ 650 µm, N'/N	32 / 32	39 / 39			
Any ocular adverse event at the study eye by SOC and PT, week 100					
Infections and infestations					
Test of heterogeneity in main analysis: **p_H=0.781**					
KESTREL					
Interaction Test:	N.E.				
< 450 µm, n (%)	7 (6.5)	4 (4.2)	1.61 [0.46; 5.68] 0.459	1.57 [0.47; 5.20] 0.460	0.02 [-0.04; 0.09] 0.450
≥ 450 - < 650 µm, n (%)	2 (2.9)	0 (0.0)	N.E.	5.07 [0.25; 103.76] 0.292	0.03 [-0.01; 0.07] 0.151
≥ 650 µm, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE					
Interaction Test:	N.E.				
< 450 µm, n (%)	3 (3.5)	2 (2.4)	1.46 [0.24; 8.99] 0.681	1.45 [0.25; 8.44] 0.681	0.01 [-0.04; 0.06] 0.678
≥ 450 - < 650 µm, n (%)	6 (8.1)	2 (2.5)	3.40 [0.66; 17.39] 0.142	3.20 [0.67; 15.37] 0.146	0.06 [-0.02; 0.13] 0.125
≥ 650 µm, n (%)	2 (10.0)	0 (0.0)	N.E.	4.76 [0.24; 93.19] 0.304	0.10 [-0.03; 0.23] 0.136

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	N.E.				
< 450 µm, n (%)	10 (5.2)	6 (3.4)	1.54 [0.51; 4.60] 0.443	1.53 [0.57; 4.12] 0.397	0.02 [-0.02; 0.06] 0.391
≥ 450 - < 650 µm, n (%)	8 (5.6)	2 (1.3)	N.E.	3.58 [0.89; 14.38] 0.053	0.04 [0.00; 0.08] 0.044 *
≥ 650 µm, n (%)	2 (6.3)	0 (0.0)	N.E.	4.76 [0.24; 93.19] 0.254	0.06 [-0.02; 0.14] 0.171
Investigations					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	N.E.				
< 450 µm, n (%)	6 (5.6)	2 (2.1)	2.79 [0.55; 14.17] 0.216	2.69 [0.56; 13.02] 0.218	0.04 [-0.02; 0.09] 0.185
≥ 450 - < 650 µm, n (%)	4 (5.7)	1 (1.4)	4.24 [0.46; 38.94] 0.201	4.06 [0.46; 35.40] 0.205	0.04 [-0.02; 0.10] 0.166
≥ 650 µm, n (%)	1 (8.3)	0 (0.0)	N.E.	4.85 [0.21; 110.30] 0.322	0.08 [-0.07; 0.24] 0.296
KITE					
Interaction Test:	N.E.				
< 450 µm, n (%)	2 (2.4)	4 (4.9)	0.47 [0.08; 2.64] 0.391	0.48 [0.09; 2.56] 0.392	-0.03 [-0.08; 0.03] 0.383
≥ 450 - < 650 µm, n (%)	3 (4.1)	0 (0.0)	N.E.	7.47 [0.39; 142.14] 0.181	0.04 [-0.00; 0.09] 0.077
≥ 650 µm, n (%)	1 (5.0)	0 (0.0)	N.E.	2.86 [0.12; 66.11] 0.512	0.05 [-0.05; 0.15] 0.305
Pooled Analysis					
Interaction Test:	N.E.				
< 450 µm, n (%)	8 (4.2)	6 (3.4)	1.17 [0.36; 3.81] 0.799	1.24 [0.43; 3.53] 0.692	0.01 [-0.03; 0.05] 0.689
≥ 450 - < 650 µm, n (%)	7 (4.9)	1 (0.7)	N.E.	5.17 [0.91; 29.32] 0.037 *	0.04 [0.00; 0.08] 0.029 *

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm, n (%)	2 (6.3)	0 (0.0)	N.E.	3.71 [0.41; 33.35] 0.213	0.06 [-0.02; 0.15] 0.140
Intraocular pressure increased					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	N.E.				
< 450 µm, n (%)	6 (5.6)	2 (2.1)	2.79 [0.55; 14.17] 0.216	2.69 [0.56; 13.02] 0.218	0.04 [-0.02; 0.09] 0.185
≥ 450 - < 650 µm, n (%)	4 (5.7)	1 (1.4)	4.24 [0.46; 38.94] 0.201	4.06 [0.46; 35.40] 0.205	0.04 [-0.02; 0.10] 0.166
≥ 650 µm, n (%)	1 (8.3)	0 (0.0)	N.E.	4.85 [0.21; 110.30] 0.322	0.08 [-0.07; 0.24] 0.296
KITE					
Interaction Test:	N.E.				
< 450 µm, n (%)	2 (2.4)	4 (4.9)	0.47 [0.08; 2.64] 0.391	0.48 [0.09; 2.56] 0.392	-0.03 [-0.08; 0.03] 0.383
≥ 450 - < 650 µm, n (%)	3 (4.1)	0 (0.0)	N.E.	7.47 [0.39; 142.14] 0.181	0.04 [-0.00; 0.09] 0.077
≥ 650 µm, n (%)	1 (5.0)	0 (0.0)	N.E.	2.86 [0.12; 66.11] 0.512	0.05 [-0.05; 0.15] 0.305
Pooled Analysis					
Interaction Test:	N.E.				
< 450 µm, n (%)	8 (4.2)	6 (3.4)	1.17 [0.36; 3.81] 0.799	1.24 [0.43; 3.53] 0.692	0.01 [-0.03; 0.05] 0.689
≥ 450 - < 650 µm, n (%)	7 (4.9)	1 (0.7)	N.E.	5.17 [0.91; 29.32] 0.037 *	0.04 [0.00; 0.08] 0.029 *

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm, n (%)	2 (6.3)	0 (0.0)	N.E.	3.71 [0.41; 33.35] 0.213	0.06 [-0.02; 0.15] 0.140

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Infections and infestations / KESTREL, Week 100 / Infections and infestations / KITE, Week 100 / Investigations / KESTREL, Week 100 / Investigations / KITE, Week 100 / Intraocular pressure increased / KESTREL, Week 100 / Intraocular pressure increased / KITE: logit(proportion) = treatment [by CSFT].
Week 100 / Infections and infestations / Pooled Analysis, Week 100 / Investigations / Pooled Analysis, Week 100 / Intraocular pressure increased / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by CSFT].

Table 16-3.11 Any ocular adverse event at the study eye by SOC, PT and status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
presence, N'/N	62 / 62	61 / 61			
absence, N'/N	127 / 127	126 / 126			
KITE, N'/N	179 / 179	181 / 181			
presence, N'/N	56 / 56	67 / 67			
absence, N'/N	123 / 123	114 / 114			
Pooled Analysis, N'/N	368 / 368	368 / 368			
presence, N'/N	118 / 118	128 / 128			
absence, N'/N	250 / 250	240 / 240			
Any ocular adverse event at the study eye by SOC and PT, week 100					
Infections and infestations					
Test of heterogeneity in main analysis: **p_H=0.781**					
KESTREL					
Interaction Test:	N.E.				
presence, n (%)	4 (6.5)	0 (0.0)	N.E.	8.86 [0.49; 161.07] 0.141	0.06 [0.00; 0.13] 0.039 *
absence, n (%)	5 (3.9)	4 (3.2)	1.25 [0.33; 4.77] 0.744	1.24 [0.34; 4.51] 0.744	0.01 [-0.04; 0.05] 0.743
KITE					
Interaction Test:	p = 0.453				
presence, n (%)	7 (12.5)	2 (3.0)	4.64 [0.92; 23.34] 0.062	4.19 [0.91; 19.36] 0.067	0.10 [-0.00; 0.19] 0.051
absence, n (%)	4 (3.3)	2 (1.8)	1.88 [0.34; 10.48] 0.470	1.85 [0.35; 9.93] 0.471	0.01 [-0.02; 0.05] 0.458
Pooled Analysis					
Interaction Test:	p = 0.113				
presence, n (%)	11 (9.3)	2 (1.6)	6.46 [1.40; 29.87] 0.017 *	5.20 [1.34; 20.12] 0.007 *	0.08 [0.02; 0.14] 0.006 *
absence, n (%)	9 (3.6)	6 (2.5)	1.44 [0.50; 4.12] 0.496	1.45 [0.52; 4.02] 0.474	0.01 [-0.02; 0.04] 0.471

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Investigations					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	N.E.				
presence, n (%)	3 (4.8)	0 (0.0)	N.E.	6.89 [0.36; 130.62] 0.199	0.05 [-0.01; 0.10] 0.076
absence, n (%)	8 (6.3)	3 (2.4)	2.76 [0.71; 10.64] 0.141	2.65 [0.72; 9.74] 0.144	0.04 [-0.01; 0.09] 0.124
KITE					
Interaction Test:	p = 0.868				
presence, n (%)	1 (1.8)	1 (1.5)	1.20 [0.07; 19.63] 0.898	1.20 [0.08; 18.70] 0.898	0.00 [-0.04; 0.05] 0.899
absence, n (%)	5 (4.1)	3 (2.6)	1.57 [0.37; 6.71] 0.545	1.54 [0.38; 6.32] 0.545	0.01 [-0.03; 0.06] 0.538
Pooled Analysis					
Interaction Test:	p = 0.548				
presence, n (%)	4 (3.4)	1 (0.8)	4.37 [0.48; 40.22] 0.193	3.22 [0.50; 20.99] 0.194	0.03 [-0.01; 0.06] 0.158
absence, n (%)	13 (5.2)	6 (2.5)	2.08 [0.77; 5.66] 0.150	2.09 [0.81; 5.39] 0.120	0.03 [-0.01; 0.06] 0.117
Intraocular pressure increased					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	N.E.				
presence, n (%)	3 (4.8)	0 (0.0)	N.E.	6.89 [0.36; 130.62] 0.199	0.05 [-0.01; 0.10] 0.076
absence, n (%)	8 (6.3)	3 (2.4)	2.76 [0.71; 10.64] 0.141	2.65 [0.72; 9.74] 0.144	0.04 [-0.01; 0.09] 0.124
KITE					
Interaction Test:	p = 0.868				
presence, n (%)	1 (1.8)	1 (1.5)	1.20 [0.07; 19.63] 0.898	1.20 [0.08; 18.70] 0.898	0.00 [-0.04; 0.05] 0.899

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence, n (%)	5 (4.1)	3 (2.6)	1.57 [0.37; 6.71] 0.545	1.54 [0.38; 6.32] 0.545	0.01 [-0.03; 0.06] 0.538
Pooled Analysis					
Interaction Test:	p = 0.548				
presence, n (%)	4 (3.4)	1 (0.8)	4.37 [0.48; 40.22] 0.193	3.22 [0.50; 20.99] 0.194	0.03 [-0.01; 0.06] 0.158
absence, n (%)	13 (5.2)	6 (2.5)	2.08 [0.77; 5.66] 0.150	2.09 [0.81; 5.39] 0.120	0.03 [-0.01; 0.06] 0.117

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Infections and infestations / KESTREL, Week 100 / Investigations / KESTREL, Week 100 / Intraocular pressure increased / KESTREL: logit(proportion) = treatment [by status of SRF].

Table 16-3.13 Any ocular adverse event at the study eye by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Non-exposed, N'/N	12 / 12	13 / 13			
Exposed, N'/N	177 / 177	174 / 174			
KITE, N'/N	179 / 179	181 / 181			
Non-exposed, N'/N	17 / 17	12 / 12			
Exposed, N'/N	162 / 162	169 / 169			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Non-exposed, N'/N	29 / 29	25 / 25			
Exposed, N'/N	339 / 339	343 / 343			
Any ocular adverse event at the study eye by SOC and PT, week 100					
Infections and infestations					
Test of heterogeneity in main analysis: **p_H=0.781**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed, n (%)	0 (0.0)	1 (7.7)	N.E.	0.36 [0.02; 8.05] 0.519	-0.08 [-0.22; 0.07] 0.298
Exposed, n (%)	9 (5.1)	3 (1.7)	3.05 [0.81; 11.47] 0.098	2.95 [0.81; 10.71] 0.100	0.03 [-0.00; 0.07] 0.081
KITE					
Interaction Test:	p = 0.301				
Non-exposed, n (%)	1 (5.9)	1 (8.3)	0.69 [0.04; 12.20] 0.798	0.71 [0.05; 10.21] 0.798	-0.02 [-0.22; 0.17] 0.803
Exposed, n (%)	10 (6.2)	3 (1.8)	3.64 [0.98; 13.48] 0.053	3.48 [0.97; 12.41] 0.055	0.04 [0.00; 0.09] 0.040 *
Pooled Analysis					
Interaction Test:	p = 0.114				
Non-exposed, n (%)	1 (3.4)	2 (8.0)	0.40 [0.03; 4.67] 0.462	0.51 [0.07; 3.82] 0.514	-0.05 [-0.17; 0.08] 0.439
Exposed, n (%)	19 (5.6)	6 (1.7)	3.32 [1.31; 8.43] 0.012 *	3.21 [1.30; 7.93] 0.007 *	0.04 [0.01; 0.07] 0.007 *

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Conjunctivitis					
Test of heterogeneity in main analysis: **p_H=0.988**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Exposed, n (%)	6 (3.4)	1 (0.6)	6.07 [0.72; 50.95] 0.097	5.90 [0.72; 48.49] 0.099	0.03 [-0.00; 0.06] 0.056
KITE					
Interaction Test:	N.E.				
Non-exposed, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Exposed, n (%)	6 (3.7)	1 (0.6)	6.46 [0.77; 54.27] 0.086	6.26 [0.76; 51.42] 0.088	0.03 [-0.00; 0.06] 0.051
Pooled Analysis					
Interaction Test:	N.E.				
Non-exposed, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Exposed, n (%)	12 (3.5)	2 (0.6)	6.26 [1.39; 28.19] 0.017 *	6.08 [1.37; 26.94] 0.007 *	0.03 [0.01; 0.05] 0.006 *
Investigations					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed, n (%)	1 (8.3)	0 (0.0)	N.E.	3.23 [0.14; 72.46] 0.460	0.08 [-0.07; 0.24] 0.296
Exposed, n (%)	10 (5.6)	3 (1.7)	3.41 [0.92; 12.62] 0.066	3.28 [0.92; 11.70] 0.068	0.04 [0.00; 0.08] 0.049 *
KITE					
Interaction Test:	N.E.				
Non-exposed, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Exposed, n (%)	6 (3.7)	4 (2.4)	1.59 [0.44; 5.73] 0.481	1.56 [0.45; 5.44] 0.481	0.01 [-0.02; 0.05] 0.479
Pooled Analysis					
Interaction Test:	N.E.				
Non-exposed, n (%)	1 (3.4)	0 (0.0)	N.E.	3.23 [0.14; 72.46] 0.438	0.04 [-0.03; 0.11] 0.279

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed, n (%)	16 (4.7)	7 (2.0)	2.34 [0.94; 5.87] 0.068	2.31 [0.96; 5.56] 0.054	0.03 [-0.00; 0.05] 0.053
Intraocular pressure increased					
Test of heterogeneity in main analysis: **p_H=0.331**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed, n (%)	1 (8.3)	0 (0.0)	N.E.	3.23 [0.14; 72.46] 0.460	0.08 [-0.07; 0.24] 0.296
Exposed, n (%)	10 (5.6)	3 (1.7)	3.41 [0.92; 12.62] 0.066	3.28 [0.92; 11.70] 0.068	0.04 [0.00; 0.08] 0.049 *
KITE					
Interaction Test:	N.E.				
Non-exposed, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Exposed, n (%)	6 (3.7)	4 (2.4)	1.59 [0.44; 5.73] 0.481	1.56 [0.45; 5.44] 0.481	0.01 [-0.02; 0.05] 0.479
Pooled Analysis					
Interaction Test:	N.E.				
Non-exposed, n (%)	1 (3.4)	0 (0.0)	N.E.	3.23 [0.14; 72.46] 0.438	0.04 [-0.03; 0.11] 0.279

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by SOC, PT and exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed, n (%)	16 (4.7)	7 (2.0)	2.34 [0.94; 5.87] 0.068	2.31 [0.96; 5.56] 0.054	0.03 [-0.00; 0.05] 0.053

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Infections and infestations / KESTREL, Week 100 / Conjunctivitis / KESTREL, Week 100 / Conjunctivitis / KITE, Week 100 / Investigations / KESTREL, Week 100 / Investigations / KITE, Week 100 / Intraocular pressure increased / KESTREL, Week 100 / Intraocular pressure increased / KITE: logit(proportion) = treatment [by exposure (week 100)].
Week 100 / Conjunctivitis / Pooled Analysis, Week 100 / Investigations / Pooled Analysis, Week 100 / Intraocular pressure increased / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by exposure (week 100)].

Table 16-4.1 Any ocular adverse event at the fellow eye by SOC and PT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular adverse event at the fellow eye by SOC and PT, week 100					
Eye disorders					
KESTREL, n (%)	84 (44.4)	67 (35.8)	1.43 [0.95; 2.17] 0.089	1.24 [0.97; 1.59] 0.090	0.09 [-0.01; 0.18] 0.087
KITE, n (%)	66 (36.9)	73 (40.3)	0.86 [0.57; 1.32] 0.500	0.91 [0.70; 1.19] 0.501	-0.03 [-0.14; 0.07] 0.500
Pooled Analysis, n (%) p_H=0.095	150 (40.8)	140 (38.0)	1.12 [0.83; 1.50] 0.460	1.07 [0.89; 1.28] 0.453	0.03 [-0.04; 0.10] 0.453
Diabetic retinal oedema					
KESTREL, n (%)	12 (6.3)	12 (6.4)	0.99 [0.43; 2.26] 0.979	0.99 [0.46; 2.15] 0.979	-0.00 [-0.05; 0.05] 0.979
KITE, n (%)	18 (10.1)	16 (8.8)	1.15 [0.57; 2.34] 0.693	1.14 [0.60; 2.16] 0.693	0.01 [-0.05; 0.07] 0.693
Pooled Analysis, n (%) p_H=0.782	30 (8.2)	28 (7.6)	1.07 [0.62; 1.84] 0.818	1.07 [0.66; 1.76] 0.778	0.01 [-0.03; 0.04] 0.778
Cataract					
KESTREL, n (%)	15 (7.9)	9 (4.8)	1.70 [0.73; 4.00] 0.220	1.65 [0.74; 3.67] 0.221	0.03 [-0.02; 0.08] 0.214
KITE, n (%)	11 (6.1)	16 (8.8)	0.68 [0.30; 1.50] 0.334	0.70 [0.33; 1.46] 0.335	-0.03 [-0.08; 0.03] 0.331
Pooled Analysis, n (%) p_H=0.120	26 (7.1)	25 (6.8)	1.08 [0.60; 1.94] 0.789	1.04 [0.61; 1.77] 0.882	0.00 [-0.03; 0.04] 0.882
Conjunctival haemorrhage					
KESTREL, n (%)	5 (2.6)	7 (3.7)	0.70 [0.22; 2.24] 0.547	0.71 [0.23; 2.19] 0.547	-0.01 [-0.05; 0.02] 0.545
KITE, n (%)	1 (0.6)	9 (5.0)	0.11 [0.01; 0.86] 0.035 *	0.11 [0.01; 0.88] 0.037 *	-0.04 [-0.08; -0.01] 0.010 *

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, n (%) p_H=0.123	6 (1.6)	16 (4.3)	0.28 [0.09; 0.91] 0.034 *	0.37 [0.15; 0.95] 0.030 *	-0.03 [-0.05; -0.00] 0.030 *
Dry eye					
KESTREL, n (%)	5 (2.6)	5 (2.7)	0.99 [0.28; 3.47] 0.986	0.99 [0.29; 3.36] 0.986	-0.00 [-0.03; 0.03] 0.986
KITE, n (%)	9 (5.0)	7 (3.9)	1.32 [0.48; 3.61] 0.594	1.30 [0.49; 3.42] 0.594	0.01 [-0.03; 0.05] 0.593
Pooled Analysis, n (%) p_H=0.729	14 (3.8)	12 (3.3)	1.14 [0.51; 2.56] 0.755	1.17 [0.55; 2.49] 0.684	0.01 [-0.02; 0.03] 0.684
Diabetic retinopathy					
KESTREL, n (%)	6 (3.2)	9 (4.8)	0.65 [0.23; 1.86] 0.420	0.66 [0.24; 1.82] 0.421	-0.02 [-0.06; 0.02] 0.417
KITE, n (%)	5 (2.8)	1 (0.6)	5.17 [0.60; 44.72] 0.135	5.06 [0.60; 42.85] 0.137	0.02 [-0.00; 0.05] 0.097
Pooled Analysis, n (%) p_H=0.090	11 (3.0)	10 (2.7)	1.79 [0.55; 5.87] 0.334	1.09 [0.47; 2.54] 0.833	0.00 [-0.02; 0.03] 0.833
Macular oedema					
KESTREL, n (%)	6 (3.2)	2 (1.1)	3.03 [0.60; 15.22] 0.178	2.97 [0.61; 14.52] 0.179	0.02 [-0.01; 0.05] 0.155
KITE, n (%)	5 (2.8)	3 (1.7)	1.70 [0.40; 7.24] 0.470	1.69 [0.41; 6.95] 0.470	0.01 [-0.02; 0.04] 0.465
Pooled Analysis, n (%) p_H=0.602	11 (3.0)	5 (1.4)	2.29 [0.77; 6.77] 0.135	2.20 [0.77; 6.28] 0.130	0.02 [-0.00; 0.04] 0.129
Vitreous haemorrhage					
KESTREL, n (%)	5 (2.6)	5 (2.7)	0.99 [0.28; 3.47] 0.986	0.99 [0.29; 3.36] 0.986	-0.00 [-0.03; 0.03] 0.986
KITE, n (%)	6 (3.4)	6 (3.3)	1.01 [0.32; 3.20] 0.984	1.01 [0.33; 3.08] 0.984	0.00 [-0.04; 0.04] 0.984
Pooled Analysis, n (%) p_H=0.979	11 (3.0)	11 (3.0)	1.00 [0.43; 2.35] 1.000	1.00 [0.44; 2.28] 0.998	0.00 [-0.02; 0.02] 0.998

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Infections and infestations					
KESTREL, n (%)	8 (4.2)	5 (2.7)	1.61 [0.52; 5.01] 0.412	1.58 [0.53; 4.75] 0.413	0.02 [-0.02; 0.05] 0.407
KITE, n (%)	5 (2.8)	2 (1.1)	2.57 [0.49; 13.43] 0.263	2.53 [0.50; 12.86] 0.264	0.02 [-0.01; 0.05] 0.246
Pooled Analysis, n (%) p_H=0.647	13 (3.5)	7 (1.9)	2.02 [0.75; 5.48] 0.165	1.85 [0.75; 4.58] 0.176	0.02 [-0.01; 0.04] 0.175
Conjunctivitis					
KESTREL, n (%)	6 (3.2)	4 (2.1)	1.50 [0.42; 5.40] 0.535	1.48 [0.43; 5.17] 0.536	0.01 [-0.02; 0.04] 0.532
KITE, n (%)	4 (2.2)	2 (1.1)	2.05 [0.37; 11.31] 0.412	2.02 [0.38; 10.90] 0.413	0.01 [-0.02; 0.04] 0.403
Pooled Analysis, n (%) p_H=0.776	10 (2.7)	6 (1.6)	1.75 [0.60; 5.05] 0.304	1.66 [0.61; 4.52] 0.315	0.01 [-0.01; 0.03] 0.314

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 16-4.2 Any ocular adverse event at the fellow eye by SOC, PT and age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
< 65 years, N'/N	104 / 104	93 / 93			
≥ 65 years, N'/N	85 / 85	94 / 94			
KITE, N'/N	179 / 179	181 / 181			
< 65 years, N'/N	100 / 100	102 / 102			
≥ 65 years, N'/N	79 / 79	79 / 79			
Pooled Analysis, N'/N	368 / 368	368 / 368			
< 65 years, N'/N	204 / 204	195 / 195			
≥ 65 years, N'/N	164 / 164	173 / 173			
Any ocular adverse event at the fellow eye by SOC and PT, week 100					
Conjunctival haemorrhage					
Test of heterogeneity in main analysis: **p_H=0.123**					
KESTREL					
Interaction Test:	N.E.				
< 65 years, n (%)	5 (4.8)	4 (4.3)	1.12 [0.29; 4.32] 0.865	1.12 [0.31; 4.04] 0.865	0.01 [-0.05; 0.06] 0.865
≥ 65 years, n (%)	0 (0.0)	3 (3.2)	N.E.	0.16 [0.01; 3.01] 0.220	-0.03 [-0.07; 0.00] 0.078
KITE					
Interaction Test:	N.E.				
< 65 years, n (%)	1 (1.0)	4 (3.9)	0.25 [0.03; 2.25] 0.215	0.26 [0.03; 2.24] 0.218	-0.03 [-0.07; 0.01] 0.177
≥ 65 years, n (%)	0 (0.0)	5 (6.3)	N.E.	0.09 [0.01; 1.62] 0.103	-0.06 [-0.12; -0.01] 0.021 *
Pooled Analysis					
Interaction Test:	N.E.				
< 65 years, n (%)	6 (2.9)	8 (4.1)	0.54 [0.15; 1.93] 0.339	0.70 [0.24; 2.00] 0.504	-0.01 [-0.05; 0.02] 0.504

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years, n (%)	0 (0.0)	8 (4.6)	N.E.	0.12 [0.01; 0.90] 0.012 *	-0.05 [-0.08; -0.02] 0.004 *

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Conjunctival haemorrhage / KESTREL, Week 100 / Conjunctival haemorrhage / KITE: logit(proportion) = treatment [by age].
Week 100 / Conjunctival haemorrhage / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by age].

Table 16-4.3 Any ocular adverse event at the fellow eye by SOC, PT and gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Male, N'/N	110 / 110	126 / 126			
Female, N'/N	79 / 79	61 / 61			
KITE, N'/N	179 / 179	181 / 181			
Male, N'/N	120 / 120	115 / 115			
Female, N'/N	59 / 59	66 / 66			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Male, N'/N	230 / 230	241 / 241			
Female, N'/N	138 / 138	127 / 127			
Any ocular adverse event at the fellow eye by SOC and PT, week 100					
Conjunctival haemorrhage					
Test of heterogeneity in main analysis: **p_H=0.123**					
KESTREL					
Interaction Test:	p = 0.660				
Male, n (%)	3 (2.7)	4 (3.2)	0.86 [0.19; 3.91] 0.840	0.86 [0.20; 3.75] 0.840	-0.00 [-0.05; 0.04] 0.839
Female, n (%)	2 (2.5)	3 (4.9)	0.50 [0.08; 3.10] 0.459	0.51 [0.09; 2.99] 0.459	-0.02 [-0.09; 0.04] 0.468
KITE					
Interaction Test:	N.E.				
Male, n (%)	0 (0.0)	7 (6.1)	N.E.	0.06 [0.00; 1.11] 0.059	-0.06 [-0.10; -0.02] 0.006 *
Female, n (%)	1 (1.7)	2 (3.0)	0.55 [0.05; 6.25] 0.631	0.56 [0.05; 6.01] 0.632	-0.01 [-0.07; 0.04] 0.621
Pooled Analysis					
Interaction Test:	p = 0.566				
Male, n (%)	3 (1.3)	11 (4.6)	0.22 [0.05; 0.94] 0.041 *	0.32 [0.10; 1.03] 0.044 *	-0.03 [-0.06; -0.00] 0.036 *

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female, n (%)	3 (2.2)	5 (3.9)	0.39 [0.08; 2.03] 0.266	0.53 [0.13; 2.18] 0.373	-0.02 [-0.06; 0.02] 0.378

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Conjunctival haemorrhage / KITE: logit(proportion) = treatment [by gender].

Table 16-4.4 Any ocular adverse event at the fellow eye by SOC, PT and BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
≤ 65 letters, N'/N	74 / 74	64 / 64			
> 65 letters, N'/N	115 / 115	123 / 123			
KITE, N'/N	179 / 179	181 / 181			
≤ 65 letters, N'/N	65 / 65	91 / 91			
> 65 letters, N'/N	114 / 114	90 / 90			
Pooled Analysis, N'/N	368 / 368	368 / 368			
≤ 65 letters, N'/N	139 / 139	155 / 155			
> 65 letters, N'/N	229 / 229	213 / 213			
Any ocular adverse event at the fellow eye by SOC and PT, week 100					
Conjunctival haemorrhage					
Test of heterogeneity in main analysis: **p_H=0.123**					
KESTREL					
Interaction Test:	N.E.				
≤ 65 letters, n (%)	3 (4.1)	0 (0.0)	N.E.	6.07 [0.32; 115.28] 0.230	0.04 [-0.00; 0.09] 0.077
> 65 letters, n (%)	2 (1.7)	7 (5.7)	0.29 [0.06; 1.44] 0.131	0.31 [0.06; 1.44] 0.134	-0.04 [-0.09; 0.01] 0.102
KITE					
Interaction Test:	N.E.				
≤ 65 letters, n (%)	0 (0.0)	5 (5.5)	N.E.	0.13 [0.01; 2.25] 0.159	-0.05 [-0.10; -0.01] 0.021 *
> 65 letters, n (%)	1 (0.9)	4 (4.4)	0.19 [0.02; 1.73] 0.141	0.20 [0.02; 1.74] 0.143	-0.04 [-0.08; 0.01] 0.128
Pooled Analysis					
Interaction Test:	p = 0.303				
≤ 65 letters, n (%)	3 (2.2)	5 (3.2)	0.52 [0.10; 2.64] 0.430	0.75 [0.19; 2.96] 0.674	-0.01 [-0.05; 0.03] 0.597

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters, n (%)	3 (1.3)	11 (5.2)	0.19 [0.04; 0.80] 0.024 *	0.26 [0.07; 0.92] 0.024 *	-0.04 [-0.07; -0.00] 0.026 *

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Conjunctival haemorrhage / KESTREL, Week 100 / Conjunctival haemorrhage / KITE: logit(proportion) = treatment [by BCVA].

Table 16-4.5 Any ocular adverse event at the fellow eye by SOC, PT and region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Region of the Americas, N'/N	90 / 90	83 / 83			
European Region, N'/N	69 / 69	75 / 75			
Western Pacific Region, N'/N	30 / 30	29 / 29			
KITE, N'/N	179 / 179	181 / 181			
South-East Asia Region and Eastern Mediterranean Region, N'/N	26 / 26	21 / 21			
European Region, N'/N	135 / 135	132 / 132			
Western Pacific Region, N'/N	18 / 18	28 / 28			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Region of the Americas, N'/N	90 / 90	83 / 83			
South-East Asia Region and Eastern Mediterranean Region, N'/N	26 / 26	21 / 21			
European Region, N'/N	204 / 204	207 / 207			
Western Pacific Region, N'/N	48 / 48	57 / 57			
Any ocular adverse event at the fellow eye by SOC and PT, week 100					
Conjunctival haemorrhage					
Test of heterogeneity in main analysis: **p_H=0.123**					
KESTREL					
Interaction Test:	N.E.				
Region of the Americas, n (%)	4 (4.4)	6 (7.2)	0.60 [0.16; 2.19] 0.437	0.61 [0.18; 2.10] 0.438	-0.03 [-0.10; 0.04] 0.436
European Region, n (%)	1 (1.4)	1 (1.3)	1.09 [0.07; 17.74] 0.953	1.09 [0.07; 17.04] 0.953	0.00 [-0.04; 0.04] 0.953
Western Pacific Region, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	N.E.				
South-East Asia Region and Eastern Mediterranean Region, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
European Region, n (%)	1 (0.7)	6 (4.5)	0.16 [0.02; 1.32] 0.088	0.16 [0.02; 1.34] 0.091	-0.04 [-0.08; 0.00] 0.052
Western Pacific Region, n (%)	0 (0.0)	3 (10.7)	N.E.	0.22 [0.01; 3.99] 0.304	-0.11 [-0.22; 0.01] 0.067
Pooled Analysis					
Interaction Test:	N.E.				
Region of the Americas, n (%)	4 (4.4)	6 (7.2)	N.E.	0.61 [0.18; 2.10] 0.434	-0.03 [-0.10; 0.04] 0.436
South-East Asia Region and Eastern Mediterranean Region, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
European Region, n (%)	2 (1.0)	7 (3.4)	0.42 [0.07; 2.46] 0.337	0.29 [0.06; 1.36] 0.093	-0.02 [-0.05; 0.00] 0.092
Western Pacific Region, n (%)	0 (0.0)	3 (5.3)	N.E.	0.22 [0.01; 3.99] 0.252	-0.05 [-0.10; 0.01] 0.103

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Conjunctival haemorrhage / KESTREL, Week 100 / Conjunctival haemorrhage / KITE: logit(proportion) = treatment [by region].
Week 100 / Conjunctival haemorrhage / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by region].

Table 16-4.6 Any ocular adverse event at the fellow eye by SOC, PT and diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Type 1, N'/N	12 / 12	6 / 6			
Type 2, N'/N	177 / 177	181 / 181			
KITE, N'/N	179 / 179	181 / 181			
Type 1, N'/N	19 / 19	7 / 7			
Type 2, N'/N	160 / 160	174 / 174			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Type 1, N'/N	31 / 31	13 / 13			
Type 2, N'/N	337 / 337	355 / 355			
Any ocular adverse event at the fellow eye by SOC and PT, week 100					
Conjunctival haemorrhage					
Test of heterogeneity in main analysis: **p_H=0.123**					
KESTREL					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2, n (%)	5 (2.8)	7 (3.9)	0.72 [0.22; 2.32] 0.585	0.73 [0.24; 2.26] 0.585	-0.01 [-0.05; 0.03] 0.583
KITE					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	1 (14.3)	N.E.	0.13 [0.01; 2.94] 0.202	-0.14 [-0.40; 0.12] 0.280
Type 2, n (%)	1 (0.6)	8 (4.6)	0.13 [0.02; 1.06] 0.056	0.14 [0.02; 1.07] 0.059	-0.04 [-0.07; -0.01] 0.020 *
Pooled Analysis					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	1 (7.7)	N.E.	0.13 [0.01; 2.94] 0.139	-0.08 [-0.23; 0.07] 0.287

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2, n (%)	6 (1.8)	15 (4.2)	0.31 [0.10; 1.02] 0.054	0.42 [0.16; 1.07] 0.060	-0.02 [-0.05; 0.00] 0.056

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Conjunctival haemorrhage / KESTREL, Week 100 / Conjunctival haemorrhage / KITE: logit(proportion) = treatment [by diabetes type].
Week 100 / Conjunctival haemorrhage / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 16-4.7 Any ocular adverse event at the fellow eye by SOC, PT and HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	188 / 188	187 / 187			
< 7.5 %, N'/N	76 / 76	107 / 107			
≥ 7.5 %, N'/N	112 / 112	80 / 80			
KITE, N'/N	179 / 179	181 / 181			
< 7.5 %, N'/N	82 / 82	96 / 96			
≥ 7.5 %, N'/N	97 / 97	85 / 85			
Pooled Analysis, N'/N	367 / 367	368 / 368			
< 7.5 %, N'/N	158 / 158	203 / 203			
≥ 7.5 %, N'/N	209 / 209	165 / 165			
Any ocular adverse event at the fellow eye by SOC and PT, week 100					
Conjunctival haemorrhage					
Test of heterogeneity in main analysis: **p_H=0.123**					
KESTREL					
Interaction Test:	N.E.				
< 7.5 %, n (%)	0 (0.0)	5 (4.7)	N.E.	0.13 [0.01; 2.27] 0.161	-0.05 [-0.09; -0.01] 0.022 *
≥ 7.5 %, n (%)	5 (4.5)	2 (2.5)	1.82 [0.34; 9.64] 0.480	1.79 [0.36; 8.97] 0.482	0.02 [-0.03; 0.07] 0.453
KITE					
Interaction Test:	N.E.				
< 7.5 %, n (%)	0 (0.0)	6 (6.3)	N.E.	0.09 [0.01; 1.57] 0.099	-0.06 [-0.11; -0.01] 0.011 *
≥ 7.5 %, n (%)	1 (1.0)	3 (3.5)	0.28 [0.03; 2.79] 0.281	0.29 [0.03; 2.76] 0.282	-0.02 [-0.07; 0.02] 0.267
Pooled Analysis					
Interaction Test:	N.E.				
< 7.5 %, n (%)	0 (0.0)	11 (5.4)	N.E.	0.11 [0.01; 0.80] 0.007 *	-0.05 [-0.09; -0.02] <.001 *

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %, n (%)	6 (2.9)	5 (3.0)	0.73 [0.18; 2.99] 0.666	0.92 [0.28; 3.05] 0.894	-0.00 [-0.04; 0.03] 0.894

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Conjunctival haemorrhage / KESTREL, Week 100 / Conjunctival haemorrhage / KITE: logit(proportion) = treatment [by HbA1c].
Week 100 / Conjunctival haemorrhage / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by HbA1c].

Table 16-4.8 Any ocular adverse event at the fellow eye by SOC, PT and duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
≤ 3 months, N'/N	120 / 120	110 / 110			
> 3 - < 12 months, N'/N	30 / 30	39 / 39			
≥ 12 months, N'/N	39 / 39	38 / 38			
KITE, N'/N	179 / 179	181 / 181			
≤ 3 months, N'/N	85 / 85	92 / 92			
> 3 - < 12 months, N'/N	51 / 51	49 / 49			
≥ 12 months, N'/N	43 / 43	40 / 40			
Pooled Analysis, N'/N	368 / 368	368 / 368			
≤ 3 months, N'/N	205 / 205	202 / 202			
> 3 - < 12 months, N'/N	81 / 81	88 / 88			
≥ 12 months, N'/N	82 / 82	78 / 78			
Any ocular adverse event at the fellow eye by SOC and PT, week 100					
Conjunctival haemorrhage					
Test of heterogeneity in main analysis: **p_H=0.123**					
KESTREL					
Interaction Test:	p = 0.832				
≤ 3 months, n (%)	3 (2.5)	5 (4.5)	0.54 [0.13; 2.31] 0.404	0.55 [0.13; 2.25] 0.405	-0.02 [-0.07; 0.03] 0.403
> 3 - < 12 months, n (%)	1 (3.3)	1 (2.6)	1.31 [0.08; 21.84] 0.851	1.30 [0.08; 19.95] 0.851	0.01 [-0.07; 0.09] 0.853
≥ 12 months, n (%)	1 (2.6)	1 (2.6)	0.97 [0.06; 16.15] 0.985	0.97 [0.06; 15.02] 0.985	-0.00 [-0.07; 0.07] 0.985
KITE					
Interaction Test:	N.E.				
≤ 3 months, n (%)	1 (1.2)	5 (5.4)	0.21 [0.02; 1.81] 0.155	0.22 [0.03; 1.82] 0.158	-0.04 [-0.09; 0.01] 0.106
> 3 - < 12 months, n (%)	0 (0.0)	4 (8.2)	N.E.	0.11 [0.01; 1.93] 0.130	-0.08 [-0.16; -0.00] 0.037 *
≥ 12 months, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.738				
≤ 3 months, n (%)	4 (2.0)	10 (5.0)	0.27 [0.07; 1.10] 0.067	0.39 [0.12; 1.24] 0.097	-0.03 [-0.07; 0.01] 0.095
> 3 - < 12 months, n (%)	1 (1.2)	5 (5.7)	0.20 [0.02; 1.86] 0.158	0.30 [0.05; 1.66] 0.139	-0.05 [-0.10; 0.01] 0.110
≥ 12 months, n (%)	1 (1.2)	1 (1.3)	0.78 [0.04; 13.68] 0.864	0.97 [0.06; 15.02] 0.985	-0.00 [-0.03; 0.03] 0.985

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Conjunctival haemorrhage / KITE: logit(proportion) = treatment [by duration of DME].

Table 16-4.9 Any ocular adverse event at the fellow eye by SOC, PT and DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	186 / 186	182 / 182			
focal, N'/N	59 / 59	48 / 48			
diffuse, N'/N	127 / 127	134 / 134			
KITE, N'/N	178 / 178	175 / 175			
focal, N'/N	63 / 63	66 / 66			
diffuse, N'/N	115 / 115	109 / 109			
Pooled Analysis, N'/N	364 / 364	357 / 357			
focal, N'/N	122 / 122	114 / 114			
diffuse, N'/N	242 / 242	243 / 243			
Any ocular adverse event at the fellow eye by SOC and PT, week 100					
Conjunctival haemorrhage					
Test of heterogeneity in main analysis: **p_H=0.123**					
KESTREL					
Interaction Test:	p = 0.597				
focal, n (%)	1 (1.7)	2 (4.2)	0.40 [0.03; 4.51] 0.456	0.41 [0.04; 4.35] 0.457	-0.02 [-0.09; 0.04] 0.459
diffuse, n (%)	4 (3.1)	5 (3.7)	0.84 [0.22; 3.20] 0.797	0.84 [0.23; 3.07] 0.797	-0.01 [-0.05; 0.04] 0.796
KITE					
Interaction Test:	N.E.				
focal, n (%)	1 (1.6)	5 (7.6)	0.20 [0.02; 1.73] 0.143	0.21 [0.03; 1.74] 0.148	-0.06 [-0.13; 0.01] 0.098
diffuse, n (%)	0 (0.0)	4 (3.7)	N.E.	0.11 [0.01; 1.93] 0.130	-0.04 [-0.07; -0.00] 0.042 *
Pooled Analysis					
Interaction Test:	p = 0.657				
focal, n (%)	2 (1.6)	7 (6.1)	0.21 [0.04; 1.16] 0.074	0.27 [0.06; 1.30] 0.079	-0.04 [-0.09; 0.01] 0.080

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse, n (%)	4 (1.7)	9 (3.7)	0.32 [0.08; 1.30] 0.112	0.48 [0.16; 1.45] 0.185	-0.02 [-0.05; 0.01] 0.172

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Conjunctival haemorrhage / KITE: logit(proportion) = treatment [by DME type].

Table 16-4.10 Any ocular adverse event at the fellow eye by SOC, PT and CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
< 450 µm, N'/N	107 / 107	96 / 96			
≥ 450 - < 650 µm, N'/N	70 / 70	71 / 71			
≥ 650 µm, N'/N	12 / 12	20 / 20			
KITE, N'/N	179 / 179	180 / 180			
< 450 µm, N'/N	85 / 85	82 / 82			
≥ 450 - < 650 µm, N'/N	74 / 74	79 / 79			
≥ 650 µm, N'/N	20 / 20	19 / 19			
Pooled Analysis, N'/N	368 / 368	367 / 367			
< 450 µm, N'/N	192 / 192	178 / 178			
≥ 450 - < 650 µm, N'/N	144 / 144	150 / 150			
≥ 650 µm, N'/N	32 / 32	39 / 39			
Any ocular adverse event at the fellow eye by SOC and PT, week 100					
Conjunctival haemorrhage					
Test of heterogeneity in main analysis: **p_H=0.123**					
KESTREL					
Interaction Test:	p = 0.575				
< 450 µm, n (%)	1 (0.9)	3 (3.1)	0.29 [0.03; 2.86] 0.291	0.30 [0.03; 2.83] 0.292	-0.02 [-0.06; 0.02] 0.275
≥ 450 - < 650 µm, n (%)	3 (4.3)	3 (4.2)	1.01 [0.20; 5.21] 0.986	1.01 [0.21; 4.86] 0.986	0.00 [-0.07; 0.07] 0.986
≥ 650 µm, n (%)	1 (8.3)	1 (5.0)	1.73 [0.10; 30.45] 0.709	1.67 [0.11; 24.26] 0.708	0.03 [-0.15; 0.22] 0.721
KITE					
Interaction Test:	N.E.				
< 450 µm, n (%)	1 (1.2)	6 (7.3)	0.15 [0.02; 1.28] 0.083	0.16 [0.02; 1.31] 0.087	-0.06 [-0.12; -0.00] 0.048 *
≥ 450 - < 650 µm, n (%)	0 (0.0)	3 (3.8)	N.E.	0.15 [0.01; 2.90] 0.211	-0.04 [-0.08; 0.00] 0.077
≥ 650 µm, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.371				
< 450 µm, n (%)	2 (1.0)	9 (5.1)	0.14 [0.02; 0.77] 0.024 *	0.21 [0.05; 0.95] 0.025 *	-0.04 [-0.07; -0.00] 0.027 *
≥ 450 - < 650 µm, n (%)	3 (2.1)	6 (4.0)	0.40 [0.08; 1.92] 0.250	0.56 [0.15; 2.01] 0.364	-0.02 [-0.06; 0.02] 0.328
≥ 650 µm, n (%)	1 (3.1)	1 (2.6)	1.13 [0.06; 19.94] 0.936	1.67 [0.11; 24.26] 0.711	0.01 [-0.06; 0.09] 0.717

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Conjunctival haemorrhage / KITE: logit(proportion) = treatment [by CSFT].

Table 16-4.11 Any ocular adverse event at the fellow eye by SOC, PT and status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
presence, N'/N	62 / 62	61 / 61			
absence, N'/N	127 / 127	126 / 126			
KITE, N'/N	179 / 179	181 / 181			
presence, N'/N	56 / 56	67 / 67			
absence, N'/N	123 / 123	114 / 114			
Pooled Analysis, N'/N	368 / 368	368 / 368			
presence, N'/N	118 / 118	128 / 128			
absence, N'/N	250 / 250	240 / 240			
Any ocular adverse event at the fellow eye by SOC and PT, week 100					
Conjunctival haemorrhage					
Test of heterogeneity in main analysis: **p_H=0.123**					
KESTREL					
Interaction Test:	p = 0.911				
presence, n (%)	2 (3.2)	3 (4.9)	0.64 [0.10; 4.00] 0.637	0.66 [0.11; 3.79] 0.637	-0.02 [-0.09; 0.05] 0.635
absence, n (%)	3 (2.4)	4 (3.2)	0.74 [0.16; 3.37] 0.695	0.74 [0.17; 3.26] 0.695	-0.01 [-0.05; 0.03] 0.694
KITE					
Interaction Test:	N.E.				
presence, n (%)	0 (0.0)	2 (3.0)	N.E.	0.24 [0.01; 4.87] 0.352	-0.03 [-0.07; 0.01] 0.151
absence, n (%)	1 (0.8)	7 (6.1)	0.13 [0.02; 1.03] 0.054	0.13 [0.02; 1.06] 0.057	-0.05 [-0.10; -0.01] 0.026 *
Pooled Analysis					
Interaction Test:	p = 0.833				
presence, n (%)	2 (1.7)	5 (3.9)	0.32 [0.05; 1.97] 0.221	0.48 [0.11; 2.11] 0.319	-0.02 [-0.06; 0.02] 0.260

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence, n (%)	4 (1.6)	11 (4.6)	0.26 [0.07; 1.00] 0.050	0.35 [0.11; 1.08] 0.055	-0.03 [-0.06; 0.00] 0.057

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Conjunctival haemorrhage / KITE: logit(proportion) = treatment [by status of SRF].

Table 16-4.13 Any ocular adverse event at the fellow eye by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Non-exposed, N'/N	12 / 12	13 / 13			
Exposed, N'/N	177 / 177	174 / 174			
KITE, N'/N	179 / 179	181 / 181			
Non-exposed, N'/N	17 / 17	12 / 12			
Exposed, N'/N	162 / 162	169 / 169			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Non-exposed, N'/N	29 / 29	25 / 25			
Exposed, N'/N	339 / 339	343 / 343			
Any ocular adverse event at the fellow eye by SOC and PT, week 100					
Conjunctival haemorrhage					
Test of heterogeneity in main analysis: **p_H=0.123**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Exposed, n (%)	5 (2.8)	7 (4.0)	0.69 [0.22; 2.23] 0.539	0.70 [0.23; 2.17] 0.539	-0.01 [-0.05; 0.03] 0.537
KITE					
Interaction Test:	N.E.				
Non-exposed, n (%)	1 (5.9)	0 (0.0)	N.E.	2.17 [0.10; 49.07] 0.627	0.06 [-0.05; 0.17] 0.303
Exposed, n (%)	0 (0.0)	9 (5.3)	N.E.	0.05 [0.00; 0.94] 0.045 *	-0.05 [-0.09; -0.02] 0.002 *
Pooled Analysis					
Interaction Test:	N.E.				
Non-exposed, n (%)	1 (3.4)	0 (0.0)	N.E.	2.17 [0.10; 49.07] 0.622	0.03 [-0.03; 0.09] 0.338

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by SOC, PT and exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed, n (%)	5 (1.5)	16 (4.7)	N.E.	0.33 [0.13; 0.87] 0.018 *	-0.03 [-0.06; -0.01] 0.015 *

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Conjunctival haemorrhage / KESTREL: logit(proportion) = treatment [by exposure (week 100)].

Table 16-5.1 Any non-ocular adverse event by SOC and PT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any non-ocular adverse event by SOC and PT, week 100					
Infections and infestations					
KESTREL, n (%)	80 (42.3)	73 (39.0)	1.15 [0.76; 1.73] 0.516	1.08 [0.85; 1.38] 0.516	0.03 [-0.07; 0.13] 0.516
KITE, n (%)	71 (39.7)	69 (38.1)	1.07 [0.70; 1.63] 0.764	1.04 [0.80; 1.35] 0.764	0.02 [-0.09; 0.12] 0.764
Pooled Analysis, n (%) p_H=0.813	151 (41.0)	142 (38.6)	1.11 [0.82; 1.49] 0.501	1.06 [0.89; 1.27] 0.500	0.02 [-0.05; 0.10] 0.499
Nasopharyngitis					
KESTREL, n (%)	18 (9.5)	16 (8.6)	1.12 [0.56; 2.28] 0.744	1.11 [0.59; 2.12] 0.744	0.01 [-0.05; 0.07] 0.743
KITE, n (%)	16 (8.9)	17 (9.4)	0.95 [0.46; 1.94] 0.881	0.95 [0.50; 1.82] 0.881	-0.00 [-0.06; 0.06] 0.881
Pooled Analysis, n (%) p_H=0.737	34 (9.2)	33 (9.0)	1.03 [0.63; 1.71] 0.897	1.03 [0.65; 1.63] 0.898	0.00 [-0.04; 0.04] 0.898
Urinary tract infection					
KESTREL, n (%)	21 (11.1)	8 (4.3)	2.80 [1.21; 6.49] 0.017 *	2.60 [1.18; 5.72] 0.018 *	0.07 [0.01; 0.12] 0.012 *
KITE, n (%)	5 (2.8)	6 (3.3)	0.84 [0.25; 2.80] 0.774	0.84 [0.26; 2.71] 0.774	-0.01 [-0.04; 0.03] 0.774
Pooled Analysis, n (%) p_H=0.108	26 (7.1)	14 (3.8)	1.55 [0.75; 3.22] 0.240	1.85 [0.98; 3.48] 0.052	0.03 [-0.00; 0.06] 0.052
COVID-19					
KESTREL, n (%)	10 (5.3)	8 (4.3)	1.25 [0.48; 3.24] 0.646	1.24 [0.50; 3.06] 0.646	0.01 [-0.03; 0.05] 0.645
KITE, n (%)	7 (3.9)	6 (3.3)	1.19 [0.39; 3.60] 0.762	1.18 [0.40; 3.44] 0.762	0.01 [-0.03; 0.04] 0.762

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, n (%) p_H=0.945	17 (4.6)	14 (3.8)	1.22 [0.59; 2.53] 0.595	1.21 [0.61; 2.42] 0.585	0.01 [-0.02; 0.04] 0.585
Influenza					
KESTREL, n (%)	8 (4.2)	7 (3.7)	1.14 [0.40; 3.20] 0.809	1.13 [0.42; 3.06] 0.809	0.00 [-0.03; 0.04] 0.808
KITE, n (%)	7 (3.9)	4 (2.2)	1.80 [0.52; 6.26] 0.355	1.77 [0.53; 5.94] 0.356	0.02 [-0.02; 0.05] 0.349
Pooled Analysis, n (%) p_H=0.578	15 (4.1)	11 (3.0)	1.42 [0.64; 3.19] 0.391	1.36 [0.63; 2.92] 0.427	0.01 [-0.02; 0.04] 0.426
Bronchitis					
KESTREL, n (%)	5 (2.6)	4 (2.1)	1.24 [0.33; 4.70] 0.748	1.24 [0.34; 4.53] 0.749	0.01 [-0.03; 0.04] 0.748
KITE, n (%)	7 (3.9)	5 (2.8)	1.43 [0.45; 4.60] 0.546	1.42 [0.46; 4.38] 0.546	0.01 [-0.03; 0.05] 0.544
Pooled Analysis, n (%) p_H=0.875	12 (3.3)	9 (2.4)	1.33 [0.55; 3.24] 0.526	1.34 [0.57; 3.13] 0.504	0.01 [-0.02; 0.03] 0.504
Pneumonia					
KESTREL, n (%)	6 (3.2)	5 (2.7)	1.19 [0.36; 3.98] 0.774	1.19 [0.37; 3.82] 0.774	0.01 [-0.03; 0.04] 0.773
KITE, n (%)	6 (3.4)	5 (2.8)	1.22 [0.37; 4.07] 0.746	1.21 [0.38; 3.90] 0.746	0.01 [-0.03; 0.04] 0.745
Pooled Analysis, n (%) p_H=0.979	12 (3.3)	10 (2.7)	1.21 [0.51; 2.83] 0.666	1.20 [0.53; 2.74] 0.665	0.01 [-0.02; 0.03] 0.665
Upper respiratory tract infection					
KESTREL, n (%)	5 (2.6)	5 (2.7)	0.99 [0.28; 3.47] 0.986	0.99 [0.29; 3.36] 0.986	-0.00 [-0.03; 0.03] 0.986
KITE, n (%)	5 (2.8)	3 (1.7)	1.70 [0.40; 7.24] 0.470	1.69 [0.41; 6.95] 0.470	0.01 [-0.02; 0.04] 0.465
Pooled Analysis, n (%) p_H=0.578	10 (2.7)	8 (2.2)	1.29 [0.50; 3.36] 0.600	1.25 [0.50; 3.13] 0.635	0.01 [-0.02; 0.03] 0.635

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Metabolism and nutrition disorders					
KESTREL, n (%)	47 (24.9)	36 (19.3)	1.39 [0.85; 2.27] 0.190	1.29 [0.88; 1.90] 0.192	0.06 [-0.03; 0.14] 0.188
KITE, n (%)	29 (16.2)	25 (13.8)	1.21 [0.68; 2.15] 0.526	1.17 [0.72; 1.92] 0.526	0.02 [-0.05; 0.10] 0.526
Pooled Analysis, n (%) p_H=0.717	76 (20.7)	61 (16.6)	1.30 [0.89; 1.89] 0.180	1.24 [0.92; 1.68] 0.158	0.04 [-0.02; 0.10] 0.157
Gastrointestinal disorders					
KESTREL, n (%)	32 (16.9)	29 (15.5)	1.11 [0.64; 1.92] 0.708	1.09 [0.69; 1.73] 0.708	0.01 [-0.06; 0.09] 0.708
KITE, n (%)	31 (17.3)	31 (17.1)	1.01 [0.59; 1.75] 0.962	1.01 [0.64; 1.59] 0.962	0.00 [-0.08; 0.08] 0.962
Pooled Analysis, n (%) p_H=0.817	63 (17.1)	60 (16.3)	1.06 [0.72; 1.56] 0.762	1.05 [0.76; 1.45] 0.766	0.01 [-0.05; 0.06] 0.765
Diarrhoea					
KESTREL, n (%)	10 (5.3)	6 (3.2)	1.69 [0.60; 4.73] 0.322	1.65 [0.61; 4.45] 0.323	0.02 [-0.02; 0.06] 0.316
KITE, n (%)	3 (1.7)	8 (4.4)	0.37 [0.10; 1.41] 0.145	0.38 [0.10; 1.41] 0.147	-0.03 [-0.06; 0.01] 0.128
Pooled Analysis, n (%) p_H=0.079	13 (3.5)	14 (3.8)	0.80 [0.34; 1.86] 0.605	0.93 [0.44; 1.95] 0.841	-0.00 [-0.03; 0.02] 0.841
Nausea					
KESTREL, n (%)	5 (2.6)	3 (1.6)	1.67 [0.39; 7.08] 0.489	1.65 [0.40; 6.80] 0.489	0.01 [-0.02; 0.04] 0.483
KITE, n (%)	5 (2.8)	5 (2.8)	1.01 [0.29; 3.56] 0.986	1.01 [0.30; 3.43] 0.986	0.00 [-0.03; 0.03] 0.986
Pooled Analysis, n (%) p_H=0.609	10 (2.7)	8 (2.2)	1.30 [0.50; 3.41] 0.587	1.25 [0.50; 3.14] 0.631	0.01 [-0.02; 0.03] 0.631
Vascular disorders					
KESTREL, n (%)	28 (14.8)	33 (17.6)	0.81 [0.47; 1.41] 0.457	0.84 [0.53; 1.33] 0.457	-0.03 [-0.10; 0.05] 0.456

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE, n (%)	28 (15.6)	30 (16.6)	0.93 [0.53; 1.64] 0.810	0.94 [0.59; 1.51] 0.810	-0.01 [-0.09; 0.07] 0.810
Pooled Analysis, n (%) p_H=0.728	56 (15.2)	63 (17.1)	0.87 [0.59; 1.29] 0.484	0.89 [0.64; 1.24] 0.484	-0.02 [-0.07; 0.03] 0.483
Hypertension					
KESTREL, n (%)	21 (11.1)	24 (12.8)	0.85 [0.45; 1.58] 0.607	0.87 [0.50; 1.50] 0.607	-0.02 [-0.08; 0.05] 0.607
KITE, n (%)	15 (8.4)	17 (9.4)	0.88 [0.43; 1.83] 0.736	0.89 [0.46; 1.73] 0.736	-0.01 [-0.07; 0.05] 0.736
Pooled Analysis, n (%) p_H=0.936	36 (9.8)	41 (11.1)	0.87 [0.54; 1.40] 0.552	0.88 [0.57; 1.34] 0.542	-0.01 [-0.06; 0.03] 0.542
Renal and urinary disorders					
KESTREL, n (%)	26 (13.8)	26 (13.9)	0.99 [0.55; 1.77] 0.967	0.99 [0.60; 1.64] 0.967	-0.00 [-0.07; 0.07] 0.967
KITE, n (%)	22 (12.3)	34 (18.8)	0.61 [0.34; 1.08] 0.091	0.65 [0.40; 1.07] 0.093	-0.06 [-0.14; 0.01] 0.088
Pooled Analysis, n (%) p_H=0.245	48 (13.0)	60 (16.3)	0.78 [0.51; 1.17] 0.232	0.80 [0.56; 1.14] 0.213	-0.03 [-0.08; 0.02] 0.212
Proteinuria					
KESTREL, n (%)	2 (1.1)	0 (0.0)	N.E.	4.95 [0.24; 102.36] 0.301	0.01 [-0.00; 0.03] 0.155
KITE, n (%)	6 (3.4)	13 (7.2)	0.45 [0.17; 1.21] 0.112	0.47 [0.18; 1.20] 0.114	-0.04 [-0.08; 0.01] 0.102
Pooled Analysis, n (%) p_H=N.E.	8 (2.2)	13 (3.5)	N.E.	0.63 [0.27; 1.47] 0.284	-0.01 [-0.04; 0.01] 0.273
Chronic kidney disease					
KESTREL, n (%)	7 (3.7)	7 (3.7)	0.99 [0.34; 2.88] 0.984	0.99 [0.35; 2.77] 0.984	-0.00 [-0.04; 0.04] 0.984
KITE, n (%)	4 (2.2)	6 (3.3)	0.67 [0.18; 2.40] 0.536	0.67 [0.19; 2.35] 0.536	-0.01 [-0.04; 0.02] 0.532
Pooled Analysis, n (%) p_H=0.643	11 (3.0)	13 (3.5)	0.82 [0.35; 1.87] 0.630	0.84 [0.38; 1.86] 0.676	-0.01 [-0.03; 0.02] 0.675

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Diabetic nephropathy					
KESTREL, n (%)	3 (1.6)	2 (1.1)	1.49 [0.25; 9.03] 0.663	1.48 [0.25; 8.78] 0.663	0.01 [-0.02; 0.03] 0.661
KITE, n (%)	6 (3.4)	9 (5.0)	0.66 [0.23; 1.90] 0.445	0.67 [0.25; 1.85] 0.445	-0.02 [-0.06; 0.03] 0.441
Pooled Analysis, n (%) p_H=0.446	9 (2.4)	11 (3.0)	1.00 [0.35; 2.88] 0.996	0.82 [0.35; 1.96] 0.659	-0.01 [-0.03; 0.02] 0.658
Nervous system disorders					
KESTREL, n (%)	24 (12.7)	29 (15.5)	0.79 [0.44; 1.42] 0.434	0.82 [0.50; 1.35] 0.435	-0.03 [-0.10; 0.04] 0.434
KITE, n (%)	29 (16.2)	28 (15.5)	1.06 [0.60; 1.86] 0.849	1.05 [0.65; 1.69] 0.849	0.01 [-0.07; 0.08] 0.849
Pooled Analysis, n (%) p_H=0.488	53 (14.4)	57 (15.5)	0.91 [0.61; 1.37] 0.659	0.93 [0.66; 1.31] 0.682	-0.01 [-0.06; 0.04] 0.682
Headache					
KESTREL, n (%)	10 (5.3)	3 (1.6)	3.43 [0.93; 12.65] 0.065	3.30 [0.92; 11.79] 0.066	0.04 [0.00; 0.07] 0.049 *
KITE, n (%)	8 (4.5)	5 (2.8)	1.65 [0.53; 5.13] 0.390	1.62 [0.54; 4.85] 0.390	0.02 [-0.02; 0.06] 0.386
Pooled Analysis, n (%) p_H=0.407	18 (4.9)	8 (2.2)	2.39 [1.00; 5.70] 0.049 *	2.25 [0.99; 5.12] 0.046 *	0.03 [0.00; 0.05] 0.045 *
Respiratory, thoracic and mediastinal disorders					
KESTREL, n (%)	30 (15.9)	28 (15.0)	1.07 [0.61; 1.88] 0.809	1.06 [0.66; 1.70] 0.809	0.01 [-0.06; 0.08] 0.809
KITE, n (%)	16 (8.9)	26 (14.4)	0.59 [0.30; 1.13] 0.112	0.62 [0.35; 1.12] 0.114	-0.05 [-0.12; 0.01] 0.107
Pooled Analysis, n (%) p_H=0.171	46 (12.5)	54 (14.7)	0.80 [0.52; 1.23] 0.302	0.85 [0.59; 1.23] 0.385	-0.02 [-0.07; 0.03] 0.384
Cough					
KESTREL, n (%)	11 (5.8)	10 (5.3)	1.09 [0.45; 2.64] 0.842	1.09 [0.47; 2.50] 0.842	0.00 [-0.04; 0.05] 0.842

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE, n (%)	5 (2.8)	10 (5.5)	0.49 [0.16; 1.47] 0.203	0.51 [0.18; 1.45] 0.204	-0.03 [-0.07; 0.01] 0.193
Pooled Analysis, n (%) p_H=0.264	16 (4.3)	20 (5.4)	0.74 [0.37; 1.49] 0.397	0.80 [0.42; 1.52] 0.492	-0.01 [-0.04; 0.02] 0.491
Musculoskeletal and connective tissue disorders					
KESTREL, n (%)	28 (14.8)	23 (12.3)	1.24 [0.69; 2.24] 0.477	1.20 [0.72; 2.01] 0.477	0.03 [-0.04; 0.09] 0.476
KITE, n (%)	25 (14.0)	25 (13.8)	1.01 [0.56; 1.84] 0.966	1.01 [0.60; 1.69] 0.966	0.00 [-0.07; 0.07] 0.966
Pooled Analysis, n (%) p_H=0.638	53 (14.4)	48 (13.0)	1.12 [0.74; 1.71] 0.589	1.10 [0.77; 1.59] 0.592	0.01 [-0.04; 0.06] 0.592
Arthralgia					
KESTREL, n (%)	6 (3.2)	5 (2.7)	1.19 [0.36; 3.98] 0.774	1.19 [0.37; 3.82] 0.774	0.01 [-0.03; 0.04] 0.773
KITE, n (%)	5 (2.8)	7 (3.9)	0.71 [0.22; 2.29] 0.572	0.72 [0.23; 2.23] 0.572	-0.01 [-0.05; 0.03] 0.570
Pooled Analysis, n (%) p_H=0.548	11 (3.0)	12 (3.3)	0.93 [0.40; 2.15] 0.861	0.92 [0.41; 2.05] 0.834	-0.00 [-0.03; 0.02] 0.834
Back pain					
KESTREL, n (%)	5 (2.6)	6 (3.2)	0.82 [0.25; 2.73] 0.746	0.82 [0.26; 2.66] 0.746	-0.01 [-0.04; 0.03] 0.746
KITE, n (%)	7 (3.9)	2 (1.1)	3.64 [0.75; 17.77] 0.110	3.54 [0.75; 16.81] 0.112	0.03 [-0.00; 0.06] 0.088
Pooled Analysis, n (%) p_H=0.142	12 (3.3)	8 (2.2)	1.70 [0.63; 4.58] 0.292	1.50 [0.62; 3.62] 0.366	0.01 [-0.01; 0.03] 0.366
Investigations					
KESTREL, n (%)	21 (11.1)	24 (12.8)	0.85 [0.45; 1.58] 0.607	0.87 [0.50; 1.50] 0.607	-0.02 [-0.08; 0.05] 0.607
KITE, n (%)	29 (16.2)	28 (15.5)	1.06 [0.60; 1.86] 0.849	1.05 [0.65; 1.69] 0.849	0.01 [-0.07; 0.08] 0.849
Pooled Analysis, n (%) p_H=0.611	50 (13.6)	52 (14.1)	0.95 [0.62; 1.44] 0.793	0.96 [0.67; 1.38] 0.837	-0.01 [-0.06; 0.04] 0.837

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
General disorders and administration site conditions					
KESTREL, n (%)	23 (12.2)	21 (11.2)	1.10 [0.58; 2.06] 0.777	1.08 [0.62; 1.89] 0.777	0.01 [-0.06; 0.07] 0.777
KITE, n (%)	26 (14.5)	26 (14.4)	1.01 [0.56; 1.82] 0.965	1.01 [0.61; 1.67] 0.965	0.00 [-0.07; 0.07] 0.965
Pooled Analysis, n (%) p_H=0.859	49 (13.3)	47 (12.8)	1.05 [0.68; 1.62] 0.811	1.04 [0.72; 1.52] 0.822	0.01 [-0.04; 0.05] 0.822
Pyrexia					
KESTREL, n (%)	8 (4.2)	4 (2.1)	2.02 [0.60; 6.83] 0.257	1.98 [0.61; 6.46] 0.258	0.02 [-0.01; 0.06] 0.247
KITE, n (%)	8 (4.5)	5 (2.8)	1.65 [0.53; 5.13] 0.390	1.62 [0.54; 4.85] 0.390	0.02 [-0.02; 0.06] 0.386
Pooled Analysis, n (%) p_H=0.809	16 (4.3)	9 (2.4)	1.83 [0.79; 4.21] 0.156	1.78 [0.80; 3.98] 0.154	0.02 [-0.01; 0.05] 0.153
Oedema peripheral					
KESTREL, n (%)	5 (2.6)	5 (2.7)	0.99 [0.28; 3.47] 0.986	0.99 [0.29; 3.36] 0.986	-0.00 [-0.03; 0.03] 0.986
KITE, n (%)	5 (2.8)	2 (1.1)	2.57 [0.49; 13.43] 0.263	2.53 [0.50; 12.86] 0.264	0.02 [-0.01; 0.05] 0.246
Pooled Analysis, n (%) p_H=0.367	10 (2.7)	7 (1.9)	1.58 [0.56; 4.44] 0.386	1.43 [0.55; 3.70] 0.464	0.01 [-0.01; 0.03] 0.464
Cardiac disorders					
KESTREL, n (%)	16 (8.5)	27 (14.4)	0.55 [0.28; 1.05] 0.072	0.59 [0.33; 1.05] 0.073	-0.06 [-0.12; 0.00] 0.068
KITE, n (%)	16 (8.9)	21 (11.6)	0.75 [0.38; 1.49] 0.407	0.77 [0.42; 1.43] 0.407	-0.03 [-0.09; 0.04] 0.405
Pooled Analysis, n (%) p_H=0.521	32 (8.7)	48 (13.0)	0.64 [0.40; 1.03] 0.063	0.67 [0.44; 1.02] 0.058	-0.04 [-0.09; 0.00] 0.057
Injury, poisoning and procedural complications					
KESTREL, n (%)	29 (15.3)	25 (13.4)	1.17 [0.66; 2.09] 0.585	1.15 [0.70; 1.88] 0.586	0.02 [-0.05; 0.09] 0.585

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE, n (%)	18 (10.1)	19 (10.5)	0.95 [0.48; 1.88] 0.890	0.96 [0.52; 1.76] 0.890	-0.00 [-0.07; 0.06] 0.890
Pooled Analysis, n (%) p_H=0.647	47 (12.8)	44 (12.0)	1.06 [0.68; 1.65] 0.796	1.07 [0.73; 1.57] 0.744	0.01 [-0.04; 0.06] 0.743
Skin and subcutaneous tissue disorders					
KESTREL, n (%)	19 (10.1)	14 (7.5)	1.38 [0.67; 2.84] 0.381	1.34 [0.69; 2.60] 0.381	0.03 [-0.03; 0.08] 0.378
KITE, n (%)	11 (6.1)	15 (8.3)	0.72 [0.32; 1.62] 0.434	0.74 [0.35; 1.57] 0.435	-0.02 [-0.07; 0.03] 0.432
Pooled Analysis, n (%) p_H=0.243	30 (8.2)	29 (7.9)	1.01 [0.59; 1.73] 0.980	1.03 [0.63; 1.69] 0.895	0.00 [-0.04; 0.04] 0.895
Blood and lymphatic system disorders					
KESTREL, n (%)	15 (7.9)	14 (7.5)	1.07 [0.50; 2.27] 0.870	1.06 [0.53; 2.13] 0.870	0.00 [-0.05; 0.06] 0.870
KITE, n (%)	10 (5.6)	13 (7.2)	0.76 [0.33; 1.79] 0.537	0.78 [0.35; 1.73] 0.537	-0.02 [-0.07; 0.03] 0.535
Pooled Analysis, n (%) p_H=0.569	25 (6.8)	27 (7.3)	0.91 [0.51; 1.60] 0.733	0.92 [0.55; 1.56] 0.771	-0.01 [-0.04; 0.03] 0.771
Anaemia					
KESTREL, n (%)	9 (4.8)	9 (4.8)	0.99 [0.38; 2.55] 0.982	0.99 [0.40; 2.44] 0.982	-0.00 [-0.04; 0.04] 0.982
KITE, n (%)	9 (5.0)	9 (5.0)	1.01 [0.39; 2.61] 0.981	1.01 [0.41; 2.49] 0.981	0.00 [-0.04; 0.05] 0.981
Pooled Analysis, n (%) p_H=0.973	18 (4.9)	18 (4.9)	1.00 [0.51; 1.95] 1.000	1.00 [0.53; 1.89] 0.999	0.00 [-0.03; 0.03] 0.999
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
KESTREL, n (%)	8 (4.2)	10 (5.3)	0.78 [0.30; 2.03] 0.613	0.79 [0.32; 1.96] 0.614	-0.01 [-0.05; 0.03] 0.613
KITE, n (%)	8 (4.5)	11 (6.1)	0.72 [0.28; 1.84] 0.497	0.74 [0.30; 1.79] 0.497	-0.02 [-0.06; 0.03] 0.494
Pooled Analysis, n (%) p_H=0.908	16 (4.3)	21 (5.7)	0.75 [0.39; 1.47] 0.404	0.76 [0.40; 1.44] 0.400	-0.01 [-0.05; 0.02] 0.400

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Psychiatric disorders					
KESTREL, n (%)	10 (5.3)	9 (4.8)	1.10 [0.44; 2.78] 0.832	1.10 [0.46; 2.64] 0.832	0.00 [-0.04; 0.05] 0.832
KITE, n (%)	7 (3.9)	7 (3.9)	1.01 [0.35; 2.95] 0.983	1.01 [0.36; 2.82] 0.983	0.00 [-0.04; 0.04] 0.983
Pooled Analysis, n (%) p_H=0.903	17 (4.6)	16 (4.3)	1.06 [0.52; 2.14] 0.875	1.06 [0.54; 2.07] 0.862	0.00 [-0.03; 0.03] 0.862
Ear and labyrinth disorders					
KESTREL, n (%)	7 (3.7)	7 (3.7)	0.99 [0.34; 2.88] 0.984	0.99 [0.35; 2.77] 0.984	-0.00 [-0.04; 0.04] 0.984
KITE, n (%)	7 (3.9)	6 (3.3)	1.19 [0.39; 3.60] 0.762	1.18 [0.40; 3.44] 0.762	0.01 [-0.03; 0.04] 0.762
Pooled Analysis, n (%) p_H=0.816	14 (3.8)	13 (3.5)	1.08 [0.50; 2.34] 0.842	1.08 [0.51; 2.26] 0.845	0.00 [-0.02; 0.03] 0.845
Reproductive system and breast disorders					
KESTREL, n (%)	5 (2.6)	5 (2.7)	0.99 [0.28; 3.47] 0.986	0.99 [0.29; 3.36] 0.986	-0.00 [-0.03; 0.03] 0.986
KITE, n (%)	5 (2.8)	7 (3.9)	0.71 [0.22; 2.29] 0.572	0.72 [0.23; 2.23] 0.572	-0.01 [-0.05; 0.03] 0.570
Pooled Analysis, n (%) p_H=0.710	10 (2.7)	12 (3.3)	0.84 [0.36; 1.99] 0.697	0.83 [0.36; 1.91] 0.668	-0.01 [-0.03; 0.02] 0.667
Hepatobiliary disorders					
KESTREL, n (%)	6 (3.2)	3 (1.6)	2.01 [0.50; 8.16] 0.328	1.98 [0.50; 7.80] 0.329	0.02 [-0.02; 0.05] 0.318
KITE, n (%)	5 (2.8)	5 (2.8)	1.01 [0.29; 3.56] 0.986	1.01 [0.30; 3.43] 0.986	0.00 [-0.03; 0.03] 0.986

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, n (%) p_H=0.474	11 (3.0)	8 (2.2)	1.44 [0.56; 3.69] 0.452	1.38 [0.56; 3.39] 0.485	0.01 [-0.01; 0.03] 0.484

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 16-5.2 Any non-ocular adverse event by SOC, PT and age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
< 65 years, N'/N	104 / 104	93 / 93			
≥ 65 years, N'/N	85 / 85	94 / 94			
KITE, N'/N	179 / 179	181 / 181			
< 65 years, N'/N	100 / 100	102 / 102			
≥ 65 years, N'/N	79 / 79	79 / 79			
Pooled Analysis, N'/N	368 / 368	368 / 368			
< 65 years, N'/N	204 / 204	195 / 195			
≥ 65 years, N'/N	164 / 164	173 / 173			
Any non-ocular adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	p = 0.721				
< 65 years, n (%)	6 (5.8)	2 (2.2)	2.79 [0.55; 14.15] 0.217	2.68 [0.55; 12.97] 0.220	0.04 [-0.02; 0.09] 0.186
≥ 65 years, n (%)	4 (4.7)	1 (1.1)	4.59 [0.50; 41.93] 0.177	4.42 [0.50; 38.80] 0.180	0.04 [-0.01; 0.09] 0.150
KITE					
Interaction Test:	p = 0.085				
< 65 years, n (%)	7 (7.0)	2 (2.0)	3.76 [0.76; 18.58] 0.104	3.57 [0.76; 16.77] 0.107	0.05 [-0.01; 0.11] 0.082
≥ 65 years, n (%)	1 (1.3)	3 (3.8)	0.32 [0.03; 3.19] 0.335	0.33 [0.04; 3.14] 0.337	-0.03 [-0.07; 0.02] 0.310
Pooled Analysis					
Interaction Test:	p = 0.297				
< 65 years, n (%)	13 (6.4)	4 (2.1)	3.43 [1.07; 10.97] 0.038 *	3.11 [1.03; 9.36] 0.032 *	0.04 [0.00; 0.08] 0.029 *

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years, n (%)	5 (3.0)	4 (2.3)	1.35 [0.35; 5.15] 0.664	1.32 [0.36; 4.76] 0.673	0.01 [-0.03; 0.04] 0.677

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 16-5.3 Any non-ocular adverse event by SOC, PT and gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Male, N'/N	110 / 110	126 / 126			
Female, N'/N	79 / 79	61 / 61			
KITE, N'/N	179 / 179	181 / 181			
Male, N'/N	120 / 120	115 / 115			
Female, N'/N	59 / 59	66 / 66			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Male, N'/N	230 / 230	241 / 241			
Female, N'/N	138 / 138	127 / 127			
Any non-ocular adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	p = 0.433				
Male, n (%)	5 (4.5)	1 (0.8)	5.95 [0.68; 51.74] 0.106	5.73 [0.68; 48.28] 0.109	0.04 [-0.00; 0.08] 0.079
Female, n (%)	5 (6.3)	2 (3.3)	1.99 [0.37; 10.64] 0.420	1.93 [0.39; 9.61] 0.422	0.03 [-0.04; 0.10] 0.392
KITE					
Interaction Test:	p = 0.115				
Male, n (%)	3 (2.5)	4 (3.5)	0.71 [0.16; 3.25] 0.661	0.72 [0.16; 3.14] 0.661	-0.01 [-0.05; 0.03] 0.660
Female, n (%)	5 (8.5)	1 (1.5)	6.02 [0.68; 53.09] 0.106	5.59 [0.67; 46.51] 0.111	0.07 [-0.01; 0.15] 0.076
Pooled Analysis					
Interaction Test:	p = 0.461				
Male, n (%)	8 (3.5)	5 (2.1)	1.75 [0.56; 5.52] 0.336	1.65 [0.56; 4.87] 0.360	0.01 [-0.02; 0.04] 0.367

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female, n (%)	10 (7.2)	3 (2.4)	3.37 [0.89; 12.84] 0.074	3.01 [0.87; 10.44] 0.067	0.05 [-0.00; 0.10] 0.061

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 16-5.4 Any non-ocular adverse event by SOC, PT and BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
≤ 65 letters, N'/N	74 / 74	64 / 64			
> 65 letters, N'/N	115 / 115	123 / 123			
KITE, N'/N	179 / 179	181 / 181			
≤ 65 letters, N'/N	65 / 65	91 / 91			
> 65 letters, N'/N	114 / 114	90 / 90			
Pooled Analysis, N'/N	368 / 368	368 / 368			
≤ 65 letters, N'/N	139 / 139	155 / 155			
> 65 letters, N'/N	229 / 229	213 / 213			
Any non-ocular adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	p = 0.956				
≤ 65 letters, n (%)	4 (5.4)	1 (1.6)	3.60 [0.39; 33.05] 0.258	3.46 [0.40; 30.17] 0.261	0.04 [-0.02; 0.10] 0.208
> 65 letters, n (%)	6 (5.2)	2 (1.6)	3.33 [0.66; 16.84] 0.146	3.21 [0.66; 15.58] 0.148	0.04 [-0.01; 0.08] 0.129
KITE					
Interaction Test:	p = 0.534				
≤ 65 letters, n (%)	2 (3.1)	1 (1.1)	2.86 [0.25; 32.19] 0.396	2.80 [0.26; 30.23] 0.396	0.02 [-0.03; 0.07] 0.411
> 65 letters, n (%)	6 (5.3)	4 (4.4)	1.19 [0.33; 4.37] 0.788	1.18 [0.34; 4.07] 0.788	0.01 [-0.05; 0.07] 0.786
Pooled Analysis					
Interaction Test:	p = 0.475				
≤ 65 letters, n (%)	6 (4.3)	2 (1.3)	3.86 [0.73; 20.26] 0.111	3.17 [0.64; 15.78] 0.136	0.03 [-0.01; 0.07] 0.140

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters, n (%)	12 (5.2)	6 (2.8)	1.92 [0.70; 5.27] 0.205	1.80 [0.70; 4.63] 0.219	0.02 [-0.01; 0.06] 0.216

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 16-5.5 Any non-ocular adverse event by SOC, PT and region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Region of the Americas, N'/N	90 / 90	83 / 83			
European Region, N'/N	69 / 69	75 / 75			
Western Pacific Region, N'/N	30 / 30	29 / 29			
KITE, N'/N	179 / 179	181 / 181			
South-East Asia Region and Eastern Mediterranean Region, N'/N	26 / 26	21 / 21			
European Region, N'/N	135 / 135	132 / 132			
Western Pacific Region, N'/N	18 / 18	28 / 28			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Region of the Americas, N'/N	90 / 90	83 / 83			
South-East Asia Region and Eastern Mediterranean Region, N'/N	26 / 26	21 / 21			
European Region, N'/N	204 / 204	207 / 207			
Western Pacific Region, N'/N	48 / 48	57 / 57			
Any non-ocular adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: $\mathbf{p_H=0.407}$					
KESTREL					
Interaction Test:	N.E.				
Region of the Americas, n (%)	5 (5.6)	0 (0.0)	N.E.	10.15 [0.57; 180.85] 0.115	0.06 [0.01; 0.10] 0.021 *
European Region, n (%)	2 (2.9)	2 (2.7)	1.09 [0.15; 7.95] 0.933	1.09 [0.16; 7.51] 0.933	0.00 [-0.05; 0.06] 0.933
Western Pacific Region, n (%)	3 (10.0)	1 (3.4)	3.11 [0.30; 31.78] 0.339	2.90 [0.32; 26.30] 0.344	0.07 [-0.06; 0.19] 0.309

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	N.E.				
South-East Asia Region and Eastern Mediterranean Region, n (%)	2 (7.7)	0 (0.0)	N.E.	4.07 [0.21; 80.51] 0.356	0.08 [-0.03; 0.18] 0.141
European Region, n (%)	6 (4.4)	5 (3.8)	1.18 [0.35; 3.97] 0.787	1.17 [0.37; 3.75] 0.788	0.01 [-0.04; 0.05] 0.787
Western Pacific Region, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Pooled Analysis					
Interaction Test:	N.E.				
Region of the Americas, n (%)	5 (5.6)	0 (0.0)	N.E.	10.15 [0.57; 180.85] 0.048 *	0.06 [0.01; 0.10] 0.021 *
South-East Asia Region and Eastern Mediterranean Region, n (%)	2 (7.7)	0 (0.0)	N.E.	4.07 [0.21; 80.51] 0.315	0.08 [-0.03; 0.18] 0.141
European Region, n (%)	8 (3.9)	7 (3.4)	1.13 [0.35; 3.67] 0.834	1.15 [0.42; 3.11] 0.784	0.01 [-0.03; 0.04] 0.784
Western Pacific Region, n (%)	3 (6.3)	1 (1.8)	N.E.	2.90 [0.32; 26.30] 0.321	0.04 [-0.04; 0.11] 0.325

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Headache / KESTREL, Week 100 / Headache / KITE: logit(proportion) = treatment [by region].
Week 100 / Headache / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by region].

Table 16-5.6 Any non-ocular adverse event by SOC, PT and diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Type 1, N'/N	12 / 12	6 / 6			
Type 2, N'/N	177 / 177	181 / 181			
KITE, N'/N	179 / 179	181 / 181			
Type 1, N'/N	19 / 19	7 / 7			
Type 2, N'/N	160 / 160	174 / 174			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Type 1, N'/N	31 / 31	13 / 13			
Type 2, N'/N	337 / 337	355 / 355			
Any non-ocular adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	N.E.				
Type 1, n (%)	2 (16.7)	0 (0.0)	N.E.	2.69 [0.15; 48.64] 0.502	0.17 [-0.04; 0.38] 0.121
Type 2, n (%)	8 (4.5)	3 (1.7)	2.81 [0.73; 10.76] 0.132	2.73 [0.74; 10.11] 0.134	0.03 [-0.01; 0.06] 0.117
KITE					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2, n (%)	8 (5.0)	5 (2.9)	1.78 [0.57; 5.55] 0.321	1.74 [0.58; 5.21] 0.322	0.02 [-0.02; 0.06] 0.320
Pooled Analysis					
Interaction Test:	N.E.				
Type 1, n (%)	2 (6.5)	0 (0.0)	N.E.	2.69 [0.15; 48.64] 0.482	0.07 [-0.02; 0.16] 0.118

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2, n (%)	16 (4.7)	8 (2.3)	2.25 [0.93; 5.43] 0.073	2.12 [0.92; 4.89] 0.072	0.03 [-0.00; 0.05] 0.073

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Headache / KESTREL, Week 100 / Headache / KITE: logit(proportion) = treatment [by diabetes type].
Week 100 / Headache / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 16-5.7 Any non-ocular adverse event by SOC, PT and HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	188 / 188	187 / 187			
< 7.5 %, N'/N	76 / 76	107 / 107			
≥ 7.5 %, N'/N	112 / 112	80 / 80			
KITE, N'/N	179 / 179	181 / 181			
< 7.5 %, N'/N	82 / 82	96 / 96			
≥ 7.5 %, N'/N	97 / 97	85 / 85			
Pooled Analysis, N'/N	367 / 367	368 / 368			
< 7.5 %, N'/N	158 / 158	203 / 203			
≥ 7.5 %, N'/N	209 / 209	165 / 165			
Any non-ocular adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	p = 0.484				
< 7.5 %, n (%)	4 (5.3)	1 (0.9)	5.89 [0.64; 53.77] 0.116	5.63 [0.64; 49.40] 0.119	0.04 [-0.01; 0.10] 0.112
≥ 7.5 %, n (%)	6 (5.4)	2 (2.5)	2.21 [0.43; 11.23] 0.340	2.14 [0.44; 10.35] 0.343	0.03 [-0.03; 0.08] 0.299
KITE					
Interaction Test:	p = 0.731				
< 7.5 %, n (%)	2 (2.4)	2 (2.1)	1.17 [0.16; 8.53] 0.873	1.17 [0.17; 8.13] 0.873	0.00 [-0.04; 0.05] 0.874
≥ 7.5 %, n (%)	6 (6.2)	3 (3.5)	1.80 [0.44; 7.44] 0.415	1.75 [0.45; 6.79] 0.417	0.03 [-0.04; 0.09] 0.401
Pooled Analysis					
Interaction Test:	p = 0.749				
< 7.5 %, n (%)	6 (3.8)	3 (1.5)	2.70 [0.66; 11.08] 0.168	2.56 [0.66; 9.85] 0.157	0.02 [-0.01; 0.06] 0.182

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %, n (%)	12 (5.7)	5 (3.0)	2.03 [0.68; 6.01] 0.203	1.92 [0.69; 5.35] 0.205	0.03 [-0.01; 0.07] 0.187

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 16-5.8 Any non-ocular adverse event by SOC, PT and duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
≤ 3 months, N'/N	120 / 120	110 / 110			
> 3 - < 12 months, N'/N	30 / 30	39 / 39			
≥ 12 months, N'/N	39 / 39	38 / 38			
KITE, N'/N	179 / 179	181 / 181			
≤ 3 months, N'/N	85 / 85	92 / 92			
> 3 - < 12 months, N'/N	51 / 51	49 / 49			
≥ 12 months, N'/N	43 / 43	40 / 40			
Pooled Analysis, N'/N	368 / 368	368 / 368			
≤ 3 months, N'/N	205 / 205	202 / 202			
> 3 - < 12 months, N'/N	81 / 81	88 / 88			
≥ 12 months, N'/N	82 / 82	78 / 78			
Any non-ocular adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months, n (%)	6 (5.0)	1 (0.9)	5.74 [0.68; 48.43] 0.108	5.50 [0.67; 44.96] 0.112	0.04 [-0.00; 0.08] 0.061
> 3 - < 12 months, n (%)	3 (10.0)	0 (0.0)	N.E.	9.03 [0.48; 168.45] 0.140	0.10 [-0.01; 0.21] 0.068
≥ 12 months, n (%)	1 (2.6)	2 (5.3)	0.47 [0.04; 5.45] 0.549	0.49 [0.05; 5.15] 0.550	-0.03 [-0.11; 0.06] 0.541
KITE					
Interaction Test:	N.E.				
≤ 3 months, n (%)	4 (4.7)	3 (3.3)	1.46 [0.32; 6.74] 0.624	1.44 [0.33; 6.26] 0.624	0.01 [-0.04; 0.07] 0.624
> 3 - < 12 months, n (%)	2 (3.9)	0 (0.0)	N.E.	4.81 [0.24; 97.68] 0.307	0.04 [-0.01; 0.09] 0.149
≥ 12 months, n (%)	2 (4.7)	2 (5.0)	0.93 [0.12; 6.91] 0.941	0.93 [0.14; 6.30] 0.941	-0.00 [-0.10; 0.09] 0.941

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	N.E.				
≤ 3 months, n (%)	10 (4.9)	4 (2.0)	2.94 [0.78; 11.01] 0.110	2.52 [0.79; 8.04] 0.105	0.03 [-0.01; 0.06] 0.101
> 3 - < 12 months, n (%)	5 (6.2)	0 (0.0)	N.E.	6.76 [0.85; 53.84] 0.035 *	0.06 [0.01; 0.12] 0.019 *
≥ 12 months, n (%)	3 (3.7)	4 (5.1)	0.66 [0.13; 3.22] 0.606	0.71 [0.16; 3.09] 0.649	-0.01 [-0.08; 0.05] 0.648

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Headache / KESTREL, Week 100 / Headache / KITE: logit(proportion) = treatment [by duration of DME].
Week 100 / Headache / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by duration of DME].

Table 16-5.9 Any non-ocular adverse event by SOC, PT and DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	186 / 186	182 / 182			
focal, N'/N	59 / 59	48 / 48			
diffuse, N'/N	127 / 127	134 / 134			
KITE, N'/N	178 / 178	175 / 175			
focal, N'/N	63 / 63	66 / 66			
diffuse, N'/N	115 / 115	109 / 109			
Pooled Analysis, N'/N	364 / 364	357 / 357			
focal, N'/N	122 / 122	114 / 114			
diffuse, N'/N	242 / 242	243 / 243			
Any non-ocular adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	N.E.				
focal, n (%)	2 (3.4)	0 (0.0)	N.E.	4.08 [0.20; 83.07] 0.360	0.03 [-0.01; 0.08] 0.150
diffuse, n (%)	8 (6.3)	3 (2.2)	2.94 [0.76; 11.32] 0.118	2.81 [0.76; 10.37] 0.120	0.04 [-0.01; 0.09] 0.105
KITE					
Interaction Test:	p = 0.797				
focal, n (%)	4 (6.3)	3 (4.5)	1.42 [0.31; 6.63] 0.653	1.40 [0.33; 5.99] 0.653	0.02 [-0.06; 0.10] 0.652
diffuse, n (%)	4 (3.5)	2 (1.8)	1.93 [0.35; 10.74] 0.454	1.90 [0.35; 10.14] 0.455	0.02 [-0.03; 0.06] 0.442
Pooled Analysis					
Interaction Test:	p = 0.838				
focal, n (%)	6 (4.9)	3 (2.6)	2.08 [0.49; 8.79] 0.321	1.82 [0.50; 6.61] 0.356	0.03 [-0.02; 0.07] 0.304

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse, n (%)	12 (5.0)	5 (2.1)	2.50 [0.86; 7.27] 0.093	2.43 [0.87; 6.79] 0.078	0.03 [-0.00; 0.06] 0.078

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Headache / KESTREL: logit(proportion) = treatment [by DME type].

Table 16-5.10 Any non-ocular adverse event by SOC, PT and CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
< 450 µm, N'/N	107 / 107	96 / 96			
≥ 450 - < 650 µm, N'/N	70 / 70	71 / 71			
≥ 650 µm, N'/N	12 / 12	20 / 20			
KITE, N'/N	179 / 179	180 / 180			
< 450 µm, N'/N	85 / 85	82 / 82			
≥ 450 - < 650 µm, N'/N	74 / 74	79 / 79			
≥ 650 µm, N'/N	20 / 20	19 / 19			
Pooled Analysis, N'/N	368 / 368	367 / 367			
< 450 µm, N'/N	192 / 192	178 / 178			
≥ 450 - < 650 µm, N'/N	144 / 144	150 / 150			
≥ 650 µm, N'/N	32 / 32	39 / 39			
Any non-ocular adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	N.E.				
< 450 µm, n (%)	6 (5.6)	1 (1.0)	5.64 [0.67; 47.75] 0.112	5.38 [0.66; 43.92] 0.116	0.05 [-0.00; 0.09] 0.063
≥ 450 - < 650 µm, n (%)	4 (5.7)	2 (2.8)	2.09 [0.37; 11.80] 0.404	2.03 [0.38; 10.72] 0.405	0.03 [-0.04; 0.10] 0.394
≥ 650 µm, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE					
Interaction Test:	N.E.				
< 450 µm, n (%)	5 (5.9)	4 (4.9)	1.22 [0.32; 4.71] 0.774	1.21 [0.34; 4.33] 0.774	0.01 [-0.06; 0.08] 0.773
≥ 450 - < 650 µm, n (%)	3 (4.1)	0 (0.0)	N.E.	7.47 [0.39; 142.14] 0.181	0.04 [-0.00; 0.09] 0.077
≥ 650 µm, n (%)	0 (0.0)	1 (5.3)	N.E.	0.32 [0.01; 7.35] 0.474	-0.05 [-0.15; 0.05] 0.304

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	N.E.				
< 450 µm, n (%)	11 (5.7)	5 (2.8)	2.66 [0.74; 9.53] 0.132	2.06 [0.73; 5.86] 0.163	0.03 [-0.01; 0.07] 0.155
≥ 450 - < 650 µm, n (%)	7 (4.9)	2 (1.3)	N.E.	3.09 [0.76; 12.63] 0.097	0.03 [-0.00; 0.07] 0.083
≥ 650 µm, n (%)	0 (0.0)	1 (2.6)	N.E.	0.32 [0.01; 7.35] 0.452	-0.03 [-0.08; 0.02] 0.279

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Headache / KESTREL, Week 100 / Headache / KITE: logit(proportion) = treatment [by CSFT].
Week 100 / Headache / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by CSFT].

Table 16-5.11 Any non-ocular adverse event by SOC, PT and status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
presence, N'/N	62 / 62	61 / 61			
absence, N'/N	127 / 127	126 / 126			
KITE, N'/N	179 / 179	181 / 181			
presence, N'/N	56 / 56	67 / 67			
absence, N'/N	123 / 123	114 / 114			
Pooled Analysis, N'/N	368 / 368	368 / 368			
presence, N'/N	118 / 118	128 / 128			
absence, N'/N	250 / 250	240 / 240			
Any non-ocular adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	p = 0.602				
presence, n (%)	5 (8.1)	1 (1.6)	5.26 [0.60; 46.44] 0.135	4.92 [0.59; 40.89] 0.140	0.06 [-0.01; 0.14] 0.093
absence, n (%)	5 (3.9)	2 (1.6)	2.54 [0.48; 13.35] 0.271	2.48 [0.49; 12.55] 0.272	0.02 [-0.02; 0.06] 0.253
KITE					
Interaction Test:	N.E.				
presence, n (%)	0 (0.0)	1 (1.5)	N.E.	0.40 [0.02; 9.57] 0.570	-0.01 [-0.04; 0.01] 0.314
absence, n (%)	8 (6.5)	4 (3.5)	1.91 [0.56; 6.53] 0.301	1.85 [0.57; 5.99] 0.302	0.03 [-0.03; 0.09] 0.287
Pooled Analysis					
Interaction Test:	p = 0.769				
presence, n (%)	5 (4.2)	2 (1.6)	2.94 [0.55; 15.74] 0.208	2.32 [0.51; 10.52] 0.260	0.02 [-0.02; 0.07] 0.242

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence, n (%)	13 (5.2)	6 (2.5)	2.20 [0.81; 5.98] 0.123	2.06 [0.80; 5.31] 0.127	0.03 [-0.01; 0.06] 0.123

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Headache / KITE: logit(proportion) = treatment [by status of SRF].

Table 16-5.13 Any non-ocular adverse event by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Non-exposed, N'/N	12 / 12	13 / 13			
Exposed, N'/N	177 / 177	174 / 174			
KITE, N'/N	179 / 179	181 / 181			
Non-exposed, N'/N	17 / 17	12 / 12			
Exposed, N'/N	162 / 162	169 / 169			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Non-exposed, N'/N	29 / 29	25 / 25			
Exposed, N'/N	339 / 339	343 / 343			
Any non-ocular adverse event by SOC and PT, week 100					
Headache					
Test of heterogeneity in main analysis: **p_H=0.407**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Exposed, n (%)	10 (5.6)	3 (1.7)	3.41 [0.92; 12.62] 0.066	3.28 [0.92; 11.70] 0.068	0.04 [0.00; 0.08] 0.049 *
KITE					
Interaction Test:	p = 0.533				
Non-exposed, n (%)	1 (5.9)	1 (8.3)	0.69 [0.04; 12.20] 0.798	0.71 [0.05; 10.21] 0.798	-0.02 [-0.22; 0.17] 0.803
Exposed, n (%)	7 (4.3)	4 (2.4)	1.86 [0.53; 6.49] 0.328	1.83 [0.54; 6.12] 0.329	0.02 [-0.02; 0.06] 0.324
Pooled Analysis					
Interaction Test:	p = 0.478				
Non-exposed, n (%)	1 (3.4)	1 (4.0)	0.89 [0.05; 15.20] 0.939	0.71 [0.05; 10.21] 0.801	-0.01 [-0.11; 0.09] 0.801

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed, n (%)	17 (5.0)	7 (2.0)	2.62 [1.05; 6.55] 0.039 *	2.46 [1.03; 5.87] 0.036 *	0.03 [0.00; 0.06] 0.035 *

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Headache / KESTREL: logit(proportion) = treatment [by exposure (week 100)].

17 Safety analysis: Any serious adverse event by SOC and PT

Table 17-1.1 Any serious adverse event by SOC and PT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any serious adverse event by SOC and PT, week 100					
Infections and infestations					
KESTREL, n (%)	17 (9.0)	15 (8.0)	1.13 [0.55; 2.34] 0.735	1.12 [0.58; 2.18] 0.735	0.01 [-0.05; 0.07] 0.735
KITE, n (%)	19 (10.6)	16 (8.8)	1.22 [0.61; 2.47] 0.570	1.20 [0.64; 2.26] 0.571	0.02 [-0.04; 0.08] 0.570
Pooled Analysis, n (%) p_H=0.880	36 (9.8)	31 (8.4)	1.18 [0.71; 1.95] 0.526	1.16 [0.74; 1.84] 0.520	0.01 [-0.03; 0.06] 0.520
Cardiac disorders					
KESTREL, n (%)	13 (6.9)	17 (9.1)	0.74 [0.35; 1.57] 0.430	0.76 [0.38; 1.51] 0.430	-0.02 [-0.08; 0.03] 0.428
KITE, n (%)	11 (6.1)	18 (9.9)	0.59 [0.27; 1.29] 0.189	0.62 [0.30; 1.27] 0.191	-0.04 [-0.09; 0.02] 0.184
Pooled Analysis, n (%) p_H=0.691	24 (6.5)	35 (9.5)	0.66 [0.39; 1.14] 0.137	0.69 [0.42; 1.13] 0.136	-0.03 [-0.07; 0.01] 0.135
Nervous system disorders					
KESTREL, n (%)	6 (3.2)	13 (7.0)	0.44 [0.16; 1.18] 0.103	0.46 [0.18; 1.18] 0.104	-0.04 [-0.08; 0.01] 0.094
KITE, n (%)	8 (4.5)	10 (5.5)	0.80 [0.31; 2.08] 0.646	0.81 [0.33; 2.00] 0.647	-0.01 [-0.06; 0.03] 0.646
Pooled Analysis, n (%) p_H=0.392	14 (3.8)	23 (6.3)	0.59 [0.30; 1.17] 0.131	0.61 [0.32; 1.16] 0.129	-0.02 [-0.06; 0.01] 0.129
Renal and urinary disorders					
KESTREL, n (%)	7 (3.7)	9 (4.8)	0.76 [0.28; 2.09] 0.595	0.77 [0.29; 2.02] 0.595	-0.01 [-0.05; 0.03] 0.594

	Treatment Groups		Comparison		
Any serious adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE, n (%)	4 (2.2)	7 (3.9)	0.57 [0.16; 1.98] 0.374	0.58 [0.17; 1.94] 0.375	-0.02 [-0.05; 0.02] 0.367
Pooled Analysis, n (%) p_H=0.721	11 (3.0)	16 (4.3)	0.66 [0.30; 1.47] 0.307	0.69 [0.32; 1.46] 0.325	-0.01 [-0.04; 0.01] 0.324
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
KESTREL, n (%)	6 (3.2)	4 (2.1)	1.50 [0.42; 5.40] 0.535	1.48 [0.43; 5.17] 0.536	0.01 [-0.02; 0.04] 0.532
KITE, n (%)	7 (3.9)	9 (5.0)	0.78 [0.28; 2.14] 0.626	0.79 [0.30; 2.07] 0.626	-0.01 [-0.05; 0.03] 0.625
Pooled Analysis, n (%) p_H=0.430	13 (3.5)	13 (3.5)	1.09 [0.48; 2.47] 0.842	1.00 [0.47; 2.13] 0.994	0.00 [-0.03; 0.03] 0.994
Eye disorders					
KESTREL, n (%)	9 (4.8)	9 (4.8)	0.99 [0.38; 2.55] 0.982	0.99 [0.40; 2.44] 0.982	-0.00 [-0.04; 0.04] 0.982
KITE, n (%)	3 (1.7)	3 (1.7)	1.01 [0.20; 5.08] 0.989	1.01 [0.21; 4.94] 0.989	0.00 [-0.03; 0.03] 0.989
Pooled Analysis, n (%) p_H=0.981	12 (3.3)	12 (3.3)	1.00 [0.40; 2.53] 1.000	0.99 [0.45; 2.18] 0.990	-0.00 [-0.03; 0.03] 0.990
Injury, poisoning and procedural complications					
KESTREL, n (%)	5 (2.6)	7 (3.7)	0.70 [0.22; 2.24] 0.547	0.71 [0.23; 2.19] 0.547	-0.01 [-0.05; 0.02] 0.545
KITE, n (%)	1 (0.6)	5 (2.8)	0.20 [0.02; 1.71] 0.141	0.20 [0.02; 1.71] 0.143	-0.02 [-0.05; 0.00] 0.100
Pooled Analysis, n (%) p_H=0.313	6 (1.6)	12 (3.3)	0.38 [0.11; 1.27] 0.114	0.50 [0.19; 1.31] 0.150	-0.02 [-0.04; 0.01] 0.149
Vascular disorders					
KESTREL, n (%)	8 (4.2)	4 (2.1)	2.02 [0.60; 6.83] 0.257	1.98 [0.61; 6.46] 0.258	0.02 [-0.01; 0.06] 0.247
KITE, n (%)	4 (2.2)	4 (2.2)	1.01 [0.25; 4.11] 0.987	1.01 [0.26; 3.98] 0.987	0.00 [-0.03; 0.03] 0.987
Pooled Analysis, n (%) p_H=0.465	12 (3.3)	8 (2.2)	1.44 [0.57; 3.63] 0.440	1.50 [0.62; 3.62] 0.367	0.01 [-0.01; 0.03] 0.366

	Treatment Groups		Comparison		
Any serious adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Metabolism and nutrition disorders					
KESTREL, n (%)	7 (3.7)	4 (2.1)	1.76 [0.51; 6.11] 0.374	1.73 [0.52; 5.82] 0.375	0.02 [-0.02; 0.05] 0.367
KITE, n (%)	4 (2.2)	4 (2.2)	1.01 [0.25; 4.11] 0.987	1.01 [0.26; 3.98] 0.987	0.00 [-0.03; 0.03] 0.987
Pooled Analysis, n (%) p_H=0.563	11 (3.0)	8 (2.2)	1.34 [0.53; 3.42] 0.538	1.37 [0.56; 3.38] 0.488	0.01 [-0.01; 0.03] 0.487

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 17-1.2 Any serious adverse event by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-1.3 Any serious adverse event by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-1.4 Any serious adverse event by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-1.5 Any serious adverse event by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-1.6 Any serious adverse event by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-1.7 Any serious adverse event by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-1.8 Any serious adverse event by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-1.9 Any serious adverse event by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-1.10 Any serious adverse event by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-1.11 Any serious adverse event by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-1.13 Any serious adverse event by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-2.1 Any serious ocular adverse event by SOC and PT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any serious ocular adverse event by SOC and PT, week 100					
Eye disorders					
KESTREL, n (%)	9 (4.8)	9 (4.8)	0.99 [0.38; 2.55] 0.982	0.99 [0.40; 2.44] 0.982	-0.00 [-0.04; 0.04] 0.982
KITE, n (%)	3 (1.7)	3 (1.7)	1.01 [0.20; 5.08] 0.989	1.01 [0.21; 4.94] 0.989	0.00 [-0.03; 0.03] 0.989
Pooled Analysis, n (%) p_H=0.981	12 (3.3)	12 (3.3)	1.00 [0.40; 2.53] 1.000	0.99 [0.45; 2.18] 0.990	-0.00 [-0.03; 0.03] 0.990

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 17-2.2 Any serious ocular adverse event by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-2.3 Any serious ocular adverse event by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-2.4 Any serious ocular adverse event by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-2.5 Any serious ocular adverse event by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-2.6 Any serious ocular adverse event by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-2.7 Any serious ocular adverse event by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-2.8 Any serious ocular adverse event by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-2.9 Any serious ocular adverse event by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-2.10 Any serious ocular adverse event by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-2.11 Any serious ocular adverse event by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-2.13 Any serious ocular adverse event by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-3.1 Any serious ocular adverse event at the study eye by SOC and PT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-3.2 Any serious ocular adverse event at the study eye by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-3.3 Any serious ocular adverse event at the study eye by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-3.4 Any serious ocular adverse event at the study eye by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-3.5 Any serious ocular adverse event at the study eye by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-3.6 Any serious ocular adverse event at the study eye by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-3.7 Any serious ocular adverse event at the study eye by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-3.8 Any serious ocular adverse event at the study eye by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-3.9 Any serious ocular adverse event at the study eye by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-3.10 Any serious ocular adverse event at the study eye by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-3.11 Any serious ocular adverse event at the study eye by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-3.13 Any serious ocular adverse event at the study eye by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-4.1 Any serious ocular adverse event at the fellow eye by SOC and PT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-4.2 Any serious ocular adverse event at the fellow eye by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-4.3 Any serious ocular adverse event at the fellow eye by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-4.4 Any serious ocular adverse event at the fellow eye by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-4.5 Any serious ocular adverse event at the fellow eye by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-4.6 Any serious ocular adverse event at the fellow eye by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-4.7 Any serious ocular adverse event at the fellow eye by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-4.8 Any serious ocular adverse event at the fellow eye by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-4.9 Any serious ocular adverse event at the fellow eye by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-4.10 Any serious ocular adverse event at the fellow eye by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-4.11 Any serious ocular adverse event at the fellow eye by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-4.13 Any serious ocular adverse event at the fellow eye by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-5.1 Any serious non-ocular adverse event by SOC and PT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any serious non-ocular adverse event by SOC and PT, week 100					
Cardiac disorders					
KESTREL, n (%)	13 (6.9)	17 (9.1)	0.74 [0.35; 1.57] 0.430	0.76 [0.38; 1.51] 0.430	-0.02 [-0.08; 0.03] 0.428
KITE, n (%)	11 (6.1)	18 (9.9)	0.59 [0.27; 1.29] 0.189	0.62 [0.30; 1.27] 0.191	-0.04 [-0.09; 0.02] 0.184
Pooled Analysis, n (%) p_H=0.691	24 (6.5)	35 (9.5)	0.66 [0.39; 1.14] 0.137	0.69 [0.42; 1.13] 0.136	-0.03 [-0.07; 0.01] 0.135
Infections and infestations					
KESTREL, n (%)	17 (9.0)	14 (7.5)	1.22 [0.58; 2.56] 0.595	1.20 [0.61; 2.37] 0.596	0.02 [-0.04; 0.07] 0.595
KITE, n (%)	17 (9.5)	15 (8.3)	1.16 [0.56; 2.40] 0.687	1.15 [0.59; 2.22] 0.687	0.01 [-0.05; 0.07] 0.687
Pooled Analysis, n (%) p_H=0.924	34 (9.2)	29 (7.9)	1.19 [0.71; 2.00] 0.508	1.17 [0.73; 1.88] 0.509	0.01 [-0.03; 0.05] 0.509
Nervous system disorders					
KESTREL, n (%)	6 (3.2)	13 (7.0)	0.44 [0.16; 1.18] 0.103	0.46 [0.18; 1.18] 0.104	-0.04 [-0.08; 0.01] 0.094
KITE, n (%)	8 (4.5)	10 (5.5)	0.80 [0.31; 2.08] 0.646	0.81 [0.33; 2.00] 0.647	-0.01 [-0.06; 0.03] 0.646
Pooled Analysis, n (%) p_H=0.392	14 (3.8)	23 (6.3)	0.59 [0.30; 1.17] 0.131	0.61 [0.32; 1.16] 0.129	-0.02 [-0.06; 0.01] 0.129
Renal and urinary disorders					
KESTREL, n (%)	7 (3.7)	9 (4.8)	0.76 [0.28; 2.09] 0.595	0.77 [0.29; 2.02] 0.595	-0.01 [-0.05; 0.03] 0.594
KITE, n (%)	4 (2.2)	7 (3.9)	0.57 [0.16; 1.98] 0.374	0.58 [0.17; 1.94] 0.375	-0.02 [-0.05; 0.02] 0.367

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, n (%) p_H=0.721	11 (3.0)	16 (4.3)	0.66 [0.30; 1.47] 0.307	0.69 [0.32; 1.46] 0.325	-0.01 [-0.04; 0.01] 0.324
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
KESTREL, n (%)	6 (3.2)	4 (2.1)	1.50 [0.42; 5.40] 0.535	1.48 [0.43; 5.17] 0.536	0.01 [-0.02; 0.04] 0.532
KITE, n (%)	7 (3.9)	9 (5.0)	0.78 [0.28; 2.14] 0.626	0.79 [0.30; 2.07] 0.626	-0.01 [-0.05; 0.03] 0.625
Pooled Analysis, n (%) p_H=0.430	13 (3.5)	13 (3.5)	1.09 [0.48; 2.47] 0.842	1.00 [0.47; 2.13] 0.994	0.00 [-0.03; 0.03] 0.994
Vascular disorders					
KESTREL, n (%)	8 (4.2)	4 (2.1)	2.02 [0.60; 6.83] 0.257	1.98 [0.61; 6.46] 0.258	0.02 [-0.01; 0.06] 0.247
KITE, n (%)	4 (2.2)	4 (2.2)	1.01 [0.25; 4.11] 0.987	1.01 [0.26; 3.98] 0.987	0.00 [-0.03; 0.03] 0.987
Pooled Analysis, n (%) p_H=0.465	12 (3.3)	8 (2.2)	1.44 [0.57; 3.63] 0.440	1.50 [0.62; 3.62] 0.367	0.01 [-0.01; 0.03] 0.366
Injury, poisoning and procedural complications					
KESTREL, n (%)	5 (2.6)	6 (3.2)	0.82 [0.25; 2.73] 0.746	0.82 [0.26; 2.66] 0.746	-0.01 [-0.04; 0.03] 0.746
KITE, n (%)	1 (0.6)	5 (2.8)	0.20 [0.02; 1.71] 0.141	0.20 [0.02; 1.71] 0.143	-0.02 [-0.05; 0.00] 0.100
Pooled Analysis, n (%) p_H=0.259	6 (1.6)	11 (3.0)	0.41 [0.12; 1.39] 0.151	0.54 [0.20; 1.46] 0.218	-0.01 [-0.04; 0.01] 0.217
Metabolism and nutrition disorders					
KESTREL, n (%)	7 (3.7)	4 (2.1)	1.76 [0.51; 6.11] 0.374	1.73 [0.52; 5.82] 0.375	0.02 [-0.02; 0.05] 0.367
KITE, n (%)	4 (2.2)	4 (2.2)	1.01 [0.25; 4.11] 0.987	1.01 [0.26; 3.98] 0.987	0.00 [-0.03; 0.03] 0.987

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, n (%) p_H=0.563	11 (3.0)	8 (2.2)	1.34 [0.53; 3.42] 0.538	1.37 [0.56; 3.38] 0.488	0.01 [-0.01; 0.03] 0.487

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 17-5.2 Any serious non-ocular adverse event by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-5.3 Any serious non-ocular adverse event by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-5.4 Any serious non-ocular adverse event by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-5.5 Any serious non-ocular adverse event by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-5.6 Any serious non-ocular adverse event by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-5.7 Any serious non-ocular adverse event by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-5.8 Any serious non-ocular adverse event by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-5.9 Any serious non-ocular adverse event by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-5.10 Any serious non-ocular adverse event by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-5.11 Any serious non-ocular adverse event by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 17-5.13 Any serious non-ocular adverse event by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

18 Safety analysis: Any severe adverse event by SOC and PT

Table 18-1.1 Any severe adverse event by SOC and PT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any severe adverse event by SOC and PT, week 100					
Cardiac disorders					
KESTREL, n (%)	11 (5.8)	11 (5.9)	0.99 [0.42; 2.34] 0.979	0.99 [0.44; 2.23] 0.979	-0.00 [-0.05; 0.05] 0.979
KITE, n (%)	8 (4.5)	12 (6.6)	0.66 [0.26; 1.65] 0.374	0.67 [0.28; 1.61] 0.375	-0.02 [-0.07; 0.03] 0.370
Pooled Analysis, n (%) p_H=0.528	19 (5.2)	23 (6.3)	0.81 [0.43; 1.52] 0.513	0.83 [0.46; 1.49] 0.525	-0.01 [-0.04; 0.02] 0.524
Eye disorders					
KESTREL, n (%)	9 (4.8)	11 (5.9)	0.80 [0.32; 1.98] 0.629	0.81 [0.34; 1.91] 0.629	-0.01 [-0.06; 0.03] 0.628
KITE, n (%)	5 (2.8)	7 (3.9)	0.71 [0.22; 2.29] 0.572	0.72 [0.23; 2.23] 0.572	-0.01 [-0.05; 0.03] 0.570
Pooled Analysis, n (%) p_H=0.880	14 (3.8)	18 (4.9)	0.76 [0.36; 1.58] 0.457	0.78 [0.39; 1.54] 0.465	-0.01 [-0.04; 0.02] 0.465
Infections and infestations					
KESTREL, n (%)	9 (4.8)	8 (4.3)	1.12 [0.42; 2.96] 0.821	1.11 [0.44; 2.82] 0.821	0.00 [-0.04; 0.05] 0.821
KITE, n (%)	9 (5.0)	5 (2.8)	1.86 [0.61; 5.67] 0.273	1.82 [0.62; 5.33] 0.274	0.02 [-0.02; 0.06] 0.266
Pooled Analysis, n (%) p_H=0.499	18 (4.9)	13 (3.5)	1.44 [0.69; 3.00] 0.336	1.38 [0.69; 2.78] 0.361	0.01 [-0.02; 0.04] 0.360
Nervous system disorders					
KESTREL, n (%)	7 (3.7)	8 (4.3)	0.86 [0.31; 2.42] 0.776	0.87 [0.32; 2.34] 0.776	-0.01 [-0.05; 0.03] 0.776

	Treatment Groups		Comparison		
Any severe adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE, n (%)	6 (3.4)	7 (3.9)	0.86 [0.28; 2.62] 0.793	0.87 [0.30; 2.53] 0.793	-0.01 [-0.04; 0.03] 0.793
Pooled Analysis, n (%) p_H=0.998	13 (3.5)	15 (4.1)	0.86 [0.40; 1.84] 0.700	0.87 [0.42; 1.79] 0.699	-0.01 [-0.03; 0.02] 0.699
Renal and urinary disorders					
KESTREL, n (%)	3 (1.6)	7 (3.7)	0.41 [0.11; 1.63] 0.207	0.42 [0.11; 1.62] 0.209	-0.02 [-0.05; 0.01] 0.194
KITE, n (%)	3 (1.7)	4 (2.2)	0.75 [0.17; 3.42] 0.715	0.76 [0.17; 3.34] 0.715	-0.01 [-0.03; 0.02] 0.713
Pooled Analysis, n (%) p_H=0.565	6 (1.6)	11 (3.0)	0.56 [0.20; 1.54] 0.258	0.54 [0.20; 1.46] 0.219	-0.01 [-0.04; 0.01] 0.218
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
KESTREL, n (%)	4 (2.1)	3 (1.6)	1.33 [0.29; 6.01] 0.714	1.32 [0.30; 5.81] 0.714	0.01 [-0.02; 0.03] 0.713
KITE, n (%)	5 (2.8)	7 (3.9)	0.71 [0.22; 2.29] 0.572	0.72 [0.23; 2.23] 0.572	-0.01 [-0.05; 0.03] 0.570
Pooled Analysis, n (%) p_H=0.525	9 (2.4)	10 (2.7)	0.98 [0.38; 2.56] 0.966	0.90 [0.37; 2.20] 0.822	-0.00 [-0.03; 0.02] 0.821
Respiratory, thoracic and mediastinal disorders					
KESTREL, n (%)	7 (3.7)	3 (1.6)	2.36 [0.60; 9.26] 0.219	2.31 [0.61; 8.79] 0.220	0.02 [-0.01; 0.05] 0.204
KITE, n (%)	3 (1.7)	2 (1.1)	1.53 [0.25; 9.24] 0.646	1.52 [0.26; 8.97] 0.646	0.01 [-0.02; 0.03] 0.644

	Treatment Groups		Comparison		
Any severe adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, n (%) p_H=0.705	10 (2.7)	5 (1.4)	1.91 [0.62; 5.87] 0.261	1.99 [0.69; 5.78] 0.195	0.01 [-0.01; 0.03] 0.193

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 18-1.2 Any severe adverse event by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-1.3 Any severe adverse event by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-1.4 Any severe adverse event by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-1.5 Any severe adverse event by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-1.6 Any severe adverse event by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-1.7 Any severe adverse event by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-1.8 Any severe adverse event by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-1.9 Any severe adverse event by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-1.10 Any severe adverse event by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-1.11 Any severe adverse event by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-1.13 Any severe adverse event by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-2.1 Any severe ocular adverse event by SOC and PT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any severe ocular adverse event by SOC and PT, week 100					
Eye disorders					
KESTREL, n (%)	9 (4.8)	11 (5.9)	0.80 [0.32; 1.98] 0.629	0.81 [0.34; 1.91] 0.629	-0.01 [-0.06; 0.03] 0.628
KITE, n (%)	5 (2.8)	7 (3.9)	0.71 [0.22; 2.29] 0.572	0.72 [0.23; 2.23] 0.572	-0.01 [-0.05; 0.03] 0.570
Pooled Analysis, n (%) p_H=0.880	14 (3.8)	18 (4.9)	0.76 [0.36; 1.58] 0.457	0.78 [0.39; 1.54] 0.465	-0.01 [-0.04; 0.02] 0.465

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 18-2.2 Any severe ocular adverse event by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-2.3 Any severe ocular adverse event by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-2.4 Any severe ocular adverse event by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-2.5 Any severe ocular adverse event by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-2.6 Any severe ocular adverse event by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-2.7 Any severe ocular adverse event by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-2.8 Any severe ocular adverse event by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-2.9 Any severe ocular adverse event by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-2.10 Any severe ocular adverse event by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-2.11 Any severe ocular adverse event by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-2.13 Any severe ocular adverse event by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-3.1 Any severe ocular adverse event at the study eye by SOC and PT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the study eye by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any severe ocular adverse event at the study eye by SOC and PT, week 100					
Eye disorders					
KESTREL, n (%)	5 (2.6)	7 (3.7)	0.70 [0.22; 2.24] 0.547	0.71 [0.23; 2.19] 0.547	-0.01 [-0.05; 0.02] 0.545
KITE, n (%)	4 (2.2)	4 (2.2)	1.01 [0.25; 4.11] 0.987	1.01 [0.26; 3.98] 0.987	0.00 [-0.03; 0.03] 0.987
Pooled Analysis, n (%) p_H=0.691	9 (2.4)	11 (3.0)	0.84 [0.34; 2.08] 0.702	0.82 [0.34; 1.95] 0.647	-0.01 [-0.03; 0.02] 0.647

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 18-3.2 Any severe ocular adverse event at the study eye by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-3.3 Any severe ocular adverse event at the study eye by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-3.4 Any severe ocular adverse event at the study eye by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-3.5 Any severe ocular adverse event at the study eye by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-3.6 Any severe ocular adverse event at the study eye by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-3.7 Any severe ocular adverse event at the study eye by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-3.8 Any severe ocular adverse event at the study eye by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-3.9 Any severe ocular adverse event at the study eye by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-3.10 Any severe ocular adverse event at the study eye by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-3.11 Any severe ocular adverse event at the study eye by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-3.13 Any severe ocular adverse event at the study eye by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-4.1 Any severe ocular adverse event at the fellow eye by SOC and PT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event at the fellow eye by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any severe ocular adverse event at the fellow eye by SOC and PT, week 100					
Eye disorders					
KESTREL, n (%)	4 (2.1)	7 (3.7)	0.56 [0.16; 1.93] 0.356	0.57 [0.17; 1.90] 0.356	-0.02 [-0.05; 0.02] 0.349
KITE, n (%)	2 (1.1)	5 (2.8)	0.40 [0.08; 2.08] 0.274	0.40 [0.08; 2.06] 0.275	-0.02 [-0.04; 0.01] 0.256
Pooled Analysis, n (%) p_H=0.751	6 (1.6)	12 (3.3)	0.47 [0.17; 1.32] 0.153	0.50 [0.19; 1.31] 0.151	-0.02 [-0.04; 0.01] 0.150

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 18-4.2 Any severe ocular adverse event at the fellow eye by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-4.3 Any severe ocular adverse event at the fellow eye by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-4.4 Any severe ocular adverse event at the fellow eye by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-4.5 Any severe ocular adverse event at the fellow eye by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-4.6 Any severe ocular adverse event at the fellow eye by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-4.7 Any severe ocular adverse event at the fellow eye by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-4.8 Any severe ocular adverse event at the fellow eye by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-4.9 Any severe ocular adverse event at the fellow eye by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-4.10 Any severe ocular adverse event at the fellow eye by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-4.11 Any severe ocular adverse event at the fellow eye by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-4.13 Any severe ocular adverse event at the fellow eye by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-5.1 Any severe non-ocular adverse event by SOC and PT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any severe non-ocular adverse event by SOC and PT, week 100					
Cardiac disorders					
KESTREL, n (%)	11 (5.8)	11 (5.9)	0.99 [0.42; 2.34] 0.979	0.99 [0.44; 2.23] 0.979	-0.00 [-0.05; 0.05] 0.979
KITE, n (%)	8 (4.5)	12 (6.6)	0.66 [0.26; 1.65] 0.374	0.67 [0.28; 1.61] 0.375	-0.02 [-0.07; 0.03] 0.370
Pooled Analysis, n (%) p_H=0.528	19 (5.2)	23 (6.3)	0.81 [0.43; 1.52] 0.513	0.83 [0.46; 1.49] 0.525	-0.01 [-0.04; 0.02] 0.524
Infections and infestations					
KESTREL, n (%)	9 (4.8)	7 (3.7)	1.29 [0.47; 3.53] 0.625	1.27 [0.48; 3.35] 0.626	0.01 [-0.03; 0.05] 0.624
KITE, n (%)	7 (3.9)	5 (2.8)	1.43 [0.45; 4.60] 0.546	1.42 [0.46; 4.38] 0.546	0.01 [-0.03; 0.05] 0.544
Pooled Analysis, n (%) p_H=0.891	16 (4.3)	12 (3.3)	1.36 [0.63; 2.93] 0.438	1.33 [0.64; 2.77] 0.443	0.01 [-0.02; 0.04] 0.443
Nervous system disorders					
KESTREL, n (%)	7 (3.7)	8 (4.3)	0.86 [0.31; 2.42] 0.776	0.87 [0.32; 2.34] 0.776	-0.01 [-0.05; 0.03] 0.776
KITE, n (%)	6 (3.4)	7 (3.9)	0.86 [0.28; 2.62] 0.793	0.87 [0.30; 2.53] 0.793	-0.01 [-0.04; 0.03] 0.793
Pooled Analysis, n (%) p_H=0.998	13 (3.5)	15 (4.1)	0.86 [0.40; 1.84] 0.700	0.87 [0.42; 1.79] 0.699	-0.01 [-0.03; 0.02] 0.699
Renal and urinary disorders					
KESTREL, n (%)	3 (1.6)	7 (3.7)	0.41 [0.11; 1.63] 0.207	0.42 [0.11; 1.62] 0.209	-0.02 [-0.05; 0.01] 0.194
KITE, n (%)	3 (1.7)	4 (2.2)	0.75 [0.17; 3.42] 0.715	0.76 [0.17; 3.34] 0.715	-0.01 [-0.03; 0.02] 0.713

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, n (%) p_H=0.565	6 (1.6)	11 (3.0)	0.56 [0.20; 1.54] 0.258	0.54 [0.20; 1.46] 0.219	-0.01 [-0.04; 0.01] 0.218
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
KESTREL, n (%)	4 (2.1)	3 (1.6)	1.33 [0.29; 6.01] 0.714	1.32 [0.30; 5.81] 0.714	0.01 [-0.02; 0.03] 0.713
KITE, n (%)	5 (2.8)	7 (3.9)	0.71 [0.22; 2.29] 0.572	0.72 [0.23; 2.23] 0.572	-0.01 [-0.05; 0.03] 0.570
Pooled Analysis, n (%) p_H=0.525	9 (2.4)	10 (2.7)	0.98 [0.38; 2.56] 0.966	0.90 [0.37; 2.20] 0.822	-0.00 [-0.03; 0.02] 0.821
Respiratory, thoracic and mediastinal disorders					
KESTREL, n (%)	7 (3.7)	3 (1.6)	2.36 [0.60; 9.26] 0.219	2.31 [0.61; 8.79] 0.220	0.02 [-0.01; 0.05] 0.204
KITE, n (%)	3 (1.7)	2 (1.1)	1.53 [0.25; 9.24] 0.646	1.52 [0.26; 8.97] 0.646	0.01 [-0.02; 0.03] 0.644
Pooled Analysis, n (%) p_H=0.705	10 (2.7)	5 (1.4)	1.91 [0.62; 5.87] 0.261	1.99 [0.69; 5.78] 0.195	0.01 [-0.01; 0.03] 0.193

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 18-5.2 Any severe non-ocular adverse event by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-5.3 Any severe non-ocular adverse event by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-5.4 Any severe non-ocular adverse event by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-5.5 Any severe non-ocular adverse event by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-5.6 Any severe non-ocular adverse event by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-5.7 Any severe non-ocular adverse event by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-5.8 Any severe non-ocular adverse event by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-5.9 Any severe non-ocular adverse event by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-5.10 Any severe non-ocular adverse event by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-5.11 Any severe non-ocular adverse event by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 18-5.13 Any severe non-ocular adverse event by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

19 Safety analysis: Any adverse event leading to study drug discontinuation by SOC and PT

Table 19.1 Any adverse event leading to study drug discontinuation by SOC and PT (SAF), binary analysis, week 100

	KESTREL		KITE	
Any adverse event leading to study drug discontinuation by SOC and PT (SAF)	**Brolucizumab** N=189	**Aflibercept** N=187	**Brolucizumab** N=179	**Aflibercept** N=181
N'	189	187	179	181
Eye disorders, n (%)	3 (1.6)	1 (0.5)	3 (1.7)	3 (1.7)
Uveitis, n (%)	1 (0.5)	0 (0.0)	2 (1.1)	1 (0.6)
Diabetic retinal oedema, n (%)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Eye inflammation, n (%)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Iritis, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Retinal aneurysm, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Retinal artery occlusion, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
Neoplasms benign, malignant and unspecified (incl cysts and polyps), n (%)	1 (0.5)	1 (0.5)	1 (0.6)	2 (1.1)
Adenocarcinoma, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Bronchial carcinoma, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Colon cancer, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Pancreatic carcinoma, n (%)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Waldenstrom's macroglobulinaemia, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Cardiac disorders, n (%)	0 (0.0)	2 (1.1)	1 (0.6)	0 (0.0)
Acute myocardial infarction, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Cardiac failure, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Coronary artery disease, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Infections and infestations, n (%)	0 (0.0)	1 (0.5)	1 (0.6)	1 (0.6)
Endophthalmitis, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.6)
COVID-19, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Nervous system disorders, n (%)	0 (0.0)	1 (0.5)	2 (1.1)	1 (0.6)
Bickerstaff's encephalitis, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Cerebellar haemorrhage, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Cerebellar stroke, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Ischaemic stroke, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Renal and urinary disorders, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.6)
Chronic kidney disease, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Renal failure, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)

	KESTREL		KITE	
Any adverse event leading to study drug discontinuation by SOC and PT (SAF)	**Brolucizumab** N=189	**Aflibercept** N=187	**Brolucizumab** N=179	**Aflibercept** N=181
Immune system disorders, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Anaphylactic reaction, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Injury, poisoning and procedural complications, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Subdural haematoma, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Metabolism and nutrition disorders, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Diabetes mellitus inadequate control, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Psychiatric disorders, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Confusional state, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Eye disorders, n (%)	3 (1.6)	1 (0.5)	4 (2.2)	3 (1.7)
Uveitis, n (%)	1 (0.5)	0 (0.0)	2 (1.1)	1 (0.6)
Diabetic retinal oedema, n (%)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Eye inflammation, n (%)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Foreign body sensation in eyes, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Iridocyclitis, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Iritis, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Retinal artery occlusion, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
Infections and infestations, n (%)	0 (0.0)	1 (0.5)	4 (2.2)	1 (0.6)
COVID-19, n (%)	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)
Endophthalmitis, n (%)	0 (0.0)	1 (0.5)	1 (0.6)	1 (0.6)
Pneumonia, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Nervous system disorders, n (%)	1 (0.5)	1 (0.5)	3 (1.7)	1 (0.6)
Cerebrovascular accident, n (%)	1 (0.5)	0 (0.0)	1 (0.6)	0 (0.0)
Bickerstaff's encephalitis, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Cerebellar haemorrhage, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Cerebellar stroke, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Ischaemic stroke, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Cardiac disorders, n (%)	0 (0.0)	3 (1.6)	1 (0.6)	0 (0.0)
Acute myocardial infarction, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Cardiac failure, n (%)	0 (0.0)	1 (0.5)	1 (0.6)	0 (0.0)
Coronary artery disease, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps), n (%)	1 (0.5)	1 (0.5)	1 (0.6)	2 (1.1)
Adenocarcinoma, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Bronchial carcinoma, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)

	KESTREL		KITE	
Any adverse event leading to study drug discontinuation by SOC and PT (SAF)	**Brolucizumab** N=189	**Aflibercept** N=187	**Brolucizumab** N=179	**Aflibercept** N=181
Colon cancer stage I, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Pancreatic carcinoma, n (%)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Waldenstrom's macroglobulinaemia, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Renal and urinary disorders, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.6)
Chronic kidney disease, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Renal failure, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Immune system disorders, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Anaphylactic reaction, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Injury, poisoning and procedural complications, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Subdural haematoma, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Metabolism and nutrition disorders, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Diabetes mellitus inadequate control, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Psychiatric disorders, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Confusional state, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Reproductive system and breast disorders, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Prostatic disorder, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
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Table 19.2 Any ocular adverse event leading to study drug discontinuation by SOC and PT (SAF), binary analysis, week 100

	KESTREL		KITE	
Any ocular adverse event leading to study drug discontinuation by SOC and PT (SAF)	**Brolucizumab** N=189	**Aflibercept** N=187	**Brolucizumab** N=179	**Aflibercept** N=181
N'	189	187	179	181
Eye disorders, n (%)	3 (1.6)	1 (0.5)	3 (1.7)	3 (1.7)
Uveitis, n (%)	1 (0.5)	0 (0.0)	2 (1.1)	1 (0.6)
Diabetic retinal oedema, n (%)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Eye inflammation, n (%)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Iritis, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Retinal aneurysm, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Retinal artery occlusion, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
Infections and infestations, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.6)
Endophthalmitis, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.6)
Eye disorders, n (%)	3 (1.6)	1 (0.5)	4 (2.2)	3 (1.7)
Uveitis, n (%)	1 (0.5)	0 (0.0)	2 (1.1)	1 (0.6)
Diabetic retinal oedema, n (%)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Eye inflammation, n (%)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Foreign body sensation in eyes, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Iridocyclitis, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Iritis, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Retinal artery occlusion, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
Infections and infestations, n (%)	0 (0.0)	1 (0.5)	1 (0.6)	1 (0.6)
Endophthalmitis, n (%)	0 (0.0)	1 (0.5)	1 (0.6)	1 (0.6)

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
.....

Table 19.3 Any ocular adverse event at the study eye leading to study drug discontinuation by SOC and PT (SAF), binary analysis, week 100

	KESTREL		KITE	
Any ocular adverse event at the study eye leading to study drug discontinuation by SOC and PT (SAF)	**Brolucizumab** N=189	**Aflibercept** N=187	**Brolucizumab** N=179	**Aflibercept** N=181
N'	189	187	179	181
Eye disorders, n (%)	3 (1.6)	1 (0.5)	3 (1.7)	3 (1.7)
Uveitis, n (%)	1 (0.5)	0 (0.0)	2 (1.1)	1 (0.6)
Diabetic retinal oedema, n (%)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Eye inflammation, n (%)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Iritis, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Retinal aneurysm, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Retinal artery occlusion, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
Infections and infestations, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.6)
Endophthalmitis, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.6)
Eye disorders, n (%)	3 (1.6)	1 (0.5)	4 (2.2)	3 (1.7)
Uveitis, n (%)	1 (0.5)	0 (0.0)	2 (1.1)	1 (0.6)
Diabetic retinal oedema, n (%)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Eye inflammation, n (%)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Foreign body sensation in eyes, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Iridocyclitis, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Iritis, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Retinal artery occlusion, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	1 (0.6)
Infections and infestations, n (%)	0 (0.0)	1 (0.5)	1 (0.6)	1 (0.6)
Endophthalmitis, n (%)	0 (0.0)	1 (0.5)	1 (0.6)	1 (0.6)

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
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Table 19.4 Any ocular adverse event at the fellow eye leading to study drug discontinuation by SOC and PT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 19.5 Any non-ocular adverse event leading to study drug discontinuation by SOC and PT (SAF), binary analysis, week 100

	KESTREL		KITE	
Any non-ocular adverse event leading to study drug discontinuation by SOC and PT (SAF)	**Brolucizumab** N=189	**Aflibercept** N=187	**Brolucizumab** N=179	**Aflibercept** N=181
N'	189	187	179	181
Neoplasms benign, malignant and unspecified (incl cysts and polyps), n (%)	1 (0.5)	1 (0.5)	1 (0.6)	2 (1.1)
Adenocarcinoma, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Bronchial carcinoma, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Colon cancer, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Pancreatic carcinoma, n (%)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Waldenstrom's macroglobulinaemia, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Cardiac disorders, n (%)	0 (0.0)	2 (1.1)	1 (0.6)	0 (0.0)
Acute myocardial infarction, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Cardiac failure, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Coronary artery disease, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Nervous system disorders, n (%)	0 (0.0)	1 (0.5)	2 (1.1)	1 (0.6)
Bickerstaff's encephalitis, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Cerebellar haemorrhage, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Cerebellar stroke, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Ischaemic stroke, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Renal and urinary disorders, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.6)
Chronic kidney disease, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Renal failure, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Immune system disorders, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Anaphylactic reaction, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Infections and infestations, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
COVID-19, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Injury, poisoning and procedural complications, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Subdural haematoma, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Metabolism and nutrition disorders, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Diabetes mellitus inadequate control, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Psychiatric disorders, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Confusional state, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)

	KESTREL		KITE	
Any non-ocular adverse event leading to study drug discontinuation by SOC and PT (SAF)	**Brolucizumab** N=189	**Aflibercept** N=187	**Brolucizumab** N=179	**Aflibercept** N=181
Nervous system disorders, n (%)	1 (0.5)	1 (0.5)	3 (1.7)	1 (0.6)
Cerebrovascular accident, n (%)	1 (0.5)	0 (0.0)	1 (0.6)	0 (0.0)
Bickerstaff's encephalitis, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Cerebellar haemorrhage, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Cerebellar stroke, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Ischaemic stroke, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Cardiac disorders, n (%)	0 (0.0)	3 (1.6)	1 (0.6)	0 (0.0)
Acute myocardial infarction, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Cardiac failure, n (%)	0 (0.0)	1 (0.5)	1 (0.6)	0 (0.0)
Coronary artery disease, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Infections and infestations, n (%)	0 (0.0)	0 (0.0)	3 (1.7)	0 (0.0)
COVID-19, n (%)	0 (0.0)	0 (0.0)	2 (1.1)	0 (0.0)
Pneumonia, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps), n (%)	1 (0.5)	1 (0.5)	1 (0.6)	2 (1.1)
Adenocarcinoma, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Bronchial carcinoma, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Colon cancer stage I, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Pancreatic carcinoma, n (%)	1 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
Waldenstrom's macroglobulinaemia, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Renal and urinary disorders, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.6)
Chronic kidney disease, n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)
Renal failure, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Immune system disorders, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Anaphylactic reaction, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Injury, poisoning and procedural complications, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Subdural haematoma, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Metabolism and nutrition disorders, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Diabetes mellitus inadequate control, n (%)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
Psychiatric disorders, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Confusional state, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Reproductive system and breast disorders, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)

	KESTREL		KITE	
Any non-ocular adverse event leading to study drug discontinuation by SOC and PT (SAF)	**Brolucizumab** N=189	**Aflibercept** N=187	**Brolucizumab** N=179	**Aflibercept** N=181
Prostatic disorder, n (%)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
.....

20 Safety analysis: Any adverse event of special interest

Table 20-1.1 Any adverse events of special interest by severity (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse events of special interest by severity (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any adverse events of special interest by severity, week 100					
Endophthalmitis					
KESTREL, n (%)	0 (0.0)	1 (0.5)	N.E.	0.33 [0.01; 8.05] 0.496	-0.01 [-0.02; 0.01] 0.316
KITE, n (%)	2 (1.1)	1 (0.6)	2.03 [0.18; 22.63] 0.564	2.02 [0.19; 22.11] 0.564	0.01 [-0.01; 0.02] 0.556
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	2 (0.5)	N.E.	1.00 [0.18; 5.73] 0.998	0.00 [-0.01; 0.01] 0.995
Endophthalmitis severe					
KESTREL, n (%)	0 (0.0)	1 (0.5)	N.E.	0.33 [0.01; 8.05] 0.496	-0.01 [-0.02; 0.01] 0.316
KITE, n (%)	2 (1.1)	0 (0.0)	N.E.	5.06 [0.24; 104.57] 0.294	0.01 [-0.00; 0.03] 0.155
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	1 (0.3)	N.E.	1.50 [0.25; 8.90] 0.652	0.00 [-0.01; 0.01] 0.562
Endophthalmitis serious					
KESTREL, n (%)	0 (0.0)	1 (0.5)	N.E.	0.33 [0.01; 8.05] 0.496	-0.01 [-0.02; 0.01] 0.316
KITE, n (%)	2 (1.1)	1 (0.6)	2.03 [0.18; 22.63] 0.564	2.02 [0.19; 22.11] 0.564	0.01 [-0.01; 0.02] 0.556
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	2 (0.5)	N.E.	1.00 [0.18; 5.73] 0.998	0.00 [-0.01; 0.01] 0.995
Intraocular inflammation					
KESTREL, n (%)	9 (4.8)	2 (1.1)	4.62 [0.99; 21.70] 0.052	4.45 [0.97; 20.33] 0.054	0.04 [0.00; 0.07] 0.032 *

	Treatment Groups		Comparison		
Any adverse events of special interest by severity (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE, n (%)	5 (2.8)	4 (2.2)	1.27 [0.34; 4.81] 0.724	1.26 [0.35; 4.63] 0.724	0.01 [-0.03; 0.04] 0.723
Pooled Analysis, n (%) p_H=0.215	14 (3.8)	6 (1.6)	2.46 [0.88; 6.83] 0.085	2.33 [0.90; 6.02] 0.070	0.02 [-0.00; 0.05] 0.069
Intraocular inflammation severe					
KESTREL, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, n (%)	2 (1.1)	0 (0.0)	N.E.	5.06 [0.24; 104.57] 0.294	0.01 [-0.00; 0.03] 0.155
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	0 (0.0)	N.E.	5.06 [0.24; 104.57] 0.243	0.01 [-0.00; 0.01] 0.155
Intraocular inflammation serious					
KESTREL, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, n (%)	1 (0.6)	1 (0.6)	1.01 [0.06; 16.29] 0.994	1.01 [0.06; 16.04] 0.994	0.00 [-0.02; 0.02] 0.994
Pooled Analysis, n (%) p_H=N.E.	1 (0.3)	1 (0.3)	N.E.	1.01 [0.06; 16.04] 0.994	0.00 [-0.01; 0.01] 0.994
Retinal vascular occlusion					
KESTREL, n (%)	3 (1.6)	1 (0.5)	3.00 [0.31; 29.10] 0.343	2.97 [0.31; 28.28] 0.344	0.01 [-0.01; 0.03] 0.318
KITE, n (%)	1 (0.6)	4 (2.2)	0.25 [0.03; 2.25] 0.215	0.25 [0.03; 2.24] 0.217	-0.02 [-0.04; 0.01] 0.178
Pooled Analysis, n (%) p_H=0.123	4 (1.1)	5 (1.4)	0.89 [0.18; 4.31] 0.880	0.80 [0.22; 2.98] 0.739	-0.00 [-0.02; 0.01] 0.739
Retinal vascular occlusion severe					
KESTREL, n (%)	1 (0.5)	1 (0.5)	0.99 [0.06; 15.93] 0.994	0.99 [0.06; 15.70] 0.994	-0.00 [-0.01; 0.01] 0.994
KITE, n (%)	1 (0.6)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.496	0.01 [-0.01; 0.02] 0.316
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	1 (0.3)	N.E.	1.67 [0.22; 12.51] 0.616	0.00 [-0.01; 0.01] 0.565
Retinal vascular occlusion serious					
KESTREL, n (%)	1 (0.5)	0 (0.0)	N.E.	2.97 [0.12; 72.41] 0.504	0.01 [-0.01; 0.02] 0.316

	Treatment Groups		Comparison		
Any adverse events of special interest by severity (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE, n (%)	1 (0.6)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.496	0.01 [-0.01; 0.02] 0.316
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	0 (0.0)	N.E.	3.00 [0.31; 28.71] 0.317	0.01 [-0.00; 0.01] 0.156

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 20-1.2 Any adverse events of special interest by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse events of special interest by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
< 65 years, N'/N	104 / 104	93 / 93			
≥ 65 years, N'/N	85 / 85	94 / 94			
KITE, N'/N	179 / 179	181 / 181			
< 65 years, N'/N	100 / 100	102 / 102			
≥ 65 years, N'/N	79 / 79	79 / 79			
Pooled Analysis, N'/N	368 / 368	368 / 368			
< 65 years, N'/N	204 / 204	195 / 195			
≥ 65 years, N'/N	164 / 164	173 / 173			
Any adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	N.E.				
< 65 years, n (%)	4 (3.8)	0 (0.0)	N.E.	8.06 [0.44; 147.68] 0.160	0.04 [0.00; 0.08] 0.041 *
≥ 65 years, n (%)	5 (5.9)	2 (2.1)	2.87 [0.54; 15.23] 0.214	2.76 [0.55; 13.88] 0.217	0.04 [-0.02; 0.10] 0.204
KITE					
Interaction Test:	p = 0.627				
< 65 years, n (%)	2 (2.0)	1 (1.0)	2.06 [0.18; 23.10] 0.557	2.04 [0.19; 22.14] 0.558	0.01 [-0.02; 0.04] 0.550
≥ 65 years, n (%)	3 (3.8)	3 (3.8)	1.00 [0.20; 5.11] 1.000	1.00 [0.21; 4.80] 1.000	0.00 [-0.06; 0.06] 1.000
Pooled Analysis					
Interaction Test:	p = 0.296				
< 65 years, n (%)	6 (2.9)	1 (0.5)	6.35 [0.73; 55.41] 0.095	4.13 [0.69; 24.64] 0.090	0.02 [-0.00; 0.05] 0.060

	Treatment Groups		Comparison		
Any adverse events of special interest by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years, n (%)	8 (4.9)	5 (2.9)	1.75 [0.54; 5.72] 0.353	1.68 [0.57; 5.02] 0.344	0.02 [-0.02; 0.06] 0.347

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL: logit(proportion) = treatment [by age].

Table 20-1.3 Any adverse events of special interest by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse events of special interest by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Male, N'/N	110 / 110	126 / 126			
Female, N'/N	79 / 79	61 / 61			
KITE, N'/N	179 / 179	181 / 181			
Male, N'/N	120 / 120	115 / 115			
Female, N'/N	59 / 59	66 / 66			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Male, N'/N	230 / 230	241 / 241			
Female, N'/N	138 / 138	127 / 127			
Any adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.695				
Male, n (%)	5 (4.5)	1 (0.8)	5.95 [0.68; 51.75] 0.106	5.73 [0.68; 48.28] 0.109	0.04 [-0.00; 0.08] 0.079
Female, n (%)	4 (5.1)	1 (1.6)	3.20 [0.35; 29.39] 0.304	3.09 [0.35; 26.93] 0.307	0.03 [-0.02; 0.09] 0.246
KITE					
Interaction Test:	p = 0.295				
Male, n (%)	1 (0.8)	2 (1.7)	0.47 [0.04; 5.31] 0.545	0.48 [0.04; 5.21] 0.546	-0.01 [-0.04; 0.02] 0.539
Female, n (%)	4 (6.8)	2 (3.0)	2.33 [0.41; 13.20] 0.340	2.24 [0.43; 11.77] 0.342	0.04 [-0.04; 0.11] 0.336
Pooled Analysis					
Interaction Test:	p = 0.868				
Male, n (%)	6 (2.6)	3 (1.2)	2.21 [0.53; 9.22] 0.276	2.12 [0.55; 8.15] 0.260	0.01 [-0.01; 0.04] 0.270

	Treatment Groups		Comparison		
Any adverse events of special interest by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female, n (%)	8 (5.8)	3 (2.4)	2.61 [0.64; 10.60] 0.180	2.56 [0.68; 9.56] 0.148	0.04 [-0.01; 0.08] 0.138

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 20-1.4 Any adverse events of special interest by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse events of special interest by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
≤ 65 letters, N'/N	74 / 74	64 / 64			
> 65 letters, N'/N	115 / 115	123 / 123			
KITE, N'/N	179 / 179	181 / 181			
≤ 65 letters, N'/N	65 / 65	91 / 91			
> 65 letters, N'/N	114 / 114	90 / 90			
Pooled Analysis, N'/N	368 / 368	368 / 368			
≤ 65 letters, N'/N	139 / 139	155 / 155			
> 65 letters, N'/N	229 / 229	213 / 213			
Any adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	N.E.				
≤ 65 letters, n (%)	2 (2.7)	0 (0.0)	N.E.	4.33 [0.21; 88.63] 0.341	0.03 [-0.01; 0.06] 0.152
> 65 letters, n (%)	7 (6.1)	2 (1.6)	3.92 [0.80; 19.28] 0.093	3.74 [0.79; 17.65] 0.095	0.04 [-0.00; 0.09] 0.075
KITE					
Interaction Test:	p = 0.228				
≤ 65 letters, n (%)	1 (1.5)	3 (3.3)	0.46 [0.05; 4.51] 0.504	0.47 [0.05; 4.39] 0.505	-0.02 [-0.06; 0.03] 0.467
> 65 letters, n (%)	4 (3.5)	1 (1.1)	3.24 [0.36; 29.45] 0.297	3.16 [0.36; 27.76] 0.300	0.02 [-0.02; 0.06] 0.242
Pooled Analysis					
Interaction Test:	p = 0.320				
≤ 65 letters, n (%)	3 (2.2)	3 (1.9)	1.20 [0.22; 6.46] 0.832	1.15 [0.24; 5.50] 0.862	0.00 [-0.03; 0.04] 0.823

	Treatment Groups		Comparison		
Any adverse events of special interest by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters, n (%)	11 (4.8)	3 (1.4)	3.46 [0.93; 12.83] 0.063	3.53 [1.00; 12.46] 0.036 *	0.04 [0.00; 0.07] 0.032 *

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL: logit(proportion) = treatment [by BCVA].

Table 20-1.5 Any adverse events of special interest by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-1.6 Any adverse events of special interest by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse events of special interest by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Type 1, N'/N	12 / 12	6 / 6			
Type 2, N'/N	177 / 177	181 / 181			
KITE, N'/N	179 / 179	181 / 181			
Type 1, N'/N	19 / 19	7 / 7			
Type 2, N'/N	160 / 160	174 / 174			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Type 1, N'/N	31 / 31	13 / 13			
Type 2, N'/N	337 / 337	355 / 355			
Any adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2, n (%)	9 (5.1)	2 (1.1)	4.79 [1.02; 22.51] 0.047 *	4.60 [1.01; 21.00] 0.049 *	0.04 [0.00; 0.08] 0.029 *
KITE					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2, n (%)	5 (3.1)	4 (2.3)	1.37 [0.36; 5.20] 0.643	1.36 [0.37; 4.97] 0.643	0.01 [-0.03; 0.04] 0.643
Pooled Analysis					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any adverse events of special interest by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2, n (%)	14 (4.2)	6 (1.7)	2.60 [0.93; 7.23] 0.068	2.46 [0.95; 6.37] 0.054	0.02 [-0.00; 0.05] 0.055

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL, Week 100 / Intraocular inflammation / KITE: logit(proportion) = treatment [by diabetes type].
Week 100 / Intraocular inflammation / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 20-1.7 Any adverse events of special interest by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse events of special interest by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	188 / 188	187 / 187			
< 7.5 %, N'/N	76 / 76	107 / 107			
≥ 7.5 %, N'/N	112 / 112	80 / 80			
KITE, N'/N	179 / 179	181 / 181			
< 7.5 %, N'/N	82 / 82	96 / 96			
≥ 7.5 %, N'/N	97 / 97	85 / 85			
Pooled Analysis, N'/N	367 / 367	368 / 368			
< 7.5 %, N'/N	158 / 158	203 / 203			
≥ 7.5 %, N'/N	209 / 209	165 / 165			
Any adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.768				
< 7.5 %, n (%)	4 (5.3)	1 (0.9)	5.89 [0.64; 53.77] 0.116	5.63 [0.64; 49.40] 0.119	0.04 [-0.01; 0.10] 0.112
≥ 7.5 %, n (%)	5 (4.5)	1 (1.3)	3.69 [0.42; 32.22] 0.237	3.57 [0.43; 29.99] 0.241	0.03 [-0.01; 0.08] 0.165
KITE					
Interaction Test:	p = 0.999				
< 7.5 %, n (%)	1 (1.2)	1 (1.0)	1.17 [0.07; 19.05] 0.911	1.17 [0.07; 18.43] 0.911	0.00 [-0.03; 0.03] 0.911
≥ 7.5 %, n (%)	4 (4.1)	3 (3.5)	1.18 [0.26; 5.41] 0.835	1.17 [0.27; 5.07] 0.835	0.01 [-0.05; 0.06] 0.834
Pooled Analysis					
Interaction Test:	p = 0.567				
< 7.5 %, n (%)	5 (3.2)	2 (1.0)	3.38 [0.63; 18.11] 0.155	3.29 [0.66; 16.30] 0.123	0.02 [-0.01; 0.05] 0.151

	Treatment Groups		Comparison		
Any adverse events of special interest by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %, n (%)	9 (4.3)	4 (2.4)	1.86 [0.53; 6.50] 0.329	1.81 [0.56; 5.87] 0.315	0.02 [-0.02; 0.06] 0.296

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 20-1.8 Any adverse events of special interest by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse events of special interest by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
≤ 3 months, N'/N	120 / 120	110 / 110			
> 3 - < 12 months, N'/N	30 / 30	39 / 39			
≥ 12 months, N'/N	39 / 39	38 / 38			
KITE, N'/N	179 / 179	181 / 181			
≤ 3 months, N'/N	85 / 85	92 / 92			
> 3 - < 12 months, N'/N	51 / 51	49 / 49			
≥ 12 months, N'/N	43 / 43	40 / 40			
Pooled Analysis, N'/N	368 / 368	368 / 368			
≤ 3 months, N'/N	205 / 205	202 / 202			
> 3 - < 12 months, N'/N	81 / 81	88 / 88			
≥ 12 months, N'/N	82 / 82	78 / 78			
Any adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months, n (%)	6 (5.0)	1 (0.9)	5.74 [0.68; 48.43] 0.108	5.50 [0.67; 44.96] 0.112	0.04 [-0.00; 0.08] 0.061
> 3 - < 12 months, n (%)	2 (6.7)	0 (0.0)	N.E.	6.45 [0.32; 129.57] 0.223	0.07 [-0.02; 0.16] 0.143
≥ 12 months, n (%)	1 (2.6)	1 (2.6)	0.97 [0.06; 16.15] 0.985	0.97 [0.06; 15.02] 0.985	-0.00 [-0.07; 0.07] 0.985
KITE					
Interaction Test:	N.E.				
≤ 3 months, n (%)	4 (4.7)	2 (2.2)	2.22 [0.40; 12.46] 0.364	2.16 [0.41; 11.52] 0.365	0.03 [-0.03; 0.08] 0.358
> 3 - < 12 months, n (%)	0 (0.0)	1 (2.0)	N.E.	0.32 [0.01; 7.68] 0.483	-0.02 [-0.06; 0.02] 0.312
≥ 12 months, n (%)	1 (2.3)	1 (2.5)	0.93 [0.06; 15.36] 0.959	0.93 [0.06; 14.38] 0.959	-0.00 [-0.07; 0.06] 0.959

	Treatment Groups		Comparison		
Any adverse events of special interest by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.619				
≤ 3 months, n (%)	10 (4.9)	3 (1.5)	3.35 [0.87; 12.82] 0.078	3.34 [0.92; 12.12] 0.051	0.03 [0.00; 0.07] 0.048 *
> 3 - < 12 months, n (%)	2 (2.5)	1 (1.1)	2.57 [0.22; 29.89] 0.451	1.68 [0.31; 9.14] 0.542	0.01 [-0.03; 0.06] 0.495
≥ 12 months, n (%)	2 (2.4)	2 (2.6)	1.02 [0.14; 7.66] 0.984	0.95 [0.14; 6.59] 0.961	-0.00 [-0.05; 0.05] 0.960

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL, Week 100 / Intraocular inflammation / KITE: logit(proportion) = treatment [by duration of DME].

Table 20-1.9 Any adverse events of special interest by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse events of special interest by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	186 / 186	182 / 182			
focal, N'/N	59 / 59	48 / 48			
diffuse, N'/N	127 / 127	134 / 134			
KITE, N'/N	178 / 178	175 / 175			
focal, N'/N	63 / 63	66 / 66			
diffuse, N'/N	115 / 115	109 / 109			
Pooled Analysis, N'/N	364 / 364	357 / 357			
focal, N'/N	122 / 122	114 / 114			
diffuse, N'/N	242 / 242	243 / 243			
Any adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	N.E.				
focal, n (%)	1 (1.7)	0 (0.0)	N.E.	2.45 [0.10; 58.81] 0.581	0.02 [-0.02; 0.05] 0.313
diffuse, n (%)	8 (6.3)	2 (1.5)	4.44 [0.92; 21.31] 0.063	4.22 [0.91; 19.50] 0.065	0.05 [0.00; 0.10] 0.045 *
KITE					
Interaction Test:	p = 0.820				
focal, n (%)	2 (3.2)	2 (3.0)	1.05 [0.14; 7.68] 0.962	1.05 [0.15; 7.21] 0.962	0.00 [-0.06; 0.06] 0.962
diffuse, n (%)	3 (2.6)	2 (1.8)	1.43 [0.23; 8.75] 0.697	1.42 [0.24; 8.35] 0.697	0.01 [-0.03; 0.05] 0.694
Pooled Analysis					
Interaction Test:	p = 0.594				
focal, n (%)	3 (2.5)	2 (1.8)	1.57 [0.24; 10.13] 0.634	1.36 [0.27; 6.87] 0.713	0.01 [-0.03; 0.04] 0.649

	Treatment Groups		Comparison		
Any adverse events of special interest by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse, n (%)	11 (4.5)	4 (1.6)	2.83 [0.86; 9.33] 0.087	2.78 [0.90; 8.56] 0.061	0.03 [-0.00; 0.06] 0.062

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL: logit(proportion) = treatment [by DME type].

Table 20-1.10 Any adverse events of special interest by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse events of special interest by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
< 450 µm, N'/N	107 / 107	96 / 96			
≥ 450 - < 650 µm, N'/N	70 / 70	71 / 71			
≥ 650 µm, N'/N	12 / 12	20 / 20			
KITE, N'/N	179 / 179	180 / 180			
< 450 µm, N'/N	85 / 85	82 / 82			
≥ 450 - < 650 µm, N'/N	74 / 74	79 / 79			
≥ 650 µm, N'/N	20 / 20	19 / 19			
Pooled Analysis, N'/N	368 / 368	367 / 367			
< 450 µm, N'/N	192 / 192	178 / 178			
≥ 450 - < 650 µm, N'/N	144 / 144	150 / 150			
≥ 650 µm, N'/N	32 / 32	39 / 39			
Any adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	N.E.				
< 450 µm, n (%)	6 (5.6)	0 (0.0)	N.E.	11.68 [0.67; 204.56] 0.093	0.06 [0.01; 0.10] 0.012 *
≥ 450 - < 650 µm, n (%)	3 (4.3)	2 (2.8)	1.54 [0.25; 9.54] 0.640	1.52 [0.26; 8.83] 0.640	0.01 [-0.05; 0.08] 0.637
≥ 650 µm, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE					
Interaction Test:	N.E.				
< 450 µm, n (%)	3 (3.5)	2 (2.4)	1.46 [0.24; 8.99] 0.681	1.45 [0.25; 8.44] 0.681	0.01 [-0.04; 0.06] 0.678
≥ 450 - < 650 µm, n (%)	2 (2.7)	2 (2.5)	1.07 [0.15; 7.79] 0.947	1.07 [0.15; 7.39] 0.947	0.00 [-0.05; 0.05] 0.947
≥ 650 µm, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any adverse events of special interest by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	N.E.				
< 450 µm, n (%)	9 (4.7)	2 (1.1)	N.E.	3.55 [0.88; 14.29] 0.056	0.04 [0.00; 0.07] 0.038 *
≥ 450 - < 650 µm, n (%)	5 (3.5)	4 (2.7)	1.29 [0.34; 4.95] 0.711	1.30 [0.35; 4.74] 0.694	0.01 [-0.03; 0.05] 0.693
≥ 650 µm, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL, Week 100 / Intraocular inflammation / KITE: logit(proportion) = treatment [by CSFT].
Week 100 / Intraocular inflammation / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by CSFT].

Table 20-1.11 Any adverse events of special interest by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse events of special interest by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
presence, N'/N	62 / 62	61 / 61			
absence, N'/N	127 / 127	126 / 126			
KITE, N'/N	179 / 179	181 / 181			
presence, N'/N	56 / 56	67 / 67			
absence, N'/N	123 / 123	114 / 114			
Pooled Analysis, N'/N	368 / 368	368 / 368			
presence, N'/N	118 / 118	128 / 128			
absence, N'/N	250 / 250	240 / 240			
Any adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.657				
presence, n (%)	3 (4.8)	1 (1.6)	3.05 [0.31; 30.17] 0.340	2.95 [0.32; 27.60] 0.343	0.03 [-0.03; 0.09] 0.313
absence, n (%)	6 (4.7)	1 (0.8)	6.20 [0.74; 52.24] 0.093	5.95 [0.73; 48.74] 0.096	0.04 [-0.00; 0.08] 0.054
KITE					
Interaction Test:	N.E.				
presence, n (%)	0 (0.0)	1 (1.5)	N.E.	0.40 [0.02; 9.57] 0.570	-0.01 [-0.04; 0.01] 0.314
absence, n (%)	5 (4.1)	3 (2.6)	1.57 [0.37; 6.71] 0.545	1.54 [0.38; 6.32] 0.545	0.01 [-0.03; 0.06] 0.538
Pooled Analysis					
Interaction Test:	p = 0.663				
presence, n (%)	3 (2.5)	2 (1.6)	1.72 [0.27; 10.91] 0.567	1.48 [0.29; 7.64] 0.637	0.01 [-0.03; 0.04] 0.631

	Treatment Groups		Comparison		
Any adverse events of special interest by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence, n (%)	11 (4.4)	4 (1.7)	2.77 [0.83; 9.19] 0.096	2.62 [0.85; 8.07] 0.081	0.03 [-0.00; 0.06] 0.077

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KITE: logit(proportion) = treatment [by status of SRF].

Table 20-1.13 Any adverse events of special interest by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse events of special interest by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Non-exposed, N'/N	12 / 12	13 / 13			
Exposed, N'/N	177 / 177	174 / 174			
KITE, N'/N	179 / 179	181 / 181			
Non-exposed, N'/N	17 / 17	12 / 12			
Exposed, N'/N	162 / 162	169 / 169			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Non-exposed, N'/N	29 / 29	25 / 25			
Exposed, N'/N	339 / 339	343 / 343			
Any adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Exposed, n (%)	9 (5.1)	2 (1.1)	4.61 [0.98; 21.64] 0.053	4.42 [0.97; 20.18] 0.055	0.04 [0.00; 0.08] 0.032 *
KITE					
Interaction Test:	N.E.				
Non-exposed, n (%)	1 (5.9)	0 (0.0)	N.E.	2.17 [0.10; 49.07] 0.627	0.06 [-0.05; 0.17] 0.303
Exposed, n (%)	4 (2.5)	4 (2.4)	1.04 [0.26; 4.25] 0.952	1.04 [0.27; 4.10] 0.952	0.00 [-0.03; 0.03] 0.952
Pooled Analysis					
Interaction Test:	N.E.				
Non-exposed, n (%)	1 (3.4)	0 (0.0)	N.E.	2.17 [0.10; 49.07] 0.622	0.03 [-0.03; 0.09] 0.338

	Treatment Groups		Comparison		
Any adverse events of special interest by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed, n (%)	13 (3.8)	6 (1.7)	2.23 [0.78; 6.34] 0.134	2.19 [0.84; 5.74] 0.100	0.02 [-0.00; 0.05] 0.099

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL, Week 100 / Intraocular inflammation / KITE: logit(proportion) = treatment [by exposure (week 100)].
Week 100 / Intraocular inflammation / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by exposure (week 100)].

Table 20-2.1 Any ocular adverse events of special interest by severity (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by severity (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular adverse events of special interest by severity, week 100					
Endophthalmitis					
KESTREL, n (%)	0 (0.0)	1 (0.5)	N.E.	0.33 [0.01; 8.05] 0.496	-0.01 [-0.02; 0.01] 0.316
KITE, n (%)	2 (1.1)	1 (0.6)	2.03 [0.18; 22.63] 0.564	2.02 [0.19; 22.11] 0.564	0.01 [-0.01; 0.02] 0.556
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	2 (0.5)	N.E.	1.00 [0.18; 5.73] 0.998	0.00 [-0.01; 0.01] 0.995
Endophthalmitis severe					
KESTREL, n (%)	0 (0.0)	1 (0.5)	N.E.	0.33 [0.01; 8.05] 0.496	-0.01 [-0.02; 0.01] 0.316
KITE, n (%)	2 (1.1)	0 (0.0)	N.E.	5.06 [0.24; 104.57] 0.294	0.01 [-0.00; 0.03] 0.155
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	1 (0.3)	N.E.	1.50 [0.25; 8.90] 0.652	0.00 [-0.01; 0.01] 0.562
Endophthalmitis serious					
KESTREL, n (%)	0 (0.0)	1 (0.5)	N.E.	0.33 [0.01; 8.05] 0.496	-0.01 [-0.02; 0.01] 0.316
KITE, n (%)	2 (1.1)	1 (0.6)	2.03 [0.18; 22.63] 0.564	2.02 [0.19; 22.11] 0.564	0.01 [-0.01; 0.02] 0.556
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	2 (0.5)	N.E.	1.00 [0.18; 5.73] 0.998	0.00 [-0.01; 0.01] 0.995
Intraocular inflammation					
KESTREL, n (%)	9 (4.8)	2 (1.1)	4.62 [0.99; 21.70] 0.052	4.45 [0.97; 20.33] 0.054	0.04 [0.00; 0.07] 0.032 *
KITE, n (%)	5 (2.8)	4 (2.2)	1.27 [0.34; 4.81] 0.724	1.26 [0.35; 4.63] 0.724	0.01 [-0.03; 0.04] 0.723

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by severity (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, n (%) p_H=0.215	14 (3.8)	6 (1.6)	2.46 [0.88; 6.83] 0.085	2.33 [0.90; 6.02] 0.070	0.02 [-0.00; 0.05] 0.069
Intraocular inflammation severe					
KESTREL, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, n (%)	2 (1.1)	0 (0.0)	N.E.	5.06 [0.24; 104.57] 0.294	0.01 [-0.00; 0.03] 0.155
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	0 (0.0)	N.E.	5.06 [0.24; 104.57] 0.243	0.01 [-0.00; 0.01] 0.155
Intraocular inflammation serious					
KESTREL, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, n (%)	1 (0.6)	1 (0.6)	1.01 [0.06; 16.29] 0.994	1.01 [0.06; 16.04] 0.994	0.00 [-0.02; 0.02] 0.994
Pooled Analysis, n (%) p_H=N.E.	1 (0.3)	1 (0.3)	N.E.	1.01 [0.06; 16.04] 0.994	0.00 [-0.01; 0.01] 0.994
Retinal vascular occlusion					
KESTREL, n (%)	3 (1.6)	1 (0.5)	3.00 [0.31; 29.10] 0.343	2.97 [0.31; 28.28] 0.344	0.01 [-0.01; 0.03] 0.318
KITE, n (%)	1 (0.6)	4 (2.2)	0.25 [0.03; 2.25] 0.215	0.25 [0.03; 2.24] 0.217	-0.02 [-0.04; 0.01] 0.178
Pooled Analysis, n (%) p_H=0.123	4 (1.1)	5 (1.4)	0.89 [0.18; 4.31] 0.880	0.80 [0.22; 2.98] 0.739	-0.00 [-0.02; 0.01] 0.739
Retinal vascular occlusion severe					
KESTREL, n (%)	1 (0.5)	1 (0.5)	0.99 [0.06; 15.93] 0.994	0.99 [0.06; 15.70] 0.994	-0.00 [-0.01; 0.01] 0.994
KITE, n (%)	1 (0.6)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.496	0.01 [-0.01; 0.02] 0.316
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	1 (0.3)	N.E.	1.67 [0.22; 12.51] 0.616	0.00 [-0.01; 0.01] 0.565
Retinal vascular occlusion serious					
KESTREL, n (%)	1 (0.5)	0 (0.0)	N.E.	2.97 [0.12; 72.41] 0.504	0.01 [-0.01; 0.02] 0.316
KITE, n (%)	1 (0.6)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.496	0.01 [-0.01; 0.02] 0.316

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by severity (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	0 (0.0)	N.E.	3.00 [0.31; 28.71] 0.317	0.01 [-0.00; 0.01] 0.156

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 20-2.2 Any ocular adverse events of special interest by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
< 65 years, N'/N	104 / 104	93 / 93			
≥ 65 years, N'/N	85 / 85	94 / 94			
KITE, N'/N	179 / 179	181 / 181			
< 65 years, N'/N	100 / 100	102 / 102			
≥ 65 years, N'/N	79 / 79	79 / 79			
Pooled Analysis, N'/N	368 / 368	368 / 368			
< 65 years, N'/N	204 / 204	195 / 195			
≥ 65 years, N'/N	164 / 164	173 / 173			
Any ocular adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	N.E.				
< 65 years, n (%)	4 (3.8)	0 (0.0)	N.E.	8.06 [0.44; 147.68] 0.160	0.04 [0.00; 0.08] 0.041 *
≥ 65 years, n (%)	5 (5.9)	2 (2.1)	2.87 [0.54; 15.23] 0.214	2.76 [0.55; 13.88] 0.217	0.04 [-0.02; 0.10] 0.204
KITE					
Interaction Test:	p = 0.627				
< 65 years, n (%)	2 (2.0)	1 (1.0)	2.06 [0.18; 23.10] 0.557	2.04 [0.19; 22.14] 0.558	0.01 [-0.02; 0.04] 0.550
≥ 65 years, n (%)	3 (3.8)	3 (3.8)	1.00 [0.20; 5.11] 1.000	1.00 [0.21; 4.80] 1.000	0.00 [-0.06; 0.06] 1.000
Pooled Analysis					
Interaction Test:	p = 0.296				
< 65 years, n (%)	6 (2.9)	1 (0.5)	6.35 [0.73; 55.41] 0.095	4.13 [0.69; 24.64] 0.090	0.02 [-0.00; 0.05] 0.060

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years, n (%)	8 (4.9)	5 (2.9)	1.75 [0.54; 5.72] 0.353	1.68 [0.57; 5.02] 0.344	0.02 [-0.02; 0.06] 0.347

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL: logit(proportion) = treatment [by age].

Table 20-2.3 Any ocular adverse events of special interest by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Male, N'/N	110 / 110	126 / 126			
Female, N'/N	79 / 79	61 / 61			
KITE, N'/N	179 / 179	181 / 181			
Male, N'/N	120 / 120	115 / 115			
Female, N'/N	59 / 59	66 / 66			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Male, N'/N	230 / 230	241 / 241			
Female, N'/N	138 / 138	127 / 127			
Any ocular adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.695				
Male, n (%)	5 (4.5)	1 (0.8)	5.95 [0.68; 51.75] 0.106	5.73 [0.68; 48.28] 0.109	0.04 [-0.00; 0.08] 0.079
Female, n (%)	4 (5.1)	1 (1.6)	3.20 [0.35; 29.39] 0.304	3.09 [0.35; 26.93] 0.307	0.03 [-0.02; 0.09] 0.246
KITE					
Interaction Test:	p = 0.295				
Male, n (%)	1 (0.8)	2 (1.7)	0.47 [0.04; 5.31] 0.545	0.48 [0.04; 5.21] 0.546	-0.01 [-0.04; 0.02] 0.539
Female, n (%)	4 (6.8)	2 (3.0)	2.33 [0.41; 13.20] 0.340	2.24 [0.43; 11.77] 0.342	0.04 [-0.04; 0.11] 0.336
Pooled Analysis					
Interaction Test:	p = 0.868				
Male, n (%)	6 (2.6)	3 (1.2)	2.21 [0.53; 9.22] 0.276	2.12 [0.55; 8.15] 0.260	0.01 [-0.01; 0.04] 0.270

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female, n (%)	8 (5.8)	3 (2.4)	2.61 [0.64; 10.60] 0.180	2.56 [0.68; 9.56] 0.148	0.04 [-0.01; 0.08] 0.138

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 20-2.4 Any ocular adverse events of special interest by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
≤ 65 letters, N'/N	74 / 74	64 / 64			
> 65 letters, N'/N	115 / 115	123 / 123			
KITE, N'/N	179 / 179	181 / 181			
≤ 65 letters, N'/N	65 / 65	91 / 91			
> 65 letters, N'/N	114 / 114	90 / 90			
Pooled Analysis, N'/N	368 / 368	368 / 368			
≤ 65 letters, N'/N	139 / 139	155 / 155			
> 65 letters, N'/N	229 / 229	213 / 213			
Any ocular adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	N.E.				
≤ 65 letters, n (%)	2 (2.7)	0 (0.0)	N.E.	4.33 [0.21; 88.63] 0.341	0.03 [-0.01; 0.06] 0.152
> 65 letters, n (%)	7 (6.1)	2 (1.6)	3.92 [0.80; 19.28] 0.093	3.74 [0.79; 17.65] 0.095	0.04 [-0.00; 0.09] 0.075
KITE					
Interaction Test:	p = 0.228				
≤ 65 letters, n (%)	1 (1.5)	3 (3.3)	0.46 [0.05; 4.51] 0.504	0.47 [0.05; 4.39] 0.505	-0.02 [-0.06; 0.03] 0.467
> 65 letters, n (%)	4 (3.5)	1 (1.1)	3.24 [0.36; 29.45] 0.297	3.16 [0.36; 27.76] 0.300	0.02 [-0.02; 0.06] 0.242
Pooled Analysis					
Interaction Test:	p = 0.320				
≤ 65 letters, n (%)	3 (2.2)	3 (1.9)	1.20 [0.22; 6.46] 0.832	1.15 [0.24; 5.50] 0.862	0.00 [-0.03; 0.04] 0.823

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters, n (%)	11 (4.8)	3 (1.4)	3.46 [0.93; 12.83] 0.063	3.53 [1.00; 12.46] 0.036 *	0.04 [0.00; 0.07] 0.032 *

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL: logit(proportion) = treatment [by BCVA].

Table 20-2.5 Any ocular adverse events of special interest by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-2.6 Any ocular adverse events of special interest by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Type 1, N'/N	12 / 12	6 / 6			
Type 2, N'/N	177 / 177	181 / 181			
KITE, N'/N	179 / 179	181 / 181			
Type 1, N'/N	19 / 19	7 / 7			
Type 2, N'/N	160 / 160	174 / 174			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Type 1, N'/N	31 / 31	13 / 13			
Type 2, N'/N	337 / 337	355 / 355			
Any ocular adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2, n (%)	9 (5.1)	2 (1.1)	4.79 [1.02; 22.51] 0.047 *	4.60 [1.01; 21.00] 0.049 *	0.04 [0.00; 0.08] 0.029 *
KITE					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2, n (%)	5 (3.1)	4 (2.3)	1.37 [0.36; 5.20] 0.643	1.36 [0.37; 4.97] 0.643	0.01 [-0.03; 0.04] 0.643
Pooled Analysis					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2, n (%)	14 (4.2)	6 (1.7)	2.60 [0.93; 7.23] 0.068	2.46 [0.95; 6.37] 0.054	0.02 [-0.00; 0.05] 0.055

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL, Week 100 / Intraocular inflammation / KITE: logit(proportion) = treatment [by diabetes type].
Week 100 / Intraocular inflammation / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 20-2.7 Any ocular adverse events of special interest by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	188 / 188	187 / 187			
< 7.5 %, N'/N	76 / 76	107 / 107			
≥ 7.5 %, N'/N	112 / 112	80 / 80			
KITE, N'/N	179 / 179	181 / 181			
< 7.5 %, N'/N	82 / 82	96 / 96			
≥ 7.5 %, N'/N	97 / 97	85 / 85			
Pooled Analysis, N'/N	367 / 367	368 / 368			
< 7.5 %, N'/N	158 / 158	203 / 203			
≥ 7.5 %, N'/N	209 / 209	165 / 165			
Any ocular adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.768				
< 7.5 %, n (%)	4 (5.3)	1 (0.9)	5.89 [0.64; 53.77] 0.116	5.63 [0.64; 49.40] 0.119	0.04 [-0.01; 0.10] 0.112
≥ 7.5 %, n (%)	5 (4.5)	1 (1.3)	3.69 [0.42; 32.22] 0.237	3.57 [0.43; 29.99] 0.241	0.03 [-0.01; 0.08] 0.165
KITE					
Interaction Test:	p = 0.999				
< 7.5 %, n (%)	1 (1.2)	1 (1.0)	1.17 [0.07; 19.05] 0.911	1.17 [0.07; 18.43] 0.911	0.00 [-0.03; 0.03] 0.911
≥ 7.5 %, n (%)	4 (4.1)	3 (3.5)	1.18 [0.26; 5.41] 0.835	1.17 [0.27; 5.07] 0.835	0.01 [-0.05; 0.06] 0.834
Pooled Analysis					
Interaction Test:	p = 0.567				
< 7.5 %, n (%)	5 (3.2)	2 (1.0)	3.38 [0.63; 18.11] 0.155	3.29 [0.66; 16.30] 0.123	0.02 [-0.01; 0.05] 0.151

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %, n (%)	9 (4.3)	4 (2.4)	1.86 [0.53; 6.50] 0.329	1.81 [0.56; 5.87] 0.315	0.02 [-0.02; 0.06] 0.296

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 20-2.8 Any ocular adverse events of special interest by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
≤ 3 months, N'/N	120 / 120	110 / 110			
> 3 - < 12 months, N'/N	30 / 30	39 / 39			
≥ 12 months, N'/N	39 / 39	38 / 38			
KITE, N'/N	179 / 179	181 / 181			
≤ 3 months, N'/N	85 / 85	92 / 92			
> 3 - < 12 months, N'/N	51 / 51	49 / 49			
≥ 12 months, N'/N	43 / 43	40 / 40			
Pooled Analysis, N'/N	368 / 368	368 / 368			
≤ 3 months, N'/N	205 / 205	202 / 202			
> 3 - < 12 months, N'/N	81 / 81	88 / 88			
≥ 12 months, N'/N	82 / 82	78 / 78			
Any ocular adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months, n (%)	6 (5.0)	1 (0.9)	5.74 [0.68; 48.43] 0.108	5.50 [0.67; 44.96] 0.112	0.04 [-0.00; 0.08] 0.061
> 3 - < 12 months, n (%)	2 (6.7)	0 (0.0)	N.E.	6.45 [0.32; 129.57] 0.223	0.07 [-0.02; 0.16] 0.143
≥ 12 months, n (%)	1 (2.6)	1 (2.6)	0.97 [0.06; 16.15] 0.985	0.97 [0.06; 15.02] 0.985	-0.00 [-0.07; 0.07] 0.985
KITE					
Interaction Test:	N.E.				
≤ 3 months, n (%)	4 (4.7)	2 (2.2)	2.22 [0.40; 12.46] 0.364	2.16 [0.41; 11.52] 0.365	0.03 [-0.03; 0.08] 0.358
> 3 - < 12 months, n (%)	0 (0.0)	1 (2.0)	N.E.	0.32 [0.01; 7.68] 0.483	-0.02 [-0.06; 0.02] 0.312
≥ 12 months, n (%)	1 (2.3)	1 (2.5)	0.93 [0.06; 15.36] 0.959	0.93 [0.06; 14.38] 0.959	-0.00 [-0.07; 0.06] 0.959

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.619				
≤ 3 months, n (%)	10 (4.9)	3 (1.5)	3.35 [0.87; 12.82] 0.078	3.34 [0.92; 12.12] 0.051	0.03 [0.00; 0.07] 0.048 *
> 3 - < 12 months, n (%)	2 (2.5)	1 (1.1)	2.57 [0.22; 29.89] 0.451	1.68 [0.31; 9.14] 0.542	0.01 [-0.03; 0.06] 0.495
≥ 12 months, n (%)	2 (2.4)	2 (2.6)	1.02 [0.14; 7.66] 0.984	0.95 [0.14; 6.59] 0.961	-0.00 [-0.05; 0.05] 0.960

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL, Week 100 / Intraocular inflammation / KITE: logit(proportion) = treatment [by duration of DME].

Table 20-2.9 Any ocular adverse events of special interest by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	186 / 186	182 / 182			
focal, N'/N	59 / 59	48 / 48			
diffuse, N'/N	127 / 127	134 / 134			
KITE, N'/N	178 / 178	175 / 175			
focal, N'/N	63 / 63	66 / 66			
diffuse, N'/N	115 / 115	109 / 109			
Pooled Analysis, N'/N	364 / 364	357 / 357			
focal, N'/N	122 / 122	114 / 114			
diffuse, N'/N	242 / 242	243 / 243			
Any ocular adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	N.E.				
focal, n (%)	1 (1.7)	0 (0.0)	N.E.	2.45 [0.10; 58.81] 0.581	0.02 [-0.02; 0.05] 0.313
diffuse, n (%)	8 (6.3)	2 (1.5)	4.44 [0.92; 21.31] 0.063	4.22 [0.91; 19.50] 0.065	0.05 [0.00; 0.10] 0.045 *
KITE					
Interaction Test:	p = 0.820				
focal, n (%)	2 (3.2)	2 (3.0)	1.05 [0.14; 7.68] 0.962	1.05 [0.15; 7.21] 0.962	0.00 [-0.06; 0.06] 0.962
diffuse, n (%)	3 (2.6)	2 (1.8)	1.43 [0.23; 8.75] 0.697	1.42 [0.24; 8.35] 0.697	0.01 [-0.03; 0.05] 0.694
Pooled Analysis					
Interaction Test:	p = 0.594				
focal, n (%)	3 (2.5)	2 (1.8)	1.57 [0.24; 10.13] 0.634	1.36 [0.27; 6.87] 0.713	0.01 [-0.03; 0.04] 0.649

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse, n (%)	11 (4.5)	4 (1.6)	2.83 [0.86; 9.33] 0.087	2.78 [0.90; 8.56] 0.061	0.03 [-0.00; 0.06] 0.062

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL: logit(proportion) = treatment [by DME type].

Table 20-2.10 Any ocular adverse events of special interest by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
< 450 µm, N'/N	107 / 107	96 / 96			
≥ 450 - < 650 µm, N'/N	70 / 70	71 / 71			
≥ 650 µm, N'/N	12 / 12	20 / 20			
KITE, N'/N	179 / 179	180 / 180			
< 450 µm, N'/N	85 / 85	82 / 82			
≥ 450 - < 650 µm, N'/N	74 / 74	79 / 79			
≥ 650 µm, N'/N	20 / 20	19 / 19			
Pooled Analysis, N'/N	368 / 368	367 / 367			
< 450 µm, N'/N	192 / 192	178 / 178			
≥ 450 - < 650 µm, N'/N	144 / 144	150 / 150			
≥ 650 µm, N'/N	32 / 32	39 / 39			
Any ocular adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	N.E.				
< 450 µm, n (%)	6 (5.6)	0 (0.0)	N.E.	11.68 [0.67; 204.56] 0.093	0.06 [0.01; 0.10] 0.012 *
≥ 450 - < 650 µm, n (%)	3 (4.3)	2 (2.8)	1.54 [0.25; 9.54] 0.640	1.52 [0.26; 8.83] 0.640	0.01 [-0.05; 0.08] 0.637
≥ 650 µm, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE					
Interaction Test:	N.E.				
< 450 µm, n (%)	3 (3.5)	2 (2.4)	1.46 [0.24; 8.99] 0.681	1.45 [0.25; 8.44] 0.681	0.01 [-0.04; 0.06] 0.678
≥ 450 - < 650 µm, n (%)	2 (2.7)	2 (2.5)	1.07 [0.15; 7.79] 0.947	1.07 [0.15; 7.39] 0.947	0.00 [-0.05; 0.05] 0.947
≥ 650 µm, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	N.E.				
< 450 µm, n (%)	9 (4.7)	2 (1.1)	N.E.	3.55 [0.88; 14.29] 0.056	0.04 [0.00; 0.07] 0.038 *
≥ 450 - < 650 µm, n (%)	5 (3.5)	4 (2.7)	1.29 [0.34; 4.95] 0.711	1.30 [0.35; 4.74] 0.694	0.01 [-0.03; 0.05] 0.693
≥ 650 µm, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL, Week 100 / Intraocular inflammation / KITE: logit(proportion) = treatment [by CSFT].
Week 100 / Intraocular inflammation / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by CSFT].

Table 20-2.11 Any ocular adverse events of special interest by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
presence, N'/N	62 / 62	61 / 61			
absence, N'/N	127 / 127	126 / 126			
KITE, N'/N	179 / 179	181 / 181			
presence, N'/N	56 / 56	67 / 67			
absence, N'/N	123 / 123	114 / 114			
Pooled Analysis, N'/N	368 / 368	368 / 368			
presence, N'/N	118 / 118	128 / 128			
absence, N'/N	250 / 250	240 / 240			
Any ocular adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.657				
presence, n (%)	3 (4.8)	1 (1.6)	3.05 [0.31; 30.17] 0.340	2.95 [0.32; 27.60] 0.343	0.03 [-0.03; 0.09] 0.313
absence, n (%)	6 (4.7)	1 (0.8)	6.20 [0.74; 52.24] 0.093	5.95 [0.73; 48.74] 0.096	0.04 [-0.00; 0.08] 0.054
KITE					
Interaction Test:	N.E.				
presence, n (%)	0 (0.0)	1 (1.5)	N.E.	0.40 [0.02; 9.57] 0.570	-0.01 [-0.04; 0.01] 0.314
absence, n (%)	5 (4.1)	3 (2.6)	1.57 [0.37; 6.71] 0.545	1.54 [0.38; 6.32] 0.545	0.01 [-0.03; 0.06] 0.538
Pooled Analysis					
Interaction Test:	p = 0.663				
presence, n (%)	3 (2.5)	2 (1.6)	1.72 [0.27; 10.91] 0.567	1.48 [0.29; 7.64] 0.637	0.01 [-0.03; 0.04] 0.631

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence, n (%)	11 (4.4)	4 (1.7)	2.77 [0.83; 9.19] 0.096	2.62 [0.85; 8.07] 0.081	0.03 [-0.00; 0.06] 0.077

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KITE: logit(proportion) = treatment [by status of SRF].

Table 20-2.13 Any ocular adverse events of special interest by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Non-exposed, N'/N	12 / 12	13 / 13			
Exposed, N'/N	177 / 177	174 / 174			
KITE, N'/N	179 / 179	181 / 181			
Non-exposed, N'/N	17 / 17	12 / 12			
Exposed, N'/N	162 / 162	169 / 169			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Non-exposed, N'/N	29 / 29	25 / 25			
Exposed, N'/N	339 / 339	343 / 343			
Any ocular adverse events of special interest, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Exposed, n (%)	9 (5.1)	2 (1.1)	4.61 [0.98; 21.64] 0.053	4.42 [0.97; 20.18] 0.055	0.04 [0.00; 0.08] 0.032 *
KITE					
Interaction Test:	N.E.				
Non-exposed, n (%)	1 (5.9)	0 (0.0)	N.E.	2.17 [0.10; 49.07] 0.627	0.06 [-0.05; 0.17] 0.303
Exposed, n (%)	4 (2.5)	4 (2.4)	1.04 [0.26; 4.25] 0.952	1.04 [0.27; 4.10] 0.952	0.00 [-0.03; 0.03] 0.952
Pooled Analysis					
Interaction Test:	N.E.				
Non-exposed, n (%)	1 (3.4)	0 (0.0)	N.E.	2.17 [0.10; 49.07] 0.622	0.03 [-0.03; 0.09] 0.338

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed, n (%)	13 (3.8)	6 (1.7)	2.23 [0.78; 6.34] 0.134	2.19 [0.84; 5.74] 0.100	0.02 [-0.00; 0.05] 0.099

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL, Week 100 / Intraocular inflammation / KITE: logit(proportion) = treatment [by exposure (week 100)].
Week 100 / Intraocular inflammation / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by exposure (week 100)].

Table 20-3.1 Any ocular adverse events of special interest at the study eye by severity (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by severity (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular adverse events of special interest at the study eye by severity, week 100					
Endophthalmitis					
KESTREL, n (%)	0 (0.0)	1 (0.5)	N.E.	0.33 [0.01; 8.05] 0.496	-0.01 [-0.02; 0.01] 0.316
KITE, n (%)	2 (1.1)	1 (0.6)	2.03 [0.18; 22.63] 0.564	2.02 [0.19; 22.11] 0.564	0.01 [-0.01; 0.02] 0.556
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	2 (0.5)	N.E.	1.00 [0.18; 5.73] 0.998	0.00 [-0.01; 0.01] 0.995
Endophthalmitis severe					
KESTREL, n (%)	0 (0.0)	1 (0.5)	N.E.	0.33 [0.01; 8.05] 0.496	-0.01 [-0.02; 0.01] 0.316
KITE, n (%)	2 (1.1)	0 (0.0)	N.E.	5.06 [0.24; 104.57] 0.294	0.01 [-0.00; 0.03] 0.155
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	1 (0.3)	N.E.	1.50 [0.25; 8.90] 0.652	0.00 [-0.01; 0.01] 0.562
Endophthalmitis serious					
KESTREL, n (%)	0 (0.0)	1 (0.5)	N.E.	0.33 [0.01; 8.05] 0.496	-0.01 [-0.02; 0.01] 0.316
KITE, n (%)	2 (1.1)	1 (0.6)	2.03 [0.18; 22.63] 0.564	2.02 [0.19; 22.11] 0.564	0.01 [-0.01; 0.02] 0.556
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	2 (0.5)	N.E.	1.00 [0.18; 5.73] 0.998	0.00 [-0.01; 0.01] 0.995
Intraocular inflammation					
KESTREL, n (%)	8 (4.2)	2 (1.1)	4.09 [0.86; 19.51] 0.077	3.96 [0.85; 18.39] 0.079	0.03 [-0.00; 0.06] 0.055
KITE, n (%)	4 (2.2)	3 (1.7)	1.36 [0.30; 6.15] 0.693	1.35 [0.31; 5.94] 0.693	0.01 [-0.02; 0.03] 0.692

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by severity (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, n (%) p_H=0.320	12 (3.3)	5 (1.4)	2.38 [0.80; 7.07] 0.118	2.40 [0.85; 6.76] 0.087	0.02 [-0.00; 0.04] 0.086
Intraocular inflammation severe					
KESTREL, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, n (%)	2 (1.1)	0 (0.0)	N.E.	5.06 [0.24; 104.57] 0.294	0.01 [-0.00; 0.03] 0.155
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	0 (0.0)	N.E.	5.06 [0.24; 104.57] 0.243	0.01 [-0.00; 0.01] 0.155
Intraocular inflammation serious					
KESTREL, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, n (%)	1 (0.6)	1 (0.6)	1.01 [0.06; 16.29] 0.994	1.01 [0.06; 16.04] 0.994	0.00 [-0.02; 0.02] 0.994
Pooled Analysis, n (%) p_H=N.E.	1 (0.3)	1 (0.3)	N.E.	1.01 [0.06; 16.04] 0.994	0.00 [-0.01; 0.01] 0.994
Retinal vascular occlusion					
KESTREL, n (%)	3 (1.6)	1 (0.5)	3.00 [0.31; 29.10] 0.343	2.97 [0.31; 28.28] 0.344	0.01 [-0.01; 0.03] 0.318
KITE, n (%)	1 (0.6)	1 (0.6)	1.01 [0.06; 16.29] 0.994	1.01 [0.06; 16.04] 0.994	0.00 [-0.02; 0.02] 0.994
Pooled Analysis, n (%) p_H=0.553	4 (1.1)	2 (0.5)	1.76 [0.29; 10.53] 0.535	2.00 [0.37; 10.85] 0.415	0.01 [-0.01; 0.02] 0.414
Retinal vascular occlusion severe					
KESTREL, n (%)	1 (0.5)	1 (0.5)	0.99 [0.06; 15.93] 0.994	0.99 [0.06; 15.70] 0.994	-0.00 [-0.01; 0.01] 0.994
KITE, n (%)	1 (0.6)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.496	0.01 [-0.01; 0.02] 0.316
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	1 (0.3)	N.E.	1.67 [0.22; 12.51] 0.616	0.00 [-0.01; 0.01] 0.565
Retinal vascular occlusion serious					
KESTREL, n (%)	1 (0.5)	0 (0.0)	N.E.	2.97 [0.12; 72.41] 0.504	0.01 [-0.01; 0.02] 0.316
KITE, n (%)	1 (0.6)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.496	0.01 [-0.01; 0.02] 0.316

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by severity (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	0 (0.0)	N.E.	3.00 [0.31; 28.71] 0.317	0.01 [-0.00; 0.01] 0.156

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 20-3.2 Any ocular adverse events of special interest at the study eye by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
< 65 years, N'/N	104 / 104	93 / 93			
≥ 65 years, N'/N	85 / 85	94 / 94			
KITE, N'/N	179 / 179	181 / 181			
< 65 years, N'/N	100 / 100	102 / 102			
≥ 65 years, N'/N	79 / 79	79 / 79			
Pooled Analysis, N'/N	368 / 368	368 / 368			
< 65 years, N'/N	204 / 204	195 / 195			
≥ 65 years, N'/N	164 / 164	173 / 173			
Any ocular adverse events of special interest at the study eye, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.320**					
KESTREL					
Interaction Test:	N.E.				
< 65 years, n (%)	4 (3.8)	0 (0.0)	N.E.	8.06 [0.44; 147.68] 0.160	0.04 [0.00; 0.08] 0.041 *
≥ 65 years, n (%)	4 (4.7)	2 (2.1)	2.27 [0.41; 12.73] 0.351	2.21 [0.42; 11.77] 0.352	0.03 [-0.03; 0.08] 0.346
KITE					
Interaction Test:	N.E.				
< 65 years, n (%)	1 (1.0)	0 (0.0)	N.E.	3.06 [0.13; 74.22] 0.492	0.01 [-0.01; 0.03] 0.315
≥ 65 years, n (%)	3 (3.8)	3 (3.8)	1.00 [0.20; 5.11] 1.000	1.00 [0.21; 4.80] 1.000	0.00 [-0.06; 0.06] 1.000
Pooled Analysis					
Interaction Test:	N.E.				
< 65 years, n (%)	5 (2.5)	0 (0.0)	N.E.	5.64 [0.67; 47.15] 0.070	0.02 [0.00; 0.05] 0.025 *

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years, n (%)	7 (4.3)	5 (2.9)	1.52 [0.46; 4.99] 0.490	1.47 [0.48; 4.52] 0.500	0.01 [-0.03; 0.05] 0.501

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL, Week 100 / Intraocular inflammation / KITE: logit(proportion) = treatment [by age].
Week 100 / Intraocular inflammation / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by age].

Table 20-3.3 Any ocular adverse events of special interest at the study eye by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Male, N'/N	110 / 110	126 / 126			
Female, N'/N	79 / 79	61 / 61			
KITE, N'/N	179 / 179	181 / 181			
Male, N'/N	120 / 120	115 / 115			
Female, N'/N	59 / 59	66 / 66			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Male, N'/N	230 / 230	241 / 241			
Female, N'/N	138 / 138	127 / 127			
Any ocular adverse events of special interest at the study eye, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.320**					
KESTREL					
Interaction Test:	p = 0.808				
Male, n (%)	4 (3.6)	1 (0.8)	4.72 [0.52; 42.85] 0.168	4.58 [0.52; 40.38] 0.170	0.03 [-0.01; 0.07] 0.145
Female, n (%)	4 (5.1)	1 (1.6)	3.20 [0.35; 29.39] 0.304	3.09 [0.35; 26.93] 0.307	0.03 [-0.02; 0.09] 0.246
KITE					
Interaction Test:	p = 0.732				
Male, n (%)	1 (0.8)	1 (0.9)	0.96 [0.06; 15.50] 0.976	0.96 [0.06; 15.14] 0.976	-0.00 [-0.02; 0.02] 0.976
Female, n (%)	3 (5.1)	2 (3.0)	1.71 [0.28; 10.63] 0.563	1.68 [0.29; 9.70] 0.563	0.02 [-0.05; 0.09] 0.563
Pooled Analysis					
Interaction Test:	p = 0.842				
Male, n (%)	5 (2.2)	2 (0.8)	2.64 [0.50; 13.90] 0.253	2.69 [0.54; 13.40] 0.209	0.01 [-0.01; 0.04] 0.217

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female, n (%)	7 (5.1)	3 (2.4)	2.12 [0.52; 8.69] 0.298	2.21 [0.57; 8.55] 0.240	0.03 [-0.02; 0.07] 0.229

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 20-3.4 Any ocular adverse events of special interest at the study eye by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
≤ 65 letters, N'/N	74 / 74	64 / 64			
> 65 letters, N'/N	115 / 115	123 / 123			
KITE, N'/N	179 / 179	181 / 181			
≤ 65 letters, N'/N	65 / 65	91 / 91			
> 65 letters, N'/N	114 / 114	90 / 90			
Pooled Analysis, N'/N	368 / 368	368 / 368			
≤ 65 letters, N'/N	139 / 139	155 / 155			
> 65 letters, N'/N	229 / 229	213 / 213			
Any ocular adverse events of special interest at the study eye, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.320**					
KESTREL					
Interaction Test:	N.E.				
≤ 65 letters, n (%)	2 (2.7)	0 (0.0)	N.E.	4.33 [0.21; 88.63] 0.341	0.03 [-0.01; 0.06] 0.152
> 65 letters, n (%)	6 (5.2)	2 (1.6)	3.33 [0.66; 16.84] 0.146	3.21 [0.66; 15.58] 0.148	0.04 [-0.01; 0.08] 0.129
KITE					
Interaction Test:	p = 0.465				
≤ 65 letters, n (%)	1 (1.5)	2 (2.2)	0.70 [0.06; 7.83] 0.769	0.70 [0.06; 7.56] 0.769	-0.01 [-0.05; 0.04] 0.761
> 65 letters, n (%)	3 (2.6)	1 (1.1)	2.41 [0.25; 23.52] 0.451	2.37 [0.25; 22.39] 0.452	0.02 [-0.02; 0.05] 0.414
Pooled Analysis					
Interaction Test:	p = 0.680				
≤ 65 letters, n (%)	3 (2.2)	2 (1.3)	1.69 [0.26; 10.81] 0.578	1.58 [0.29; 8.71] 0.594	0.01 [-0.02; 0.04] 0.532

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters, n (%)	9 (3.9)	3 (1.4)	2.72 [0.72; 10.34] 0.142	2.90 [0.80; 10.53] 0.089	0.03 [-0.00; 0.06] 0.084

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL: logit(proportion) = treatment [by BCVA].

Table 20-3.5 Any ocular adverse events of special interest at the study eye by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-3.6 Any ocular adverse events of special interest at the study eye by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Type 1, N'/N	12 / 12	6 / 6			
Type 2, N'/N	177 / 177	181 / 181			
KITE, N'/N	179 / 179	181 / 181			
Type 1, N'/N	19 / 19	7 / 7			
Type 2, N'/N	160 / 160	174 / 174			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Type 1, N'/N	31 / 31	13 / 13			
Type 2, N'/N	337 / 337	355 / 355			
Any ocular adverse events of special interest at the study eye, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.320**					
KESTREL					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2, n (%)	8 (4.5)	2 (1.1)	4.24 [0.89; 20.24] 0.070	4.09 [0.88; 19.00] 0.072	0.03 [-0.00; 0.07] 0.050
KITE					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2, n (%)	4 (2.5)	3 (1.7)	1.46 [0.32; 6.63] 0.623	1.45 [0.33; 6.38] 0.623	0.01 [-0.02; 0.04] 0.623
Pooled Analysis					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2, n (%)	12 (3.6)	5 (1.4)	2.51 [0.85; 7.47] 0.097	2.53 [0.90; 7.13] 0.069	0.02 [-0.00; 0.04] 0.071

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL, Week 100 / Intraocular inflammation / KITE: logit(proportion) = treatment [by diabetes type].
Week 100 / Intraocular inflammation / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 20-3.7 Any ocular adverse events of special interest at the study eye by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	188 / 188	187 / 187			
< 7.5 %, N'/N	76 / 76	107 / 107			
≥ 7.5 %, N'/N	112 / 112	80 / 80			
KITE, N'/N	179 / 179	181 / 181			
< 7.5 %, N'/N	82 / 82	96 / 96			
≥ 7.5 %, N'/N	97 / 97	85 / 85			
Pooled Analysis, N'/N	367 / 367	368 / 368			
< 7.5 %, N'/N	158 / 158	203 / 203			
≥ 7.5 %, N'/N	209 / 209	165 / 165			
Any ocular adverse events of special interest at the study eye, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.320**					
KESTREL					
Interaction Test:	p = 0.661				
< 7.5 %, n (%)	4 (5.3)	1 (0.9)	5.89 [0.64; 53.77] 0.116	5.63 [0.64; 49.40] 0.119	0.04 [-0.01; 0.10] 0.112
≥ 7.5 %, n (%)	4 (3.6)	1 (1.3)	2.93 [0.32; 26.68] 0.341	2.86 [0.33; 25.08] 0.344	0.02 [-0.02; 0.07] 0.280
KITE					
Interaction Test:	p = 0.943				
< 7.5 %, n (%)	1 (1.2)	1 (1.0)	1.17 [0.07; 19.05] 0.911	1.17 [0.07; 18.43] 0.911	0.00 [-0.03; 0.03] 0.911
≥ 7.5 %, n (%)	3 (3.1)	2 (2.4)	1.32 [0.22; 8.12] 0.761	1.31 [0.22; 7.68] 0.761	0.01 [-0.04; 0.05] 0.759
Pooled Analysis					
Interaction Test:	p = 0.597				
< 7.5 %, n (%)	5 (3.2)	2 (1.0)	3.23 [0.61; 17.11] 0.169	3.29 [0.66; 16.30] 0.123	0.02 [-0.01; 0.05] 0.151

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %, n (%)	7 (3.3)	3 (1.8)	1.81 [0.44; 7.35] 0.409	1.86 [0.48; 7.19] 0.361	0.02 [-0.02; 0.05] 0.341

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 20-3.8 Any ocular adverse events of special interest at the study eye by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
≤ 3 months, N'/N	120 / 120	110 / 110			
> 3 - < 12 months, N'/N	30 / 30	39 / 39			
≥ 12 months, N'/N	39 / 39	38 / 38			
KITE, N'/N	179 / 179	181 / 181			
≤ 3 months, N'/N	85 / 85	92 / 92			
> 3 - < 12 months, N'/N	51 / 51	49 / 49			
≥ 12 months, N'/N	43 / 43	40 / 40			
Pooled Analysis, N'/N	368 / 368	368 / 368			
≤ 3 months, N'/N	205 / 205	202 / 202			
> 3 - < 12 months, N'/N	81 / 81	88 / 88			
≥ 12 months, N'/N	82 / 82	78 / 78			
Any ocular adverse events of special interest at the study eye, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.320**					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months, n (%)	5 (4.2)	1 (0.9)	4.74 [0.54; 41.22] 0.159	4.58 [0.54; 38.62] 0.162	0.03 [-0.01; 0.07] 0.110
> 3 - < 12 months, n (%)	2 (6.7)	0 (0.0)	N.E.	6.45 [0.32; 129.57] 0.223	0.07 [-0.02; 0.16] 0.143
≥ 12 months, n (%)	1 (2.6)	1 (2.6)	0.97 [0.06; 16.15] 0.985	0.97 [0.06; 15.02] 0.985	-0.00 [-0.07; 0.07] 0.985
KITE					
Interaction Test:	N.E.				
≤ 3 months, n (%)	3 (3.5)	2 (2.2)	1.65 [0.27; 10.10] 0.590	1.62 [0.28; 9.48] 0.590	0.01 [-0.04; 0.06] 0.590
> 3 - < 12 months, n (%)	0 (0.0)	1 (2.0)	N.E.	0.32 [0.01; 7.68] 0.483	-0.02 [-0.06; 0.02] 0.312
≥ 12 months, n (%)	1 (2.3)	0 (0.0)	N.E.	2.80 [0.12; 66.70] 0.525	0.02 [-0.02; 0.07] 0.312

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.985				
≤ 3 months, n (%)	8 (3.9)	3 (1.5)	2.50 [0.63; 9.87] 0.191	2.67 [0.71; 10.06] 0.132	0.02 [-0.01; 0.06] 0.127
> 3 - < 12 months, n (%)	2 (2.5)	1 (1.1)	2.43 [0.21; 27.95] 0.476	1.68 [0.31; 9.14] 0.542	0.01 [-0.03; 0.06] 0.495
≥ 12 months, n (%)	2 (2.4)	1 (1.3)	1.95 [0.17; 22.36] 0.590	1.59 [0.21; 11.84] 0.649	0.01 [-0.03; 0.05] 0.580

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL, Week 100 / Intraocular inflammation / KITE: logit(proportion) = treatment [by duration of DME].

Table 20-3.9 Any ocular adverse events of special interest at the study eye by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	186 / 186	182 / 182			
focal, N'/N	59 / 59	48 / 48			
diffuse, N'/N	127 / 127	134 / 134			
KITE, N'/N	178 / 178	175 / 175			
focal, N'/N	63 / 63	66 / 66			
diffuse, N'/N	115 / 115	109 / 109			
Pooled Analysis, N'/N	364 / 364	357 / 357			
focal, N'/N	122 / 122	114 / 114			
diffuse, N'/N	242 / 242	243 / 243			
Any ocular adverse events of special interest at the study eye, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.320**					
KESTREL					
Interaction Test:	N.E.				
focal, n (%)	1 (1.7)	0 (0.0)	N.E.	2.45 [0.10; 58.81] 0.581	0.02 [-0.02; 0.05] 0.313
diffuse, n (%)	7 (5.5)	2 (1.5)	3.85 [0.78; 18.89] 0.097	3.69 [0.78; 17.44] 0.099	0.04 [-0.00; 0.08] 0.078
KITE					
Interaction Test:	p = 0.854				
focal, n (%)	1 (1.6)	1 (1.5)	1.05 [0.06; 17.13] 0.974	1.05 [0.07; 16.39] 0.974	0.00 [-0.04; 0.04] 0.974
diffuse, n (%)	3 (2.6)	2 (1.8)	1.43 [0.23; 8.75] 0.697	1.42 [0.24; 8.35] 0.697	0.01 [-0.03; 0.05] 0.694
Pooled Analysis					
Interaction Test:	p = 0.871				
focal, n (%)	2 (1.6)	1 (0.9)	1.97 [0.17; 22.80] 0.587	1.55 [0.20; 11.93] 0.671	0.01 [-0.02; 0.04] 0.575

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse, n (%)	10 (4.1)	4 (1.6)	2.46 [0.74; 8.17] 0.141	2.53 [0.81; 7.90] 0.098	0.03 [-0.00; 0.06] 0.098

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL: logit(proportion) = treatment [by DME type].

Table 20-3.10 Any ocular adverse events of special interest at the study eye by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-3.11 Any ocular adverse events of special interest at the study eye by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
presence, N'/N	62 / 62	61 / 61			
absence, N'/N	127 / 127	126 / 126			
KITE, N'/N	179 / 179	181 / 181			
presence, N'/N	56 / 56	67 / 67			
absence, N'/N	123 / 123	114 / 114			
Pooled Analysis, N'/N	368 / 368	368 / 368			
presence, N'/N	118 / 118	128 / 128			
absence, N'/N	250 / 250	240 / 240			
Any ocular adverse events of special interest at the study eye, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.320**					
KESTREL					
Interaction Test:	p = 0.493				
presence, n (%)	2 (3.2)	1 (1.6)	2.00 [0.18; 22.65] 0.576	1.97 [0.18; 21.14] 0.576	0.02 [-0.04; 0.07] 0.567
absence, n (%)	6 (4.7)	1 (0.8)	6.20 [0.74; 52.25] 0.093	5.95 [0.73; 48.74] 0.096	0.04 [-0.00; 0.08] 0.054
KITE					
Interaction Test:	N.E.				
presence, n (%)	0 (0.0)	1 (1.5)	N.E.	0.40 [0.02; 9.57] 0.570	-0.01 [-0.04; 0.01] 0.314
absence, n (%)	4 (3.3)	2 (1.8)	1.88 [0.34; 10.48] 0.470	1.85 [0.35; 9.93] 0.471	0.01 [-0.02; 0.05] 0.458
Pooled Analysis					
Interaction Test:	p = 0.362				
presence, n (%)	2 (1.7)	2 (1.6)	1.06 [0.14; 7.84] 0.956	1.06 [0.18; 6.24] 0.946	0.00 [-0.03; 0.03] 0.974

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence, n (%)	10 (4.0)	3 (1.3)	3.18 [0.85; 11.99] 0.087	3.19 [0.89; 11.39] 0.058	0.03 [-0.00; 0.06] 0.055

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KITE: logit(proportion) = treatment [by status of SRF].

Table 20-3.13 Any ocular adverse events of special interest at the study eye by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
Non-exposed, N'/N	12 / 12	13 / 13			
Exposed, N'/N	177 / 177	174 / 174			
KITE, N'/N	179 / 179	181 / 181			
Non-exposed, N'/N	17 / 17	12 / 12			
Exposed, N'/N	162 / 162	169 / 169			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Non-exposed, N'/N	29 / 29	25 / 25			
Exposed, N'/N	339 / 339	343 / 343			
Any ocular adverse events of special interest at the study eye, week 100					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.320**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Exposed, n (%)	8 (4.5)	2 (1.1)	4.07 [0.85; 19.45] 0.079	3.93 [0.85; 18.26] 0.080	0.03 [-0.00; 0.07] 0.055
KITE					
Interaction Test:	N.E.				
Non-exposed, n (%)	1 (5.9)	0 (0.0)	N.E.	2.17 [0.10; 49.07] 0.627	0.06 [-0.05; 0.17] 0.303
Exposed, n (%)	3 (1.9)	3 (1.8)	1.04 [0.21; 5.25] 0.958	1.04 [0.21; 5.09] 0.958	0.00 [-0.03; 0.03] 0.958
Pooled Analysis					
Interaction Test:	N.E.				
Non-exposed, n (%)	1 (3.4)	0 (0.0)	N.E.	2.17 [0.10; 49.07] 0.622	0.03 [-0.03; 0.09] 0.338

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the study eye by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed, n (%)	11 (3.2)	5 (1.5)	2.09 [0.68; 6.43] 0.199	2.22 [0.77; 6.36] 0.127	0.02 [-0.00; 0.04] 0.126

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 100 / Intraocular inflammation / KESTREL, Week 100 / Intraocular inflammation / KITE: logit(proportion) = treatment [by exposure (week 100)].
Week 100 / Intraocular inflammation / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by exposure (week 100)].

Table 20-4.1 Any ocular adverse events of special interest at the fellow eye by severity (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the fellow eye by severity (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular adverse events of special interest at the fellow eye by severity, week 100					
Intraocular inflammation					
KESTREL, n (%)	1 (0.5)	1 (0.5)	0.99 [0.06; 15.93] 0.994	0.99 [0.06; 15.70] 0.994	-0.00 [-0.01; 0.01] 0.994
KITE, n (%)	1 (0.6)	2 (1.1)	0.50 [0.05; 5.59] 0.576	0.51 [0.05; 5.53] 0.576	-0.01 [-0.02; 0.01] 0.568
Pooled Analysis, n (%) p_H=0.718	2 (0.5)	3 (0.8)	0.71 [0.11; 4.49] 0.716	0.67 [0.11; 3.98] 0.656	-0.00 [-0.01; 0.01] 0.655
Intraocular inflammation severe					
KESTREL, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Pooled Analysis, n (%) p_H=N.E.	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Intraocular inflammation serious					
KESTREL, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, n (%)	0 (0.0)	1 (0.6)	N.E.	0.34 [0.01; 8.22] 0.505	-0.01 [-0.02; 0.01] 0.316
Pooled Analysis, n (%) p_H=N.E.	0 (0.0)	1 (0.3)	N.E.	0.34 [0.01; 8.22] 0.484	-0.00 [-0.01; 0.00] 0.318
Retinal vascular occlusion					
KESTREL, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, n (%)	0 (0.0)	3 (1.7)	N.E.	0.14 [0.01; 2.78] 0.200	-0.02 [-0.04; 0.00] 0.081
Pooled Analysis, n (%) p_H=N.E.	0 (0.0)	3 (0.8)	N.E.	0.14 [0.01; 2.78] 0.135	-0.01 [-0.02; 0.00] 0.083
Retinal vascular occlusion severe					
KESTREL, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any ocular adverse events of special interest at the fellow eye by severity (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
p_H=N.E.					
Retinal vascular occlusion serious					
KESTREL, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Pooled Analysis, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
p_H=N.E.					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 20-4.2 Any ocular adverse events of special interest at the fellow eye by age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-4.3 Any ocular adverse events of special interest at the fellow eye by gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-4.4 Any ocular adverse events of special interest at the fellow eye by BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-4.5 Any ocular adverse events of special interest at the fellow eye by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-4.6 Any ocular adverse events of special interest at the fellow eye by diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-4.7 Any ocular adverse events of special interest at the fellow eye by HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-4.8 Any ocular adverse events of special interest at the fellow eye by duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-4.9 Any ocular adverse events of special interest at the fellow eye by DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-4.10 Any ocular adverse events of special interest at the fellow eye by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-4.11 Any ocular adverse events of special interest at the fellow eye by status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-4.13 Any ocular adverse events of special interest at the fellow eye by exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-5.1 Any non-ocular adverse events of special interest by severity (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-5.2 Any non-ocular adverse events of special interest by age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-5.3 Any non-ocular adverse events of special interest by gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-5.4 Any non-ocular adverse events of special interest by BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-5.5 Any non-ocular adverse events of special interest by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-5.6 Any non-ocular adverse events of special interest by diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-5.7 Any non-ocular adverse events of special interest by HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-5.8 Any non-ocular adverse events of special interest by duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-5.9 Any non-ocular adverse events of special interest by DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-5.10 Any non-ocular adverse events of special interest by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-5.11 Any non-ocular adverse events of special interest by status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 20-5.13 Any non-ocular adverse events of special interest by exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

21 Safety analysis: Any adverse event of potential relevance to intravitreal anti-VEGF injection

Table 21-1.1 Any adverse event of potential relevance to intravitreal anti-VEGF injection (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	25 (13.2)	32 (17.1)	0.74 [0.42; 1.30] 0.295	0.77 [0.48; 1.25] 0.296	-0.04 [-0.11; 0.03] 0.293
KITE, N'/N	179 / 179	181 / 181			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	21 (11.7)	14 (7.7)	1.59 [0.78; 3.23] 0.204	1.52 [0.80; 2.89] 0.205	0.04 [-0.02; 0.10] 0.200
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	46 (12.5)	46 (12.5)	1.07 [0.68; 1.69] 0.758	1.00 [0.68; 1.46] 0.990	-0.00 [-0.05; 0.05] 0.990
p_H=0.099					
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	31 (16.4)	40 (21.4)	0.72 [0.43; 1.21] 0.218	0.77 [0.50; 1.17] 0.219	-0.05 [-0.13; 0.03] 0.216
KITE, N'/N	179 / 179	181 / 181			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	26 (14.5)	19 (10.5)	1.45 [0.77; 2.72] 0.250	1.38 [0.79; 2.41] 0.251	0.04 [-0.03; 0.11] 0.247

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	57 (15.5)	59 (16.0)	1.02 [0.68; 1.53] 0.943	0.96 [0.69; 1.35] 0.829	-0.01 [-0.06; 0.05] 0.829
p_H=0.095					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-1.2 Any adverse event of potential relevance to intravitreal anti-VEGF injection by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.099**					
KESTREL					
Interaction Test:	p = 0.654				
< 65 years					
N'/N	104 / 104	93 / 93			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	16 (15.4)	17 (18.3)	0.81 [0.38; 1.72] 0.587	0.84 [0.45; 1.57] 0.587	-0.03 [-0.13; 0.08] 0.588
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	9 (10.6)	15 (16.0)	0.62 [0.26; 1.51] 0.295	0.66 [0.31; 1.44] 0.298	-0.05 [-0.15; 0.05] 0.287
KITE					
Interaction Test:	p = 0.336				
< 65 years					
N'/N	100 / 100	102 / 102			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	15 (15.0)	8 (7.8)	2.07 [0.84; 5.14] 0.115	1.91 [0.85; 4.31] 0.118	0.07 [-0.02; 0.16] 0.108
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	6 (7.6)	6 (7.6)	1.00 [0.31; 3.25] 1.000	1.00 [0.34; 2.97] 1.000	0.00 [-0.08; 0.08] 1.000
Pooled Analysis					
Interaction Test:	p = 0.325				
< 65 years					
N'/N	204 / 204	195 / 195			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	31 (15.2)	25 (12.8)	1.27 [0.71; 2.27] 0.412	1.17 [0.72; 1.90] 0.527	0.02 [-0.05; 0.09] 0.527

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	15 (9.1)	21 (12.1)	0.81 [0.39; 1.65] 0.558	0.76 [0.41; 1.43] 0.397	-0.03 [-0.09; 0.04] 0.393
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.095**					
KESTREL					
Interaction Test:	p = 0.757				
< 65 years					
N'/N	104 / 104	93 / 93			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	19 (18.3)	21 (22.6)	0.77 [0.38; 1.54] 0.453	0.81 [0.46; 1.41] 0.453	-0.04 [-0.16; 0.07] 0.454
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (14.1)	19 (20.2)	0.65 [0.29; 1.43] 0.284	0.70 [0.36; 1.35] 0.287	-0.06 [-0.17; 0.05] 0.277
KITE					
Interaction Test:	p = 0.373				
< 65 years					
N'/N	100 / 100	102 / 102			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	18 (18.0)	11 (10.8)	1.82 [0.81; 4.07] 0.147	1.67 [0.83; 3.35] 0.150	0.07 [-0.02; 0.17] 0.142
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	8 (10.1)	8 (10.1)	1.00 [0.36; 2.81] 1.000	1.00 [0.39; 2.53] 1.000	0.00 [-0.09; 0.09] 1.000
Pooled Analysis					
Interaction Test:	p = 0.398				
< 65 years					
N'/N	204 / 204	195 / 195			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	37 (18.1)	32 (16.4)	1.16 [0.69; 1.97] 0.574	1.09 [0.71; 1.68] 0.686	0.02 [-0.06; 0.09] 0.686

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	20 (12.2)	27 (15.6)	0.82 [0.43; 1.54] 0.535	0.79 [0.46; 1.35] 0.391	-0.03 [-0.11; 0.04] 0.388

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-1.3 Any adverse event of potential relevance to intravitreal anti-VEGF injection by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.099**					
KESTREL					
Interaction Test:	p = 0.795				
Male					
N'/N	110 / 110	126 / 126			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	16 (14.5)	24 (19.0)	0.72 [0.36; 1.44] 0.359	0.76 [0.43; 1.36] 0.361	-0.05 [-0.14; 0.05] 0.353
Female					
N'/N	79 / 79	61 / 61			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	9 (11.4)	8 (13.1)	0.85 [0.31; 2.36] 0.757	0.87 [0.36; 2.12] 0.757	-0.02 [-0.13; 0.09] 0.759
KITE					
Interaction Test:	p = 0.603				
Male					
N'/N	120 / 120	115 / 115			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	14 (11.7)	10 (8.7)	1.39 [0.59; 3.26] 0.454	1.34 [0.62; 2.90] 0.454	0.03 [-0.05; 0.11] 0.450
Female					
N'/N	59 / 59	66 / 66			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	7 (11.9)	4 (6.1)	2.09 [0.58; 7.52] 0.261	1.96 [0.60; 6.35] 0.263	0.06 [-0.04; 0.16] 0.258
Pooled Analysis					
Interaction Test:	p = 0.571				
Male					
N'/N	230 / 230	241 / 241			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	30 (13.0)	34 (14.1)	0.99 [0.58; 1.71] 0.980	0.94 [0.60; 1.49] 0.808	-0.01 [-0.07; 0.05] 0.807

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	16 (11.6)	12 (9.4)	1.31 [0.59; 2.92] 0.509	1.19 [0.59; 2.39] 0.626	0.02 [-0.06; 0.09] 0.627
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.095**					
KESTREL					
Interaction Test:	p = 0.406				
Male					
N'/N	110 / 110	126 / 126			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	19 (17.3)	31 (24.6)	0.64 [0.34; 1.21] 0.171	0.70 [0.42; 1.17] 0.174	-0.07 [-0.18; 0.03] 0.164
Female					
N'/N	79 / 79	61 / 61			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (15.2)	9 (14.8)	1.03 [0.41; 2.64] 0.943	1.03 [0.46; 2.28] 0.943	0.00 [-0.11; 0.12] 0.943
KITE					
Interaction Test:	p = 0.857				
Male					
N'/N	120 / 120	115 / 115			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	18 (15.0)	13 (11.3)	1.38 [0.64; 2.97] 0.404	1.33 [0.68; 2.58] 0.405	0.04 [-0.05; 0.12] 0.401
Female					
N'/N	59 / 59	66 / 66			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	8 (13.6)	6 (9.1)	1.57 [0.51; 4.82] 0.432	1.49 [0.55; 4.05] 0.433	0.04 [-0.07; 0.16] 0.432
Pooled Analysis					
Interaction Test:	p = 0.431				
Male					
N'/N	230 / 230	241 / 241			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	37 (16.1)	44 (18.3)	0.92 [0.56; 1.50] 0.734	0.90 [0.60; 1.34] 0.600	-0.02 [-0.09; 0.05] 0.599

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	20 (14.5)	15 (11.8)	1.30 [0.63; 2.69] 0.476	1.19 [0.64; 2.22] 0.575	0.02 [-0.06; 0.11] 0.573

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-1.4 Any adverse event of potential relevance to intravitreal anti-VEGF injection by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.099**					
KESTREL					
Interaction Test:	p = 0.678				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (16.2)	12 (18.8)	0.84 [0.35; 2.02] 0.696	0.86 [0.42; 1.79] 0.695	-0.03 [-0.15; 0.10] 0.696
> 65 letters					
N'/N	115 / 115	123 / 123			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	13 (11.3)	20 (16.3)	0.66 [0.31; 1.39] 0.271	0.70 [0.36; 1.33] 0.273	-0.05 [-0.14; 0.04] 0.265
KITE					
Interaction Test:	p = 0.393				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (7.7)	7 (7.7)	1.00 [0.30; 3.30] 1.000	1.00 [0.33; 3.01] 1.000	0.00 [-0.08; 0.08] 1.000
> 65 letters					
N'/N	114 / 114	90 / 90			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	16 (14.0)	7 (7.8)	1.94 [0.76; 4.93] 0.166	1.80 [0.78; 4.20] 0.170	0.06 [-0.02; 0.15] 0.146
Pooled Analysis					
Interaction Test:	p = 0.741				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	17 (12.2)	19 (12.3)	0.98 [0.49; 1.99] 0.959	0.91 [0.49; 1.66] 0.754	-0.01 [-0.09; 0.06] 0.753

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	29 (12.7)	27 (12.7)	1.14 [0.64; 2.05] 0.652	1.01 [0.61; 1.68] 0.954	0.00 [-0.06; 0.06] 0.954
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.095**					
KESTREL					
Interaction Test:	p = 0.863				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	13 (17.6)	14 (21.9)	0.76 [0.33; 1.77] 0.525	0.80 [0.41; 1.58] 0.525	-0.04 [-0.18; 0.09] 0.527
> 65 letters					
N'/N	115 / 115	123 / 123			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	18 (15.7)	26 (21.1)	0.69 [0.36; 1.34] 0.278	0.74 [0.43; 1.28] 0.279	-0.05 [-0.15; 0.04] 0.273
KITE					
Interaction Test:	p = 0.907				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	8 (12.3)	8 (8.8)	1.46 [0.52; 4.10] 0.477	1.40 [0.55; 3.54] 0.477	0.04 [-0.06; 0.13] 0.485
> 65 letters					
N'/N	114 / 114	90 / 90			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	18 (15.8)	11 (12.2)	1.35 [0.60; 3.02] 0.470	1.29 [0.64; 2.59] 0.472	0.04 [-0.06; 0.13] 0.463
Pooled Analysis					
Interaction Test:	p = 0.889				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	21 (15.1)	22 (14.2)	1.05 [0.55; 2.01] 0.886	0.99 [0.57; 1.70] 0.961	-0.00 [-0.08; 0.08] 0.962

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	36 (15.7)	37 (17.4)	0.99 [0.59; 1.66] 0.966	0.92 [0.60; 1.41] 0.706	-0.01 [-0.08; 0.06] 0.705

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-1.5 Any adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.099**					
KESTREL					
Interaction Test:	p = 0.684				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	13 (14.4)	18 (21.7)	0.61 [0.28; 1.34] 0.217	0.67 [0.35; 1.27] 0.219	-0.07 [-0.19; 0.04] 0.216
European Region					
N'/N	69 / 69	75 / 75			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	8 (11.6)	11 (14.7)	0.76 [0.29; 2.02] 0.587	0.79 [0.34; 1.85] 0.588	-0.03 [-0.14; 0.08] 0.584
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	4 (13.3)	3 (10.3)	1.33 [0.27; 6.56] 0.723	1.29 [0.32; 5.26] 0.724	0.03 [-0.13; 0.19] 0.722
KITE					
Interaction Test:	p = 0.871				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	3 (11.5)	2 (9.5)	1.24 [0.19; 8.20] 0.824	1.21 [0.22; 6.59] 0.824	0.02 [-0.16; 0.20] 0.822
European Region					
N'/N	135 / 135	132 / 132			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	13 (9.6)	8 (6.1)	1.65 [0.66; 4.13] 0.283	1.59 [0.68; 3.71] 0.284	0.04 [-0.03; 0.10] 0.277
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (27.8)	4 (14.3)	2.31 [0.53; 10.12] 0.267	1.94 [0.60; 6.29] 0.267	0.13 [-0.11; 0.38] 0.279

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.789				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	13 (14.4)	18 (21.7)	0.88 [0.33; 2.32] 0.797	0.67 [0.35; 1.27] 0.216	-0.07 [-0.19; 0.04] 0.216
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	3 (11.5)	2 (9.5)	0.85 [0.12; 6.12] 0.868	1.21 [0.22; 6.59] 0.826	0.02 [-0.16; 0.20] 0.822
European Region					
N'/N	204 / 204	207 / 207			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	21 (10.3)	19 (9.2)	1.05 [0.54; 2.06] 0.885	1.14 [0.63; 2.05] 0.670	0.01 [-0.04; 0.07] 0.669
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	9 (18.8)	7 (12.3)	1.73 [0.59; 5.11] 0.321	1.62 [0.66; 3.98] 0.293	0.07 [-0.07; 0.21] 0.297
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.095**					
KESTREL					
Interaction Test:	p = 0.977				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	16 (17.8)	19 (22.9)	0.73 [0.35; 1.53] 0.404	0.78 [0.43; 1.41] 0.404	-0.05 [-0.17; 0.07] 0.404
European Region					
N'/N	69 / 69	75 / 75			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	10 (14.5)	14 (18.7)	0.74 [0.30; 1.79] 0.503	0.78 [0.37; 1.63] 0.504	-0.04 [-0.16; 0.08] 0.499
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (16.7)	7 (24.1)	0.63 [0.17; 2.27] 0.478	0.69 [0.25; 1.93] 0.480	-0.07 [-0.28; 0.13] 0.475

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.409				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	3 (11.5)	4 (19.0)	0.55 [0.11; 2.81] 0.476	0.61 [0.15; 2.41] 0.477	-0.08 [-0.28; 0.13] 0.479
European Region					
N'/N	135 / 135	132 / 132			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	18 (13.3)	10 (7.6)	1.88 [0.83; 4.23] 0.129	1.76 [0.84; 3.67] 0.132	0.06 [-0.02; 0.13] 0.122
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (27.8)	5 (17.9)	1.77 [0.43; 7.28] 0.429	1.56 [0.52; 4.62] 0.427	0.10 [-0.15; 0.35] 0.438
Pooled Analysis					
Interaction Test:	p = 0.637				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	16 (17.8)	19 (22.9)	1.15 [0.47; 2.83] 0.760	0.78 [0.43; 1.41] 0.404	-0.05 [-0.17; 0.07] 0.404
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	3 (11.5)	4 (19.0)	0.34 [0.06; 1.90] 0.221	0.61 [0.15; 2.41] 0.477	-0.08 [-0.28; 0.13] 0.479
European Region					
N'/N	204 / 204	207 / 207			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	28 (13.7)	24 (11.6)	1.12 [0.61; 2.05] 0.707	1.20 [0.72; 2.00] 0.486	0.02 [-0.04; 0.09] 0.485

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	10 (20.8)	12 (21.1)	1.05 [0.40; 2.73] 0.924	1.00 [0.48; 2.08] 0.994	-0.00 [-0.16; 0.16] 0.994

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-1.6 Any adverse event of potential relevance to intravitreal anti-VEGF injection by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.099**					
KESTREL					
Interaction Test:	p = 0.290				
Type 1					
N'/N	12 / 12	6 / 6			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (8.3)	2 (33.3)	0.18 [0.01; 2.60] 0.209	0.25 [0.03; 2.24] 0.215	-0.25 [-0.66; 0.16] 0.230
Type 2					
N'/N	177 / 177	181 / 181			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	24 (13.6)	30 (16.6)	0.79 [0.44; 1.41] 0.426	0.82 [0.50; 1.34] 0.427	-0.03 [-0.10; 0.04] 0.425
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	4 (21.1)	0 (0.0)	N.E.	3.60 [0.22; 59.46] 0.371	0.21 [0.03; 0.39] 0.024 *
Type 2					
N'/N	160 / 160	174 / 174			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	17 (10.6)	14 (8.0)	1.36 [0.65; 2.85] 0.418	1.32 [0.67; 2.59] 0.419	0.03 [-0.04; 0.09] 0.419
Pooled Analysis					
Interaction Test:	p = 0.958				
Type 1					
N'/N	31 / 31	13 / 13			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (16.1)	2 (15.4)	1.10 [0.18; 6.71] 0.914	0.96 [0.22; 4.08] 0.953	0.01 [-0.23; 0.25] 0.945

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	41 (12.2)	44 (12.4)	1.05 [0.66; 1.68] 0.836	0.97 [0.66; 1.45] 0.899	-0.00 [-0.05; 0.05] 0.899
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.095**					
KESTREL					
Interaction Test:	p = 0.298				
Type 1					
N'/N	12 / 12	6 / 6			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (8.3)	2 (33.3)	0.18 [0.01; 2.60] 0.209	0.25 [0.03; 2.24] 0.215	-0.25 [-0.66; 0.16] 0.230
Type 2					
N'/N	177 / 177	181 / 181			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	30 (16.9)	38 (21.0)	0.77 [0.45; 1.31] 0.330	0.81 [0.52; 1.24] 0.331	-0.04 [-0.12; 0.04] 0.328
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	6 (31.6)	0 (0.0)	N.E.	5.20 [0.33; 81.92] 0.241	0.32 [0.11; 0.52] 0.003 *
Type 2					
N'/N	160 / 160	174 / 174			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	20 (12.5)	19 (10.9)	1.17 [0.60; 2.27] 0.653	1.14 [0.63; 2.07] 0.653	0.02 [-0.05; 0.08] 0.654
Pooled Analysis					
Interaction Test:	p = 0.547				
Type 1					
N'/N	31 / 31	13 / 13			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	7 (22.6)	2 (15.4)	1.67 [0.29; 9.53] 0.565	1.30 [0.32; 5.21] 0.701	0.07 [-0.19; 0.32] 0.607

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	50 (14.8)	57 (16.1)	0.96 [0.63; 1.47] 0.857	0.92 [0.65; 1.30] 0.627	-0.01 [-0.07; 0.04] 0.626

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KITE, Week 100 / KITE: logit(proportion) = treatment [by diabetes type].

Table 21-1.7 Any adverse event of potential relevance to intravitreal anti-VEGF injection by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.099**					
KESTREL					
Interaction Test:	p = 0.169				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	15 (19.7)	19 (17.8)	1.14 [0.54; 2.41] 0.734	1.11 [0.60; 2.05] 0.734	0.02 [-0.10; 0.13] 0.736
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	10 (8.9)	13 (16.3)	0.51 [0.21; 1.22] 0.128	0.55 [0.25; 1.19] 0.129	-0.07 [-0.17; 0.02] 0.137
KITE					
Interaction Test:	p = 0.674				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	9 (11.0)	6 (6.3)	1.85 [0.63; 5.44] 0.264	1.76 [0.65; 4.73] 0.265	0.05 [-0.04; 0.13] 0.266
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (12.4)	8 (9.4)	1.36 [0.53; 3.50] 0.525	1.31 [0.56; 3.06] 0.526	0.03 [-0.06; 0.12] 0.520
Pooled Analysis					
Interaction Test:	p = 0.262				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	24 (15.2)	25 (12.3)	1.40 [0.75; 2.60] 0.286	1.28 [0.76; 2.15] 0.352	0.03 [-0.04; 0.10] 0.356

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	22 (10.5)	21 (12.7)	0.84 [0.44; 1.61] 0.609	0.82 [0.47; 1.44] 0.498	-0.02 [-0.09; 0.04] 0.504
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.095**					
KESTREL					
Interaction Test:	p = 0.597				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	17 (22.4)	26 (24.3)	0.90 [0.45; 1.80] 0.762	0.92 [0.54; 1.57] 0.762	-0.02 [-0.14; 0.10] 0.760
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	14 (12.5)	14 (17.5)	0.67 [0.30; 1.50] 0.335	0.71 [0.36; 1.41] 0.334	-0.05 [-0.15; 0.05] 0.343
KITE					
Interaction Test:	p = 0.252				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (14.6)	7 (7.3)	2.18 [0.82; 5.83] 0.120	2.01 [0.83; 4.86] 0.123	0.07 [-0.02; 0.17] 0.120
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	14 (14.4)	12 (14.1)	1.03 [0.45; 2.36] 0.952	1.02 [0.50; 2.09] 0.952	0.00 [-0.10; 0.10] 0.952
Pooled Analysis					
Interaction Test:	p = 0.353				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	29 (18.4)	33 (16.3)	1.25 [0.71; 2.19] 0.435	1.17 [0.74; 1.84] 0.495	0.03 [-0.05; 0.10] 0.497

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	28 (13.4)	26 (15.8)	0.85 [0.48; 1.53] 0.598	0.85 [0.52; 1.39] 0.517	-0.02 [-0.10; 0.05] 0.520

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-1.8 Any adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.099**					
KESTREL					
Interaction Test:	p = 0.545				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	17 (14.2)	18 (16.4)	0.84 [0.41; 1.73] 0.643	0.87 [0.47; 1.59] 0.643	-0.02 [-0.12; 0.07] 0.644
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	3 (10.0)	9 (23.1)	0.37 [0.09; 1.51] 0.166	0.43 [0.13; 1.46] 0.178	-0.13 [-0.30; 0.04] 0.132
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (12.8)	5 (13.2)	0.97 [0.26; 3.67] 0.965	0.97 [0.31; 3.10] 0.965	-0.00 [-0.15; 0.15] 0.965
KITE					
Interaction Test:	p = 0.613				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (14.1)	9 (9.8)	1.52 [0.60; 3.80] 0.375	1.44 [0.64; 3.25] 0.376	0.04 [-0.05; 0.14] 0.375
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	3 (5.9)	3 (6.1)	0.96 [0.18; 4.99] 0.960	0.96 [0.20; 4.53] 0.960	-0.00 [-0.10; 0.09] 0.960
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	6 (14.0)	2 (5.0)	3.08 [0.58; 16.25] 0.185	2.79 [0.60; 13.03] 0.192	0.09 [-0.03; 0.21] 0.156

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.254				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	29 (14.1)	27 (13.4)	1.18 [0.66; 2.12] 0.580	1.05 [0.65; 1.70] 0.851	0.01 [-0.06; 0.07] 0.851
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	6 (7.4)	12 (13.6)	0.52 [0.18; 1.46] 0.214	0.58 [0.23; 1.49] 0.249	-0.05 [-0.14; 0.04] 0.239
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	11 (13.4)	7 (9.0)	1.68 [0.61; 4.62] 0.318	1.50 [0.61; 3.69] 0.372	0.04 [-0.05; 0.14] 0.367
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 100 Test of heterogeneity in main analysis: **p_H=0.095**					
KESTREL					
Interaction Test:	p = 0.442				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	21 (17.5)	23 (20.9)	0.80 [0.42; 1.55] 0.512	0.84 [0.49; 1.42] 0.512	-0.03 [-0.14; 0.07] 0.512
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	3 (10.0)	10 (25.6)	0.32 [0.08; 1.30] 0.111	0.39 [0.12; 1.29] 0.124	-0.16 [-0.33; 0.02] 0.078
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	7 (17.9)	7 (18.4)	0.97 [0.30; 3.08] 0.957	0.97 [0.38; 2.51] 0.957	-0.00 [-0.18; 0.17] 0.957

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.921				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	14 (16.5)	12 (13.0)	1.31 [0.57; 3.03] 0.521	1.26 [0.62; 2.57] 0.521	0.03 [-0.07; 0.14] 0.521
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (9.8)	3 (6.1)	1.67 [0.38; 7.38] 0.501	1.60 [0.40; 6.34] 0.503	0.04 [-0.07; 0.14] 0.495
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	7 (16.3)	4 (10.0)	1.75 [0.47; 6.50] 0.403	1.63 [0.52; 5.14] 0.406	0.06 [-0.08; 0.21] 0.394
Pooled Analysis					
Interaction Test:	p = 0.530				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	35 (17.1)	35 (17.3)	1.06 [0.63; 1.80] 0.824	0.98 [0.64; 1.49] 0.907	-0.00 [-0.08; 0.07] 0.907
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	8 (9.9)	13 (14.8)	0.64 [0.25; 1.65] 0.358	0.71 [0.30; 1.65] 0.414	-0.04 [-0.14; 0.06] 0.407

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	14 (17.1)	11 (14.1)	1.31 [0.55; 3.12] 0.540	1.22 [0.59; 2.51] 0.600	0.03 [-0.08; 0.14] 0.596

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-1.9 Any adverse event of potential relevance to intravitreal anti-VEGF injection by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.099**					
KESTREL					
Interaction Test:	p = 0.097				
focal					
N'/N	59 / 59	48 / 48			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	6 (10.2)	12 (25.0)	0.34 [0.12; 0.99] 0.047 *	0.41 [0.16; 1.00] 0.051	-0.15 [-0.29; -0.00] 0.045 *
diffuse					
N'/N	127 / 127	134 / 134			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	18 (14.2)	19 (14.2)	1.00 [0.50; 2.00] 0.999	1.00 [0.55; 1.82] 0.999	-0.00 [-0.08; 0.08] 0.999
KITE					
Interaction Test:	p = 0.440				
focal					
N'/N	63 / 63	66 / 66			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	6 (9.5)	6 (9.1)	1.05 [0.32; 3.45] 0.933	1.05 [0.36; 3.08] 0.933	0.00 [-0.10; 0.10] 0.933
diffuse					
N'/N	115 / 115	109 / 109			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	15 (13.0)	8 (7.3)	1.89 [0.77; 4.66] 0.165	1.78 [0.79; 4.02] 0.168	0.06 [-0.02; 0.14] 0.155
Pooled Analysis					
Interaction Test:	p = 0.066				
focal					
N'/N	122 / 122	114 / 114			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (9.8)	18 (15.8)	0.58 [0.26; 1.27] 0.170	0.60 [0.31; 1.18] 0.137	-0.06 [-0.15; 0.02] 0.141

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	33 (13.6)	27 (11.1)	1.42 [0.81; 2.50] 0.223	1.24 [0.77; 2.00] 0.379	0.03 [-0.03; 0.08] 0.378
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.095**					
KESTREL					
Interaction Test:	p = 0.168				
focal					
N'/N	59 / 59	48 / 48			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	8 (13.6)	13 (27.1)	0.42 [0.16; 1.13] 0.085	0.50 [0.23; 1.11] 0.088	-0.14 [-0.29; 0.02] 0.083
diffuse					
N'/N	127 / 127	134 / 134			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	22 (17.3)	24 (17.9)	0.96 [0.51; 1.82] 0.901	0.97 [0.57; 1.64] 0.901	-0.01 [-0.10; 0.09] 0.901
KITE					
Interaction Test:	p = 0.330				
focal					
N'/N	63 / 63	66 / 66			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	7 (11.1)	8 (12.1)	0.91 [0.31; 2.67] 0.858	0.92 [0.35; 2.38] 0.858	-0.01 [-0.12; 0.10] 0.858
diffuse					
N'/N	115 / 115	109 / 109			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	19 (16.5)	11 (10.1)	1.76 [0.80; 3.90] 0.162	1.64 [0.82; 3.28] 0.164	0.06 [-0.02; 0.15] 0.154
Pooled Analysis					
Interaction Test:	p = 0.084				
focal					
N'/N	122 / 122	114 / 114			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	15 (12.3)	21 (18.4)	0.61 [0.30; 1.25] 0.178	0.65 [0.35; 1.18] 0.155	-0.07 [-0.16; 0.03] 0.157

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	41 (16.9)	35 (14.4)	1.32 [0.80; 2.19] 0.282	1.19 [0.78; 1.80] 0.422	0.03 [-0.04; 0.09] 0.421

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-1.10 Any adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.099**					
KESTREL					
Interaction Test:	p = 0.882				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	16 (15.0)	17 (17.7)	0.82 [0.39; 1.72] 0.596	0.84 [0.45; 1.58] 0.596	-0.03 [-0.13; 0.07] 0.596
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	8 (11.4)	12 (16.9)	0.63 [0.24; 1.66] 0.354	0.68 [0.29; 1.55] 0.356	-0.05 [-0.17; 0.06] 0.350
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (8.3)	3 (15.0)	0.52 [0.05; 5.60] 0.586	0.56 [0.06; 4.76] 0.592	-0.07 [-0.29; 0.15] 0.555
KITE					
Interaction Test:	p = 0.958				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	10 (11.8)	7 (8.5)	1.43 [0.52; 3.95] 0.492	1.38 [0.55; 3.45] 0.493	0.03 [-0.06; 0.12] 0.489
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	9 (12.2)	6 (7.6)	1.68 [0.57; 4.99] 0.346	1.60 [0.60; 4.28] 0.348	0.05 [-0.05; 0.14] 0.344
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	2 (10.0)	1 (5.3)	2.00 [0.17; 24.07] 0.585	1.90 [0.19; 19.27] 0.587	0.05 [-0.12; 0.21] 0.575

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.986				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	26 (13.5)	24 (13.5)	1.10 [0.60; 2.03] 0.761	1.00 [0.60; 1.66] 0.989	-0.00 [-0.07; 0.07] 0.989
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	17 (11.8)	18 (12.0)	1.03 [0.50; 2.10] 0.945	0.98 [0.53; 1.82] 0.947	-0.00 [-0.08; 0.07] 0.947
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	3 (9.4)	4 (10.3)	0.99 [0.20; 4.86] 0.994	0.98 [0.22; 4.39] 0.975	-0.00 [-0.14; 0.14] 0.975
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.095**					
KESTREL					
Interaction Test:	p = 0.941				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	18 (16.8)	22 (22.9)	0.68 [0.34; 1.36] 0.277	0.73 [0.42; 1.28] 0.278	-0.06 [-0.17; 0.05] 0.277
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (17.1)	15 (21.1)	0.77 [0.33; 1.79] 0.548	0.81 [0.41; 1.61] 0.549	-0.04 [-0.17; 0.09] 0.547
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (8.3)	3 (15.0)	0.52 [0.05; 5.60] 0.586	0.56 [0.06; 4.76] 0.592	-0.07 [-0.29; 0.15] 0.555

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.485				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (14.1)	11 (13.4)	1.06 [0.44; 2.56] 0.895	1.05 [0.49; 2.25] 0.895	0.01 [-0.10; 0.11] 0.895
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	10 (13.5)	7 (8.9)	1.61 [0.58; 4.47] 0.363	1.53 [0.61; 3.80] 0.365	0.05 [-0.05; 0.15] 0.362
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	4 (20.0)	1 (5.3)	4.50 [0.45; 44.51] 0.199	3.80 [0.47; 31.01] 0.213	0.15 [-0.05; 0.35] 0.153
Pooled Analysis					
Interaction Test:	p = 0.631				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	30 (15.6)	33 (18.5)	0.87 [0.50; 1.52] 0.627	0.84 [0.53; 1.31] 0.440	-0.03 [-0.11; 0.05] 0.440
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	22 (15.3)	22 (14.7)	1.08 [0.57; 2.07] 0.810	1.03 [0.60; 1.78] 0.902	0.01 [-0.08; 0.09] 0.902

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (15.6)	4 (10.3)	1.77 [0.43; 7.29] 0.431	1.57 [0.41; 6.04] 0.504	0.05 [-0.10; 0.21] 0.499

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-1.11 Any adverse event of potential relevance to intravitreal anti-VEGF injection by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.099**					
KESTREL					
Interaction Test:	p = 0.696				
presence					
N'/N	62 / 62	61 / 61			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	9 (14.5)	10 (16.4)	0.87 [0.33; 2.31] 0.773	0.89 [0.39; 2.03] 0.774	-0.02 [-0.15; 0.11] 0.773
absence					
N'/N	127 / 127	126 / 126			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	16 (12.6)	22 (17.5)	0.68 [0.34; 1.37] 0.281	0.72 [0.40; 1.31] 0.282	-0.05 [-0.14; 0.04] 0.278
KITE					
Interaction Test:	p = 0.649				
presence					
N'/N	56 / 56	67 / 67			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (8.9)	5 (7.5)	1.22 [0.33; 4.43] 0.767	1.20 [0.36; 3.92] 0.767	0.01 [-0.08; 0.11] 0.769
absence					
N'/N	123 / 123	114 / 114			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	16 (13.0)	9 (7.9)	1.74 [0.74; 4.12] 0.205	1.65 [0.76; 3.58] 0.207	0.05 [-0.03; 0.13] 0.195
Pooled Analysis					
Interaction Test:	p = 0.970				
presence					
N'/N	118 / 118	128 / 128			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	14 (11.9)	15 (11.7)	1.06 [0.48; 2.32] 0.888	0.98 [0.50; 1.94] 0.959	-0.00 [-0.08; 0.08] 0.959

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	32 (12.8)	31 (12.9)	1.08 [0.63; 1.86] 0.788	1.00 [0.63; 1.58] 0.989	-0.00 [-0.06; 0.06] 0.989
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.095**					
KESTREL					
Interaction Test:	p = 0.276				
presence					
N'/N	62 / 62	61 / 61			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (19.4)	11 (18.0)	1.09 [0.44; 2.70] 0.851	1.07 [0.51; 2.24] 0.851	0.01 [-0.12; 0.15] 0.851
absence					
N'/N	127 / 127	126 / 126			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	19 (15.0)	29 (23.0)	0.59 [0.31; 1.12] 0.105	0.65 [0.39; 1.10] 0.107	-0.08 [-0.18; 0.02] 0.101
KITE					
Interaction Test:	p = 0.522				
presence					
N'/N	56 / 56	67 / 67			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (8.9)	6 (9.0)	1.00 [0.29; 3.46] 0.996	1.00 [0.32; 3.09] 0.996	-0.00 [-0.10; 0.10] 0.996
absence					
N'/N	123 / 123	114 / 114			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	21 (17.1)	13 (11.4)	1.60 [0.76; 3.37] 0.216	1.50 [0.79; 2.85] 0.219	0.06 [-0.03; 0.15] 0.209
Pooled Analysis					
Interaction Test:	p = 0.708				
presence					
N'/N	118 / 118	128 / 128			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	17 (14.4)	17 (13.3)	1.13 [0.55; 2.36] 0.737	1.05 [0.56; 1.95] 0.882	0.01 [-0.08; 0.09] 0.882

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	40 (16.0)	42 (17.5)	0.96 [0.59; 1.56] 0.868	0.92 [0.62; 1.37] 0.674	-0.01 [-0.08; 0.05] 0.674

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-1.12 Any adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 52) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.099**					
KESTREL					
Interaction Test:	p = 0.630				
Non-exposed					
N'/N	71 / 71	75 / 75			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	11 (15.5)	13 (17.3)	0.87 [0.36; 2.10] 0.764	0.89 [0.43; 1.86] 0.765	-0.02 [-0.14; 0.10] 0.764
Exposed					
N'/N	118 / 118	112 / 112			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	14 (11.9)	19 (17.0)	0.66 [0.31; 1.39] 0.273	0.70 [0.37; 1.33] 0.274	-0.05 [-0.14; 0.04] 0.271
KITE					
Interaction Test:	p = 0.201				
Non-exposed					
N'/N	85 / 85	90 / 90			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	10 (11.8)	4 (4.4)	2.87 [0.86; 9.52] 0.086	2.65 [0.86; 8.12] 0.089	0.07 [-0.01; 0.15] 0.075
Exposed					
N'/N	94 / 94	91 / 91			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	11 (11.7)	10 (11.0)	1.07 [0.43; 2.67] 0.879	1.06 [0.48; 2.39] 0.879	0.01 [-0.08; 0.10] 0.878
Pooled Analysis					
Interaction Test:	p = 0.312				
Non-exposed					
N'/N	156 / 156	165 / 165			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	21 (13.5)	17 (10.3)	1.40 [0.70; 2.79] 0.338	1.31 [0.72; 2.37] 0.380	0.03 [-0.04; 0.10] 0.380

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	212 / 212	203 / 203			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	25 (11.8)	29 (14.3)	0.88 [0.49; 1.59] 0.674	0.82 [0.50; 1.36] 0.448	-0.03 [-0.09; 0.04] 0.448

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-1.13 Any adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.095**					
KESTREL					
Interaction Test:	p = 0.772				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (8.3)	1 (7.7)	1.09 [0.06; 19.62] 0.953	1.08 [0.08; 15.46] 0.953	0.01 [-0.21; 0.22] 0.953
Exposed					
N'/N	177 / 177	174 / 174			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	30 (16.9)	39 (22.4)	0.71 [0.42; 1.20] 0.199	0.76 [0.49; 1.16] 0.200	-0.05 [-0.14; 0.03] 0.197
KITE					
Interaction Test:	p = 0.595				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (5.9)	1 (8.3)	0.69 [0.04; 12.20] 0.799	0.71 [0.05; 10.21] 0.798	-0.02 [-0.22; 0.17] 0.803
Exposed					
N'/N	162 / 162	169 / 169			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	25 (15.4)	18 (10.7)	1.53 [0.80; 2.93] 0.198	1.45 [0.82; 2.55] 0.199	0.05 [-0.02; 0.12] 0.196
Pooled Analysis					
Interaction Test:	p = 0.930				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	2 (6.9)	2 (8.0)	0.93 [0.12; 7.23] 0.948	0.88 [0.13; 5.70] 0.892	-0.01 [-0.15; 0.13] 0.891

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any AE of potential relevance to intravitreal anti-VEGF injection, n (%)	55 (16.2)	57 (16.6)	1.03 [0.68; 1.56] 0.904	0.97 [0.69; 1.36] 0.862	-0.00 [-0.06; 0.05] 0.862

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-2.1 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	24 (12.7)	32 (17.1)	0.70 [0.40; 1.25] 0.231	0.74 [0.46; 1.21] 0.232	-0.04 [-0.12; 0.03] 0.229
KITE, N'/N	179 / 179	181 / 181			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	20 (11.2)	14 (7.7)	1.50 [0.73; 3.07] 0.267	1.44 [0.75; 2.77] 0.268	0.03 [-0.03; 0.09] 0.264
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	44 (12.0)	46 (12.5)	1.02 [0.65; 1.61] 0.931	0.95 [0.65; 1.40] 0.812	-0.01 [-0.05; 0.04] 0.812
p_H=0.106					
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	30 (15.9)	40 (21.4)	0.69 [0.41; 1.17] 0.171	0.74 [0.48; 1.14] 0.172	-0.06 [-0.13; 0.02] 0.169
KITE, N'/N	179 / 179	181 / 181			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	25 (14.0)	19 (10.5)	1.38 [0.73; 2.61] 0.316	1.33 [0.76; 2.33] 0.317	0.03 [-0.03; 0.10] 0.315

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	55 (14.9)	59 (16.0)	0.97 [0.65; 1.47] 0.896	0.93 [0.66; 1.30] 0.673	-0.01 [-0.06; 0.04] 0.674
p_H=0.100					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-2.2 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.751				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	15 (14.4)	17 (18.3)	0.75 [0.35; 1.61] 0.465	0.79 [0.42; 1.49] 0.465	-0.04 [-0.14; 0.07] 0.466
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	9 (10.6)	15 (16.0)	0.62 [0.26; 1.51] 0.295	0.66 [0.31; 1.44] 0.298	-0.05 [-0.15; 0.05] 0.287
KITE					
Interaction Test:	p = 0.394				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	14 (14.0)	8 (7.8)	1.91 [0.76; 4.78] 0.165	1.79 [0.78; 4.07] 0.168	0.06 [-0.02; 0.15] 0.159
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	6 (7.6)	6 (7.6)	1.00 [0.31; 3.25] 1.000	1.00 [0.34; 2.97] 1.000	0.00 [-0.08; 0.08] 1.000
Pooled Analysis					
Interaction Test:	p = 0.417				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	29 (14.2)	25 (12.8)	1.18 [0.66; 2.12] 0.584	1.09 [0.67; 1.79] 0.722	0.01 [-0.06; 0.08] 0.722

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	15 (9.1)	21 (12.1)	0.81 [0.39; 1.65] 0.558	0.76 [0.41; 1.43] 0.397	-0.03 [-0.09; 0.04] 0.393
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.853				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	18 (17.3)	21 (22.6)	0.72 [0.36; 1.45] 0.355	0.77 [0.44; 1.35] 0.355	-0.05 [-0.16; 0.06] 0.355
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (14.1)	19 (20.2)	0.65 [0.29; 1.43] 0.284	0.70 [0.36; 1.35] 0.287	-0.06 [-0.17; 0.05] 0.277
KITE					
Interaction Test:	p = 0.432				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	17 (17.0)	11 (10.8)	1.69 [0.75; 3.83] 0.205	1.58 [0.78; 3.20] 0.207	0.06 [-0.03; 0.16] 0.200
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	8 (10.1)	8 (10.1)	1.00 [0.36; 2.81] 1.000	1.00 [0.39; 2.53] 1.000	0.00 [-0.09; 0.09] 1.000
Pooled Analysis					
Interaction Test:	p = 0.496				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	35 (17.2)	32 (16.4)	1.09 [0.64; 1.85] 0.758	1.03 [0.67; 1.60] 0.883	0.01 [-0.07; 0.08] 0.883

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	20 (12.2)	27 (15.6)	0.82 [0.43; 1.54] 0.535	0.79 [0.46; 1.35] 0.391	-0.03 [-0.11; 0.04] 0.388

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-2.3 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.961				
Male					
N'/N	110 / 110	126 / 126			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	16 (14.5)	24 (19.0)	0.72 [0.36; 1.44] 0.359	0.76 [0.43; 1.36] 0.361	-0.05 [-0.14; 0.05] 0.353
Female					
N'/N	79 / 79	61 / 61			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	8 (10.1)	8 (13.1)	0.75 [0.26; 2.12] 0.583	0.77 [0.31; 1.94] 0.582	-0.03 [-0.14; 0.08] 0.587
KITE					
Interaction Test:	p = 0.769				
Male					
N'/N	120 / 120	115 / 115			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	14 (11.7)	10 (8.7)	1.39 [0.59; 3.26] 0.454	1.34 [0.62; 2.90] 0.454	0.03 [-0.05; 0.11] 0.450
Female					
N'/N	59 / 59	66 / 66			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	6 (10.2)	4 (6.1)	1.75 [0.47; 6.55] 0.403	1.68 [0.50; 5.66] 0.404	0.04 [-0.06; 0.14] 0.403
Pooled Analysis					
Interaction Test:	p = 0.802				
Male					
N'/N	230 / 230	241 / 241			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	30 (13.0)	34 (14.1)	0.99 [0.58; 1.71] 0.980	0.94 [0.60; 1.49] 0.808	-0.01 [-0.07; 0.05] 0.807

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	14 (10.1)	12 (9.4)	1.13 [0.49; 2.56] 0.779	1.04 [0.50; 2.14] 0.917	0.00 [-0.07; 0.08] 0.917
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.517				
Male					
N'/N	110 / 110	126 / 126			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	19 (17.3)	31 (24.6)	0.64 [0.34; 1.21] 0.171	0.70 [0.42; 1.17] 0.174	-0.07 [-0.18; 0.03] 0.164
Female					
N'/N	79 / 79	61 / 61			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	11 (13.9)	9 (14.8)	0.93 [0.36; 2.42] 0.889	0.94 [0.42; 2.13] 0.889	-0.01 [-0.13; 0.11] 0.890
KITE					
Interaction Test:	p = 0.968				
Male					
N'/N	120 / 120	115 / 115			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	18 (15.0)	13 (11.3)	1.38 [0.64; 2.97] 0.404	1.33 [0.68; 2.58] 0.405	0.04 [-0.05; 0.12] 0.401
Female					
N'/N	59 / 59	66 / 66			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	7 (11.9)	6 (9.1)	1.35 [0.43; 4.26] 0.613	1.31 [0.46; 3.66] 0.613	0.03 [-0.08; 0.14] 0.614
Pooled Analysis					
Interaction Test:	p = 0.616				
Male					
N'/N	230 / 230	241 / 241			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	37 (16.1)	44 (18.3)	0.92 [0.56; 1.50] 0.734	0.90 [0.60; 1.34] 0.600	-0.02 [-0.09; 0.05] 0.599

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	138 / 138	127 / 127			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	18 (13.0)	15 (11.8)	1.15 [0.55; 2.41] 0.711	1.07 [0.57; 2.03] 0.829	0.01 [-0.07; 0.09] 0.829

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-2.4 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.812				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	11 (14.9)	12 (18.8)	0.76 [0.31; 1.85] 0.542	0.79 [0.38; 1.67] 0.542	-0.04 [-0.16; 0.09] 0.544
> 65 letters					
N'/N	115 / 115	123 / 123			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	13 (11.3)	20 (16.3)	0.66 [0.31; 1.39] 0.271	0.70 [0.36; 1.33] 0.273	-0.05 [-0.14; 0.04] 0.265
KITE					
Interaction Test:	p = 0.451				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (7.7)	7 (7.7)	1.00 [0.30; 3.30] 1.000	1.00 [0.33; 3.01] 1.000	0.00 [-0.08; 0.08] 1.000
> 65 letters					
N'/N	114 / 114	90 / 90			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	15 (13.2)	7 (7.8)	1.80 [0.70; 4.61] 0.224	1.69 [0.72; 3.97] 0.227	0.05 [-0.03; 0.14] 0.205
Pooled Analysis					
Interaction Test:	p = 0.697				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	16 (11.5)	19 (12.3)	0.92 [0.45; 1.87] 0.810	0.86 [0.46; 1.59] 0.627	-0.02 [-0.09; 0.06] 0.625

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	28 (12.2)	27 (12.7)	1.10 [0.61; 1.98] 0.753	0.98 [0.59; 1.63] 0.945	-0.00 [-0.06; 0.06] 0.945
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.998				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (16.2)	14 (21.9)	0.69 [0.29; 1.63] 0.398	0.74 [0.37; 1.48] 0.398	-0.06 [-0.19; 0.07] 0.399
> 65 letters					
N'/N	115 / 115	123 / 123			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	18 (15.7)	26 (21.1)	0.69 [0.36; 1.34] 0.277	0.74 [0.43; 1.28] 0.279	-0.05 [-0.15; 0.04] 0.273
KITE					
Interaction Test:	p = 0.828				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	8 (12.3)	8 (8.8)	1.46 [0.52; 4.10] 0.477	1.40 [0.55; 3.54] 0.477	0.04 [-0.06; 0.13] 0.485
> 65 letters					
N'/N	114 / 114	90 / 90			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	17 (14.9)	11 (12.2)	1.26 [0.56; 2.84] 0.580	1.22 [0.60; 2.47] 0.581	0.03 [-0.07; 0.12] 0.575
Pooled Analysis					
Interaction Test:	p = 0.935				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	20 (14.4)	22 (14.2)	0.99 [0.51; 1.91] 0.976	0.94 [0.54; 1.64] 0.837	-0.01 [-0.09; 0.07] 0.838

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	229 / 229	213 / 213			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	35 (15.3)	37 (17.4)	0.96 [0.57; 1.61] 0.866	0.90 [0.59; 1.38] 0.622	-0.02 [-0.09; 0.05] 0.621

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-2.5 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.613				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (13.3)	18 (21.7)	0.56 [0.25; 1.24] 0.150	0.61 [0.32; 1.20] 0.153	-0.08 [-0.20; 0.03] 0.148
European Region					
N'/N	69 / 69	75 / 75			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	8 (11.6)	11 (14.7)	0.76 [0.29; 2.02] 0.587	0.79 [0.34; 1.85] 0.588	-0.03 [-0.14; 0.08] 0.584
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	4 (13.3)	3 (10.3)	1.33 [0.27; 6.56] 0.723	1.29 [0.32; 5.26] 0.724	0.03 [-0.13; 0.19] 0.722
KITE					
Interaction Test:	p = 0.708				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	2 (7.7)	2 (9.5)	0.79 [0.10; 6.15] 0.823	0.81 [0.12; 5.26] 0.823	-0.02 [-0.18; 0.14] 0.825
European Region					
N'/N	135 / 135	132 / 132			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	13 (9.6)	8 (6.1)	1.65 [0.66; 4.13] 0.283	1.59 [0.68; 3.71] 0.284	0.04 [-0.03; 0.10] 0.277
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (27.8)	4 (14.3)	2.31 [0.53; 10.12] 0.267	1.94 [0.60; 6.29] 0.267	0.13 [-0.11; 0.38] 0.279

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.651				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (13.3)	18 (21.7)	0.80 [0.30; 2.14] 0.660	0.61 [0.32; 1.20] 0.148	-0.08 [-0.20; 0.03] 0.148
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	2 (7.7)	2 (9.5)	0.54 [0.06; 4.56] 0.571	0.81 [0.12; 5.26] 0.825	-0.02 [-0.18; 0.14] 0.825
European Region					
N'/N	204 / 204	207 / 207			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	21 (10.3)	19 (9.2)	1.05 [0.54; 2.06] 0.885	1.14 [0.63; 2.05] 0.670	0.01 [-0.04; 0.07] 0.669
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	9 (18.8)	7 (12.3)	1.73 [0.59; 5.11] 0.321	1.62 [0.66; 3.98] 0.293	0.07 [-0.07; 0.21] 0.297
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.977				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	15 (16.7)	19 (22.9)	0.67 [0.32; 1.43] 0.305	0.73 [0.40; 1.34] 0.306	-0.06 [-0.18; 0.06] 0.304
European Region					
N'/N	69 / 69	75 / 75			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	10 (14.5)	14 (18.7)	0.74 [0.30; 1.79] 0.503	0.78 [0.37; 1.63] 0.504	-0.04 [-0.16; 0.08] 0.499
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (16.7)	7 (24.1)	0.63 [0.17; 2.27] 0.478	0.69 [0.25; 1.93] 0.480	-0.07 [-0.28; 0.13] 0.475

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.247				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	2 (7.7)	4 (19.0)	0.35 [0.06; 2.16] 0.260	0.40 [0.08; 1.99] 0.266	-0.11 [-0.31; 0.08] 0.258
European Region					
N'/N	135 / 135	132 / 132			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	18 (13.3)	10 (7.6)	1.88 [0.83; 4.23] 0.129	1.76 [0.84; 3.67] 0.132	0.06 [-0.02; 0.13] 0.122
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (27.8)	5 (17.9)	1.77 [0.43; 7.28] 0.429	1.56 [0.52; 4.62] 0.427	0.10 [-0.15; 0.35] 0.438
Pooled Analysis					
Interaction Test:	p = 0.442				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	15 (16.7)	19 (22.9)	1.06 [0.43; 2.64] 0.893	0.73 [0.40; 1.34] 0.305	-0.06 [-0.18; 0.06] 0.304
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	2 (7.7)	4 (19.0)	0.22 [0.03; 1.45] 0.115	0.40 [0.08; 1.99] 0.251	-0.11 [-0.31; 0.08] 0.258
European Region					
N'/N	204 / 204	207 / 207			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	28 (13.7)	24 (11.6)	1.12 [0.61; 2.05] 0.707	1.20 [0.72; 2.00] 0.486	0.02 [-0.04; 0.09] 0.485

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	10 (20.8)	12 (21.1)	1.05 [0.40; 2.73] 0.924	1.00 [0.48; 2.08] 0.994	-0.00 [-0.16; 0.16] 0.994

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-2.6 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.307				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (8.3)	2 (33.3)	0.18 [0.01; 2.60] 0.209	0.25 [0.03; 2.24] 0.215	-0.25 [-0.66; 0.16] 0.230
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	23 (13.0)	30 (16.6)	0.75 [0.42; 1.35] 0.341	0.78 [0.47; 1.30] 0.342	-0.04 [-0.11; 0.04] 0.339
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	4 (21.1)	0 (0.0)	N.E.	3.60 [0.22; 59.46] 0.371	0.21 [0.03; 0.39] 0.024 *
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	16 (10.0)	14 (8.0)	1.27 [0.60; 2.69] 0.533	1.24 [0.63; 2.46] 0.534	0.02 [-0.04; 0.08] 0.534
Pooled Analysis					
Interaction Test:	p = 0.909				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (16.1)	2 (15.4)	1.11 [0.18; 6.72] 0.913	0.96 [0.22; 4.08] 0.953	0.01 [-0.23; 0.25] 0.945

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	39 (11.6)	44 (12.4)	0.99 [0.62; 1.60] 0.975	0.93 [0.62; 1.39] 0.712	-0.01 [-0.06; 0.04] 0.711
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.312				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (8.3)	2 (33.3)	0.18 [0.01; 2.60] 0.209	0.25 [0.03; 2.24] 0.215	-0.25 [-0.66; 0.16] 0.230
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	29 (16.4)	38 (21.0)	0.74 [0.43; 1.26] 0.264	0.78 [0.50; 1.21] 0.266	-0.05 [-0.13; 0.03] 0.262
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	6 (31.6)	0 (0.0)	N.E.	5.20 [0.33; 81.92] 0.241	0.32 [0.11; 0.52] 0.003 *
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	19 (11.9)	19 (10.9)	1.10 [0.56; 2.16] 0.784	1.09 [0.60; 1.98] 0.784	0.01 [-0.06; 0.08] 0.784
Pooled Analysis					
Interaction Test:	p = 0.512				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	7 (22.6)	2 (15.4)	1.67 [0.29; 9.54] 0.564	1.30 [0.32; 5.21] 0.701	0.07 [-0.19; 0.32] 0.607

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	48 (14.2)	57 (16.1)	0.92 [0.60; 1.41] 0.689	0.88 [0.62; 1.25] 0.479	-0.02 [-0.07; 0.03] 0.478

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KITE, Week 100 / KITE: logit(proportion) = treatment [by diabetes type].

Table 21-2.7 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.221				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	14 (18.4)	19 (17.8)	1.05 [0.49; 2.24] 0.908	1.04 [0.56; 1.94] 0.908	0.01 [-0.11; 0.12] 0.909
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	10 (8.9)	13 (16.3)	0.51 [0.21; 1.22] 0.128	0.55 [0.25; 1.19] 0.129	-0.07 [-0.17; 0.02] 0.137
KITE					
Interaction Test:	p = 0.581				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	9 (11.0)	6 (6.3)	1.85 [0.63; 5.44] 0.264	1.76 [0.65; 4.73] 0.265	0.05 [-0.04; 0.13] 0.266
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	11 (11.3)	8 (9.4)	1.23 [0.47; 3.22] 0.672	1.20 [0.51; 2.86] 0.672	0.02 [-0.07; 0.11] 0.669
Pooled Analysis					
Interaction Test:	p = 0.264				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	23 (14.6)	25 (12.3)	1.33 [0.71; 2.48] 0.368	1.22 [0.72; 2.07] 0.452	0.03 [-0.04; 0.10] 0.454

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	21 (10.0)	21 (12.7)	0.80 [0.42; 1.54] 0.507	0.79 [0.45; 1.38] 0.402	-0.03 [-0.09; 0.04] 0.409
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.701				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	16 (21.1)	26 (24.3)	0.83 [0.41; 1.68] 0.607	0.87 [0.50; 1.50] 0.609	-0.03 [-0.15; 0.09] 0.603
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	14 (12.5)	14 (17.5)	0.67 [0.30; 1.50] 0.335	0.71 [0.36; 1.41] 0.334	-0.05 [-0.15; 0.05] 0.343
KITE					
Interaction Test:	p = 0.204				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (14.6)	7 (7.3)	2.18 [0.82; 5.83] 0.120	2.01 [0.83; 4.86] 0.123	0.07 [-0.02; 0.17] 0.120
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	13 (13.4)	12 (14.1)	0.94 [0.40; 2.19] 0.889	0.95 [0.46; 1.97] 0.889	-0.01 [-0.11; 0.09] 0.889
Pooled Analysis					
Interaction Test:	p = 0.357				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	28 (17.7)	33 (16.3)	1.20 [0.68; 2.10] 0.531	1.13 [0.71; 1.79] 0.605	0.02 [-0.06; 0.10] 0.606

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	27 (12.9)	26 (15.8)	0.82 [0.45; 1.48] 0.507	0.82 [0.50; 1.34] 0.428	-0.03 [-0.10; 0.04] 0.432

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-2.8 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.575				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	16 (13.3)	18 (16.4)	0.79 [0.38; 1.63] 0.518	0.81 [0.44; 1.52] 0.519	-0.03 [-0.12; 0.06] 0.519
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	3 (10.0)	9 (23.1)	0.37 [0.09; 1.51] 0.166	0.43 [0.13; 1.46] 0.178	-0.13 [-0.30; 0.04] 0.132
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (12.8)	5 (13.2)	0.97 [0.26; 3.67] 0.965	0.97 [0.31; 3.10] 0.965	-0.00 [-0.15; 0.15] 0.965
KITE					
Interaction Test:	p = 0.730				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (14.1)	9 (9.8)	1.52 [0.60; 3.80] 0.375	1.44 [0.64; 3.25] 0.376	0.04 [-0.05; 0.14] 0.375
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	3 (5.9)	3 (6.1)	0.96 [0.18; 4.99] 0.960	0.96 [0.20; 4.53] 0.960	-0.00 [-0.10; 0.09] 0.960
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (11.6)	2 (5.0)	2.50 [0.46; 13.69] 0.291	2.33 [0.48; 11.32] 0.296	0.07 [-0.05; 0.18] 0.268

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.317				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	28 (13.7)	27 (13.4)	1.13 [0.63; 2.04] 0.681	1.01 [0.62; 1.65] 0.959	0.00 [-0.06; 0.07] 0.959
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	6 (7.4)	12 (13.6)	0.52 [0.18; 1.47] 0.215	0.58 [0.23; 1.49] 0.249	-0.05 [-0.14; 0.04] 0.239
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	10 (12.2)	7 (9.0)	1.50 [0.54; 4.21] 0.439	1.37 [0.55; 3.42] 0.503	0.03 [-0.06; 0.13] 0.499
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.461				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	20 (16.7)	23 (20.9)	0.76 [0.39; 1.47] 0.411	0.80 [0.46; 1.37] 0.411	-0.04 [-0.14; 0.06] 0.411
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	3 (10.0)	10 (25.6)	0.32 [0.08; 1.30] 0.111	0.39 [0.12; 1.29] 0.124	-0.16 [-0.33; 0.02] 0.078
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	7 (17.9)	7 (18.4)	0.97 [0.30; 3.08] 0.957	0.97 [0.38; 2.51] 0.957	-0.00 [-0.18; 0.17] 0.957

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.962				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	14 (16.5)	12 (13.0)	1.31 [0.57; 3.03] 0.521	1.26 [0.62; 2.57] 0.521	0.03 [-0.07; 0.14] 0.521
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (9.8)	3 (6.1)	1.67 [0.38; 7.38] 0.501	1.60 [0.40; 6.34] 0.503	0.04 [-0.07; 0.14] 0.495
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	6 (14.0)	4 (10.0)	1.46 [0.38; 5.61] 0.582	1.40 [0.42; 4.58] 0.583	0.04 [-0.10; 0.18] 0.578
Pooled Analysis					
Interaction Test:	p = 0.607				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	34 (16.6)	35 (17.3)	1.02 [0.60; 1.75] 0.928	0.95 [0.62; 1.45] 0.808	-0.01 [-0.08; 0.06] 0.808
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	8 (9.9)	13 (14.8)	0.64 [0.25; 1.65] 0.359	0.71 [0.30; 1.65] 0.414	-0.04 [-0.14; 0.06] 0.407

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	13 (15.9)	11 (14.1)	1.20 [0.50; 2.89] 0.684	1.13 [0.54; 2.37] 0.748	0.02 [-0.09; 0.13] 0.746

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-2.9 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.121				
focal					
N'/N	59 / 59	48 / 48			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	6 (10.2)	12 (25.0)	0.34 [0.12; 0.99] 0.047 *	0.41 [0.16; 1.00] 0.051	-0.15 [-0.29; -0.00] 0.045 *
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	17 (13.4)	19 (14.2)	0.94 [0.46; 1.89] 0.853	0.94 [0.51; 1.73] 0.853	-0.01 [-0.09; 0.08] 0.853
KITE					
Interaction Test:	p = 0.506				
focal					
N'/N	63 / 63	66 / 66			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	6 (9.5)	6 (9.1)	1.05 [0.32; 3.45] 0.933	1.05 [0.36; 3.08] 0.933	0.00 [-0.10; 0.10] 0.933
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	14 (12.2)	8 (7.3)	1.75 [0.70; 4.35] 0.229	1.66 [0.72; 3.80] 0.231	0.05 [-0.03; 0.13] 0.220
Pooled Analysis					
Interaction Test:	p = 0.092				
focal					
N'/N	122 / 122	114 / 114			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (9.8)	18 (15.8)	0.58 [0.26; 1.27] 0.170	0.60 [0.31; 1.18] 0.137	-0.06 [-0.15; 0.02] 0.141

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	31 (12.8)	27 (11.1)	1.32 [0.75; 2.34] 0.339	1.16 [0.72; 1.89] 0.540	0.02 [-0.04; 0.08] 0.539
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.201				
focal					
N'/N	59 / 59	48 / 48			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	8 (13.6)	13 (27.1)	0.42 [0.16; 1.13] 0.085	0.50 [0.23; 1.11] 0.088	-0.14 [-0.29; 0.02] 0.083
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	21 (16.5)	24 (17.9)	0.91 [0.48; 1.73] 0.769	0.92 [0.54; 1.57] 0.769	-0.01 [-0.11; 0.08] 0.769
KITE					
Interaction Test:	p = 0.380				
focal					
N'/N	63 / 63	66 / 66			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	7 (11.1)	8 (12.1)	0.91 [0.31; 2.67] 0.858	0.92 [0.35; 2.38] 0.858	-0.01 [-0.12; 0.10] 0.858
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	18 (15.7)	11 (10.1)	1.65 [0.74; 3.68] 0.218	1.55 [0.77; 3.13] 0.221	0.06 [-0.03; 0.14] 0.211
Pooled Analysis					
Interaction Test:	p = 0.113				
focal					
N'/N	122 / 122	114 / 114			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	15 (12.3)	21 (18.4)	0.61 [0.30; 1.25] 0.178	0.65 [0.35; 1.18] 0.155	-0.07 [-0.16; 0.03] 0.157

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	39 (16.1)	35 (14.4)	1.24 [0.75; 2.07] 0.404	1.13 [0.74; 1.72] 0.576	0.02 [-0.05; 0.08] 0.575

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-2.10 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.930				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	15 (14.0)	17 (17.7)	0.76 [0.36; 1.61] 0.472	0.79 [0.42; 1.50] 0.472	-0.04 [-0.14; 0.06] 0.473
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	8 (11.4)	12 (16.9)	0.63 [0.24; 1.66] 0.354	0.68 [0.29; 1.55] 0.356	-0.05 [-0.17; 0.06] 0.350
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (8.3)	3 (15.0)	0.52 [0.05; 5.60] 0.586	0.56 [0.06; 4.76] 0.592	-0.07 [-0.29; 0.15] 0.555
KITE					
Interaction Test:	p = 0.970				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	10 (11.8)	7 (8.5)	1.43 [0.52; 3.95] 0.492	1.38 [0.55; 3.45] 0.493	0.03 [-0.06; 0.12] 0.489
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	8 (10.8)	6 (7.6)	1.47 [0.49; 4.47] 0.493	1.42 [0.52; 3.91] 0.493	0.03 [-0.06; 0.12] 0.492
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	2 (10.0)	1 (5.3)	2.00 [0.17; 24.07] 0.585	1.90 [0.19; 19.27] 0.587	0.05 [-0.12; 0.21] 0.575

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.981				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	25 (13.0)	24 (13.5)	1.05 [0.57; 1.95] 0.876	0.96 [0.57; 1.61] 0.873	-0.01 [-0.07; 0.06] 0.873
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	16 (11.1)	18 (12.0)	0.96 [0.46; 1.98] 0.907	0.92 [0.49; 1.73] 0.798	-0.01 [-0.08; 0.06] 0.798
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	3 (9.4)	4 (10.3)	1.00 [0.20; 4.87] 0.995	0.98 [0.22; 4.39] 0.975	-0.00 [-0.14; 0.14] 0.975
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.916				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	17 (15.9)	22 (22.9)	0.64 [0.31; 1.28] 0.206	0.69 [0.39; 1.23] 0.208	-0.07 [-0.18; 0.04] 0.206
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (17.1)	15 (21.1)	0.77 [0.33; 1.79] 0.548	0.81 [0.41; 1.61] 0.549	-0.04 [-0.17; 0.09] 0.547
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (8.3)	3 (15.0)	0.52 [0.05; 5.60] 0.586	0.56 [0.06; 4.76] 0.592	-0.07 [-0.29; 0.15] 0.555

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE					
Interaction Test:	p = 0.508				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	12 (14.1)	11 (13.4)	1.06 [0.44; 2.56] 0.895	1.05 [0.49; 2.25] 0.895	0.01 [-0.10; 0.11] 0.895
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	9 (12.2)	7 (8.9)	1.42 [0.50; 4.04] 0.506	1.37 [0.54; 3.50] 0.507	0.03 [-0.06; 0.13] 0.506
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	4 (20.0)	1 (5.3)	4.50 [0.45; 44.52] 0.199	3.80 [0.47; 31.01] 0.213	0.15 [-0.05; 0.35] 0.153
Pooled Analysis					
Interaction Test:	p = 0.609				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	29 (15.1)	33 (18.5)	0.84 [0.48; 1.46] 0.532	0.81 [0.51; 1.28] 0.363	-0.04 [-0.11; 0.04] 0.364
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	21 (14.6)	22 (14.7)	1.02 [0.53; 1.97] 0.941	0.99 [0.57; 1.71] 0.962	-0.00 [-0.08; 0.08] 0.962

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (15.6)	4 (10.3)	1.77 [0.43; 7.30] 0.430	1.57 [0.41; 6.04] 0.504	0.05 [-0.10; 0.21] 0.499

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-2.11 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.869				
presence					
N'/N	62 / 62	61 / 61			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	8 (12.9)	10 (16.4)	0.76 [0.28; 2.06] 0.585	0.79 [0.33; 1.86] 0.585	-0.03 [-0.16; 0.09] 0.584
absence					
N'/N	127 / 127	126 / 126			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	16 (12.6)	22 (17.5)	0.68 [0.34; 1.37] 0.281	0.72 [0.40; 1.31] 0.282	-0.05 [-0.14; 0.04] 0.278
KITE					
Interaction Test:	p = 0.718				
presence					
N'/N	56 / 56	67 / 67			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (8.9)	5 (7.5)	1.22 [0.33; 4.43] 0.767	1.20 [0.36; 3.92] 0.767	0.01 [-0.08; 0.11] 0.769
absence					
N'/N	123 / 123	114 / 114			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	15 (12.2)	9 (7.9)	1.62 [0.68; 3.86] 0.276	1.54 [0.70; 3.39] 0.278	0.04 [-0.03; 0.12] 0.268
Pooled Analysis					
Interaction Test:	p = 0.893				
presence					
N'/N	118 / 118	128 / 128			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	13 (11.0)	15 (11.7)	0.97 [0.44; 2.16] 0.946	0.91 [0.46; 1.83] 0.801	-0.01 [-0.09; 0.07] 0.800

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	31 (12.4)	31 (12.9)	1.04 [0.60; 1.80] 0.891	0.97 [0.61; 1.54] 0.885	-0.00 [-0.06; 0.05] 0.885
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.373				
presence					
N'/N	62 / 62	61 / 61			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	11 (17.7)	11 (18.0)	0.98 [0.39; 2.47] 0.966	0.98 [0.46; 2.10] 0.966	-0.00 [-0.14; 0.13] 0.966
absence					
N'/N	127 / 127	126 / 126			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	19 (15.0)	29 (23.0)	0.59 [0.31; 1.12] 0.104	0.65 [0.39; 1.10] 0.107	-0.08 [-0.18; 0.02] 0.101
KITE					
Interaction Test:	p = 0.576				
presence					
N'/N	56 / 56	67 / 67			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	5 (8.9)	6 (9.0)	1.00 [0.29; 3.46] 0.996	1.00 [0.32; 3.09] 0.996	-0.00 [-0.10; 0.10] 0.996
absence					
N'/N	123 / 123	114 / 114			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	20 (16.3)	13 (11.4)	1.51 [0.71; 3.19] 0.283	1.43 [0.74; 2.73] 0.285	0.05 [-0.04; 0.14] 0.277
Pooled Analysis					
Interaction Test:	p = 0.779				
presence					
N'/N	118 / 118	128 / 128			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	16 (13.6)	17 (13.3)	1.06 [0.50; 2.22] 0.885	0.99 [0.53; 1.86] 0.971	-0.00 [-0.09; 0.08] 0.971

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	250 / 250	240 / 240			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	39 (15.6)	42 (17.5)	0.93 [0.57; 1.52] 0.774	0.90 [0.60; 1.34] 0.589	-0.02 [-0.08; 0.05] 0.589

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-2.12 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 52) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.774				
Non-exposed					
N'/N	71 / 71	75 / 75			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	10 (14.1)	13 (17.3)	0.78 [0.32; 1.92] 0.591	0.81 [0.38; 1.73] 0.591	-0.03 [-0.15; 0.09] 0.589
Exposed					
N'/N	118 / 118	112 / 112			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	14 (11.9)	19 (17.0)	0.66 [0.31; 1.39] 0.273	0.70 [0.37; 1.33] 0.274	-0.05 [-0.14; 0.04] 0.271
KITE					
Interaction Test:	p = 0.159				
Non-exposed					
N'/N	85 / 85	90 / 90			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	10 (11.8)	4 (4.4)	2.87 [0.86; 9.52] 0.085	2.65 [0.86; 8.12] 0.089	0.07 [-0.01; 0.15] 0.075
Exposed					
N'/N	94 / 94	91 / 91			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	10 (10.6)	10 (11.0)	0.96 [0.38; 2.44] 0.939	0.97 [0.42; 2.22] 0.939	-0.00 [-0.09; 0.09] 0.939
Pooled Analysis					
Interaction Test:	p = 0.326				
Non-exposed					
N'/N	156 / 156	165 / 165			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	20 (12.8)	17 (10.3)	1.32 [0.66; 2.65] 0.429	1.24 [0.68; 2.28] 0.479	0.03 [-0.04; 0.09] 0.480

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	212 / 212	203 / 203			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	24 (11.3)	29 (14.3)	0.84 [0.46; 1.53] 0.568	0.79 [0.48; 1.31] 0.363	-0.03 [-0.09; 0.03] 0.363

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-2.13 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.751				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (8.3)	1 (7.7)	1.09 [0.06; 19.62] 0.953	1.08 [0.08; 15.46] 0.953	0.01 [-0.21; 0.22] 0.953
Exposed					
N'/N	177 / 177	174 / 174			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	29 (16.4)	39 (22.4)	0.68 [0.40; 1.16] 0.154	0.73 [0.47; 1.13] 0.156	-0.06 [-0.14; 0.02] 0.152
KITE					
Interaction Test:	p = 0.617				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (5.9)	1 (8.3)	0.69 [0.04; 12.20] 0.799	0.71 [0.05; 10.21] 0.798	-0.02 [-0.22; 0.17] 0.803
Exposed					
N'/N	162 / 162	169 / 169			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	24 (14.8)	18 (10.7)	1.46 [0.76; 2.80] 0.257	1.39 [0.79; 2.46] 0.258	0.04 [-0.03; 0.11] 0.256
Pooled Analysis					
Interaction Test:	p = 0.963				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	2 (6.9)	2 (8.0)	0.93 [0.12; 7.23] 0.948	0.88 [0.13; 5.70] 0.892	-0.01 [-0.15; 0.13] 0.891

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed					
N'/N	339 / 339	343 / 343			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	53 (15.6)	57 (16.6)	0.98 [0.65; 1.49] 0.931	0.94 [0.66; 1.32] 0.700	-0.01 [-0.07; 0.04] 0.700

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-3.1 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	24 (12.7)	32 (17.1)	0.70 [0.40; 1.25] 0.231	0.74 [0.46; 1.21] 0.232	-0.04 [-0.12; 0.03] 0.229
KITE, N'/N	179 / 179	181 / 181			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	20 (11.2)	14 (7.7)	1.50 [0.73; 3.07] 0.267	1.44 [0.75; 2.77] 0.268	0.03 [-0.03; 0.09] 0.264
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	44 (12.0)	46 (12.5)	1.02 [0.65; 1.61] 0.931	0.95 [0.65; 1.40] 0.812	-0.01 [-0.05; 0.04] 0.812
p_H=0.106					
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	30 (15.9)	40 (21.4)	0.69 [0.41; 1.17] 0.171	0.74 [0.48; 1.14] 0.172	-0.06 [-0.13; 0.02] 0.169
KITE, N'/N	179 / 179	181 / 181			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	25 (14.0)	19 (10.5)	1.38 [0.73; 2.61] 0.316	1.33 [0.76; 2.33] 0.317	0.03 [-0.03; 0.10] 0.315

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	55 (14.9)	59 (16.0)	0.97 [0.65; 1.47] 0.896	0.93 [0.66; 1.30] 0.673	-0.01 [-0.06; 0.04] 0.674
p_H=0.100					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-3.2 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by age (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.751				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	15 (14.4)	17 (18.3)	0.75 [0.35; 1.61] 0.465	0.79 [0.42; 1.49] 0.465	-0.04 [-0.14; 0.07] 0.466
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	9 (10.6)	15 (16.0)	0.62 [0.26; 1.51] 0.295	0.66 [0.31; 1.44] 0.298	-0.05 [-0.15; 0.05] 0.287
KITE					
Interaction Test:	p = 0.394				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	14 (14.0)	8 (7.8)	1.91 [0.76; 4.78] 0.165	1.79 [0.78; 4.07] 0.168	0.06 [-0.02; 0.15] 0.159
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	6 (7.6)	6 (7.6)	1.00 [0.31; 3.25] 1.000	1.00 [0.34; 2.97] 1.000	0.00 [-0.08; 0.08] 1.000

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.417				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	29 (14.2)	25 (12.8)	1.18 [0.66; 2.12] 0.584	1.09 [0.67; 1.79] 0.722	0.01 [-0.06; 0.08] 0.722
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	15 (9.1)	21 (12.1)	0.81 [0.39; 1.65] 0.558	0.76 [0.41; 1.43] 0.397	-0.03 [-0.09; 0.04] 0.393
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 100 Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.853				
< 65 years					
N'/N	104 / 104	93 / 93			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	18 (17.3)	21 (22.6)	0.72 [0.36; 1.45] 0.355	0.77 [0.44; 1.35] 0.355	-0.05 [-0.16; 0.06] 0.355
≥ 65 years					
N'/N	85 / 85	94 / 94			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	12 (14.1)	19 (20.2)	0.65 [0.29; 1.43] 0.284	0.70 [0.36; 1.35] 0.287	-0.06 [-0.17; 0.05] 0.277
KITE					
Interaction Test:	p = 0.432				
< 65 years					
N'/N	100 / 100	102 / 102			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	17 (17.0)	11 (10.8)	1.69 [0.75; 3.83] 0.205	1.58 [0.78; 3.20] 0.207	0.06 [-0.03; 0.16] 0.200

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by age (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 65 years					
N'/N	79 / 79	79 / 79			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	8 (10.1)	8 (10.1)	1.00 [0.36; 2.81] 1.000	1.00 [0.39; 2.53] 1.000	0.00 [-0.09; 0.09] 1.000
Pooled Analysis					
Interaction Test:	p = 0.496				
< 65 years					
N'/N	204 / 204	195 / 195			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	35 (17.2)	32 (16.4)	1.09 [0.64; 1.85] 0.758	1.03 [0.67; 1.60] 0.883	0.01 [-0.07; 0.08] 0.883
≥ 65 years					
N'/N	164 / 164	173 / 173			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	20 (12.2)	27 (15.6)	0.82 [0.43; 1.54] 0.535	0.79 [0.46; 1.35] 0.391	-0.03 [-0.11; 0.04] 0.388

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + age + treatment * age.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + age + treatment * age.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-3.3 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by gender (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.961				
Male					
N'/N	110 / 110	126 / 126			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	16 (14.5)	24 (19.0)	0.72 [0.36; 1.44] 0.359	0.76 [0.43; 1.36] 0.361	-0.05 [-0.14; 0.05] 0.353
Female					
N'/N	79 / 79	61 / 61			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	8 (10.1)	8 (13.1)	0.75 [0.26; 2.12] 0.583	0.77 [0.31; 1.94] 0.582	-0.03 [-0.14; 0.08] 0.587
KITE					
Interaction Test:	p = 0.769				
Male					
N'/N	120 / 120	115 / 115			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	14 (11.7)	10 (8.7)	1.39 [0.59; 3.26] 0.454	1.34 [0.62; 2.90] 0.454	0.03 [-0.05; 0.11] 0.450
Female					
N'/N	59 / 59	66 / 66			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	6 (10.2)	4 (6.1)	1.75 [0.47; 6.55] 0.403	1.68 [0.50; 5.66] 0.404	0.04 [-0.06; 0.14] 0.403

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.802				
Male					
N'/N	230 / 230	241 / 241			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	30 (13.0)	34 (14.1)	0.99 [0.58; 1.71] 0.980	0.94 [0.60; 1.49] 0.808	-0.01 [-0.07; 0.05] 0.807
Female					
N'/N	138 / 138	127 / 127			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	14 (10.1)	12 (9.4)	1.13 [0.49; 2.56] 0.779	1.04 [0.50; 2.14] 0.917	0.00 [-0.07; 0.08] 0.917
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 100 Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.517				
Male					
N'/N	110 / 110	126 / 126			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	19 (17.3)	31 (24.6)	0.64 [0.34; 1.21] 0.171	0.70 [0.42; 1.17] 0.174	-0.07 [-0.18; 0.03] 0.164
Female					
N'/N	79 / 79	61 / 61			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	11 (13.9)	9 (14.8)	0.93 [0.36; 2.42] 0.889	0.94 [0.42; 2.13] 0.889	-0.01 [-0.13; 0.11] 0.890
KITE					
Interaction Test:	p = 0.968				
Male					
N'/N	120 / 120	115 / 115			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	18 (15.0)	13 (11.3)	1.38 [0.64; 2.97] 0.404	1.33 [0.68; 2.58] 0.405	0.04 [-0.05; 0.12] 0.401

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by gender (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Female					
N'/N	59 / 59	66 / 66			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	7 (11.9)	6 (9.1)	1.35 [0.43; 4.26] 0.613	1.31 [0.46; 3.66] 0.613	0.03 [-0.08; 0.14] 0.614
Pooled Analysis					
Interaction Test:	p = 0.616				
Male					
N'/N	230 / 230	241 / 241			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	37 (16.1)	44 (18.3)	0.92 [0.56; 1.50] 0.734	0.90 [0.60; 1.34] 0.600	-0.02 [-0.09; 0.05] 0.599
Female					
N'/N	138 / 138	127 / 127			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	18 (13.0)	15 (11.8)	1.15 [0.55; 2.41] 0.711	1.07 [0.57; 2.03] 0.829	0.01 [-0.07; 0.09] 0.829

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + gender + treatment * gender.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + gender + treatment * gender.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-3.4 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by BCVA (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.812				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	11 (14.9)	12 (18.8)	0.76 [0.31; 1.85] 0.542	0.79 [0.38; 1.67] 0.542	-0.04 [-0.16; 0.09] 0.544
> 65 letters					
N'/N	115 / 115	123 / 123			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	13 (11.3)	20 (16.3)	0.66 [0.31; 1.39] 0.271	0.70 [0.36; 1.33] 0.273	-0.05 [-0.14; 0.04] 0.265
KITE					
Interaction Test:	p = 0.451				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	5 (7.7)	7 (7.7)	1.00 [0.30; 3.30] 1.000	1.00 [0.33; 3.01] 1.000	0.00 [-0.08; 0.08] 1.000
> 65 letters					
N'/N	114 / 114	90 / 90			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	15 (13.2)	7 (7.8)	1.80 [0.70; 4.61] 0.224	1.69 [0.72; 3.97] 0.227	0.05 [-0.03; 0.14] 0.205

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.697				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	16 (11.5)	19 (12.3)	0.92 [0.45; 1.87] 0.810	0.86 [0.46; 1.59] 0.627	-0.02 [-0.09; 0.06] 0.625
> 65 letters					
N'/N	229 / 229	213 / 213			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	28 (12.2)	27 (12.7)	1.10 [0.61; 1.98] 0.753	0.98 [0.59; 1.63] 0.945	-0.00 [-0.06; 0.06] 0.945
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 100 Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.998				
≤ 65 letters					
N'/N	74 / 74	64 / 64			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	12 (16.2)	14 (21.9)	0.69 [0.29; 1.63] 0.398	0.74 [0.37; 1.48] 0.398	-0.06 [-0.19; 0.07] 0.399
> 65 letters					
N'/N	115 / 115	123 / 123			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	18 (15.7)	26 (21.1)	0.69 [0.36; 1.34] 0.277	0.74 [0.43; 1.28] 0.279	-0.05 [-0.15; 0.04] 0.273
KITE					
Interaction Test:	p = 0.828				
≤ 65 letters					
N'/N	65 / 65	91 / 91			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	8 (12.3)	8 (8.8)	1.46 [0.52; 4.10] 0.477	1.40 [0.55; 3.54] 0.477	0.04 [-0.06; 0.13] 0.485

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by BCVA (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 65 letters					
N'/N	114 / 114	90 / 90			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	17 (14.9)	11 (12.2)	1.26 [0.56; 2.84] 0.580	1.22 [0.60; 2.47] 0.581	0.03 [-0.07; 0.12] 0.575
Pooled Analysis					
Interaction Test:	p = 0.935				
≤ 65 letters					
N'/N	139 / 139	155 / 155			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	20 (14.4)	22 (14.2)	0.99 [0.51; 1.91] 0.976	0.94 [0.54; 1.64] 0.837	-0.01 [-0.09; 0.07] 0.838
> 65 letters					
N'/N	229 / 229	213 / 213			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	35 (15.3)	37 (17.4)	0.96 [0.57; 1.61] 0.866	0.90 [0.59; 1.38] 0.622	-0.02 [-0.09; 0.05] 0.621

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + BCVA + treatment * BCVA.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + BCVA + treatment * BCVA.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-3.5 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by region (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.613				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	12 (13.3)	18 (21.7)	0.56 [0.25; 1.24] 0.150	0.61 [0.32; 1.20] 0.153	-0.08 [-0.20; 0.03] 0.148
European Region					
N'/N	69 / 69	75 / 75			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	8 (11.6)	11 (14.7)	0.76 [0.29; 2.02] 0.587	0.79 [0.34; 1.85] 0.588	-0.03 [-0.14; 0.08] 0.584
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	4 (13.3)	3 (10.3)	1.33 [0.27; 6.56] 0.723	1.29 [0.32; 5.26] 0.724	0.03 [-0.13; 0.19] 0.722
KITE					
Interaction Test:	p = 0.708				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	2 (7.7)	2 (9.5)	0.79 [0.10; 6.15] 0.823	0.81 [0.12; 5.26] 0.823	-0.02 [-0.18; 0.14] 0.825
European Region					
N'/N	135 / 135	132 / 132			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	13 (9.6)	8 (6.1)	1.65 [0.66; 4.13] 0.283	1.59 [0.68; 3.71] 0.284	0.04 [-0.03; 0.10] 0.277

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	5 (27.8)	4 (14.3)	2.31 [0.53; 10.12] 0.267	1.94 [0.60; 6.29] 0.267	0.13 [-0.11; 0.38] 0.279
Pooled Analysis					
Interaction Test:	p = 0.651				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	12 (13.3)	18 (21.7)	0.80 [0.30; 2.14] 0.660	0.61 [0.32; 1.20] 0.148	-0.08 [-0.20; 0.03] 0.148
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	2 (7.7)	2 (9.5)	0.54 [0.06; 4.56] 0.571	0.81 [0.12; 5.26] 0.825	-0.02 [-0.18; 0.14] 0.825
European Region					
N'/N	204 / 204	207 / 207			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	21 (10.3)	19 (9.2)	1.05 [0.54; 2.06] 0.885	1.14 [0.63; 2.05] 0.670	0.01 [-0.04; 0.07] 0.669
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	9 (18.8)	7 (12.3)	1.73 [0.59; 5.11] 0.321	1.62 [0.66; 3.98] 0.293	0.07 [-0.07; 0.21] 0.297
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.100**					

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL					
Interaction Test:	p = 0.977				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	15 (16.7)	19 (22.9)	0.67 [0.32; 1.43] 0.305	0.73 [0.40; 1.34] 0.306	-0.06 [-0.18; 0.06] 0.304
European Region					
N'/N	69 / 69	75 / 75			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	10 (14.5)	14 (18.7)	0.74 [0.30; 1.79] 0.503	0.78 [0.37; 1.63] 0.504	-0.04 [-0.16; 0.08] 0.499
Western Pacific Region					
N'/N	30 / 30	29 / 29			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	5 (16.7)	7 (24.1)	0.63 [0.17; 2.27] 0.478	0.69 [0.25; 1.93] 0.480	-0.07 [-0.28; 0.13] 0.475
KITE					
Interaction Test:	p = 0.247				
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	2 (7.7)	4 (19.0)	0.35 [0.06; 2.16] 0.260	0.40 [0.08; 1.99] 0.266	-0.11 [-0.31; 0.08] 0.258
European Region					
N'/N	135 / 135	132 / 132			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	18 (13.3)	10 (7.6)	1.88 [0.83; 4.23] 0.129	1.76 [0.84; 3.67] 0.132	0.06 [-0.02; 0.13] 0.122
Western Pacific Region					
N'/N	18 / 18	28 / 28			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	5 (27.8)	5 (17.9)	1.77 [0.43; 7.28] 0.429	1.56 [0.52; 4.62] 0.427	0.10 [-0.15; 0.35] 0.438

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by region (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.442				
Region of the Americas					
N'/N	90 / 90	83 / 83			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	15 (16.7)	19 (22.9)	1.06 [0.43; 2.64] 0.893	0.73 [0.40; 1.34] 0.305	-0.06 [-0.18; 0.06] 0.304
South-East Asia Region and Eastern Mediterranean Region					
N'/N	26 / 26	21 / 21			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	2 (7.7)	4 (19.0)	0.22 [0.03; 1.45] 0.115	0.40 [0.08; 1.99] 0.251	-0.11 [-0.31; 0.08] 0.258
European Region					
N'/N	204 / 204	207 / 207			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	28 (13.7)	24 (11.6)	1.12 [0.61; 2.05] 0.707	1.20 [0.72; 2.00] 0.486	0.02 [-0.04; 0.09] 0.485
Western Pacific Region					
N'/N	48 / 48	57 / 57			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	10 (20.8)	12 (21.1)	1.05 [0.40; 2.73] 0.924	1.00 [0.48; 2.08] 0.994	-0.00 [-0.16; 0.16] 0.994

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + region + treatment * region.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + region + treatment * region.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-3.6 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by diabetes type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.307				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	1 (8.3)	2 (33.3)	0.18 [0.01; 2.60] 0.209	0.25 [0.03; 2.24] 0.215	-0.25 [-0.66; 0.16] 0.230
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	23 (13.0)	30 (16.6)	0.75 [0.42; 1.35] 0.341	0.78 [0.47; 1.30] 0.342	-0.04 [-0.11; 0.04] 0.339
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	4 (21.1)	0 (0.0)	N.E.	3.60 [0.22; 59.46] 0.371	0.21 [0.03; 0.39] 0.024 *
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	16 (10.0)	14 (8.0)	1.27 [0.60; 2.69] 0.533	1.24 [0.63; 2.46] 0.534	0.02 [-0.04; 0.08] 0.534

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.909				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	5 (16.1)	2 (15.4)	1.11 [0.18; 6.72] 0.913	0.96 [0.22; 4.08] 0.953	0.01 [-0.23; 0.25] 0.945
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	39 (11.6)	44 (12.4)	0.99 [0.62; 1.60] 0.975	0.93 [0.62; 1.39] 0.712	-0.01 [-0.06; 0.04] 0.711
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 100 Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.312				
Type 1					
N'/N	12 / 12	6 / 6			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	1 (8.3)	2 (33.3)	0.18 [0.01; 2.60] 0.209	0.25 [0.03; 2.24] 0.215	-0.25 [-0.66; 0.16] 0.230
Type 2					
N'/N	177 / 177	181 / 181			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	29 (16.4)	38 (21.0)	0.74 [0.43; 1.26] 0.264	0.78 [0.50; 1.21] 0.266	-0.05 [-0.13; 0.03] 0.262
KITE					
Interaction Test:	N.E.				
Type 1					
N'/N	19 / 19	7 / 7			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	6 (31.6)	0 (0.0)	N.E.	5.20 [0.33; 81.92] 0.241	0.32 [0.11; 0.52] 0.003 *

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2					
N'/N	160 / 160	174 / 174			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	19 (11.9)	19 (10.9)	1.10 [0.56; 2.16] 0.784	1.09 [0.60; 1.98] 0.784	0.01 [-0.06; 0.08] 0.784
Pooled Analysis					
Interaction Test:	p = 0.512				
Type 1					
N'/N	31 / 31	13 / 13			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	7 (22.6)	2 (15.4)	1.67 [0.29; 9.54] 0.564	1.30 [0.32; 5.21] 0.701	0.07 [-0.19; 0.32] 0.607
Type 2					
N'/N	337 / 337	355 / 355			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	48 (14.2)	57 (16.1)	0.92 [0.60; 1.41] 0.689	0.88 [0.62; 1.25] 0.479	-0.02 [-0.07; 0.03] 0.478

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + diabetes type + treatment * diabetes type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + diabetes type + treatment * diabetes type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Exceptionally applied model (due to nonconvergence):
Week 52 / KITE, Week 100 / KITE: logit(proportion) = treatment [by diabetes type].

Table 21-3.7 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by HbA1c (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.221				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	14 (18.4)	19 (17.8)	1.05 [0.49; 2.24] 0.908	1.04 [0.56; 1.94] 0.908	0.01 [-0.11; 0.12] 0.909
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	10 (8.9)	13 (16.3)	0.51 [0.21; 1.22] 0.128	0.55 [0.25; 1.19] 0.129	-0.07 [-0.17; 0.02] 0.137
KITE					
Interaction Test:	p = 0.581				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	9 (11.0)	6 (6.3)	1.85 [0.63; 5.44] 0.264	1.76 [0.65; 4.73] 0.265	0.05 [-0.04; 0.13] 0.266
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	11 (11.3)	8 (9.4)	1.23 [0.47; 3.22] 0.672	1.20 [0.51; 2.86] 0.672	0.02 [-0.07; 0.11] 0.669

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.264				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	23 (14.6)	25 (12.3)	1.33 [0.71; 2.48] 0.368	1.22 [0.72; 2.07] 0.452	0.03 [-0.04; 0.10] 0.454
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	21 (10.0)	21 (12.7)	0.80 [0.42; 1.54] 0.507	0.79 [0.45; 1.38] 0.402	-0.03 [-0.09; 0.04] 0.409
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 100 Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.701				
< 7.5 %					
N'/N	76 / 76	107 / 107			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	16 (21.1)	26 (24.3)	0.83 [0.41; 1.68] 0.607	0.87 [0.50; 1.50] 0.609	-0.03 [-0.15; 0.09] 0.603
≥ 7.5 %					
N'/N	112 / 112	80 / 80			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	14 (12.5)	14 (17.5)	0.67 [0.30; 1.50] 0.335	0.71 [0.36; 1.41] 0.334	-0.05 [-0.15; 0.05] 0.343
KITE					
Interaction Test:	p = 0.204				
< 7.5 %					
N'/N	82 / 82	96 / 96			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	12 (14.6)	7 (7.3)	2.18 [0.82; 5.83] 0.120	2.01 [0.83; 4.86] 0.123	0.07 [-0.02; 0.17] 0.120

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by HbA1c (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 7.5 %					
N'/N	97 / 97	85 / 85			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	13 (13.4)	12 (14.1)	0.94 [0.40; 2.19] 0.889	0.95 [0.46; 1.97] 0.889	-0.01 [-0.11; 0.09] 0.889
Pooled Analysis					
Interaction Test:	p = 0.357				
< 7.5 %					
N'/N	158 / 158	203 / 203			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	28 (17.7)	33 (16.3)	1.20 [0.68; 2.10] 0.531	1.13 [0.71; 1.79] 0.605	0.02 [-0.06; 0.10] 0.606
≥ 7.5 %					
N'/N	209 / 209	165 / 165			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	27 (12.9)	26 (15.8)	0.82 [0.45; 1.48] 0.507	0.82 [0.50; 1.34] 0.428	-0.03 [-0.10; 0.04] 0.432

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + HbA1c + treatment * HbA1c.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + HbA1c + treatment * HbA1c.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-3.8 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by duration of DME (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.575				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	16 (13.3)	18 (16.4)	0.79 [0.38; 1.63] 0.518	0.81 [0.44; 1.52] 0.519	-0.03 [-0.12; 0.06] 0.519
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	3 (10.0)	9 (23.1)	0.37 [0.09; 1.51] 0.166	0.43 [0.13; 1.46] 0.178	-0.13 [-0.30; 0.04] 0.132
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	5 (12.8)	5 (13.2)	0.97 [0.26; 3.67] 0.965	0.97 [0.31; 3.10] 0.965	-0.00 [-0.15; 0.15] 0.965
KITE					
Interaction Test:	p = 0.730				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	12 (14.1)	9 (9.8)	1.52 [0.60; 3.80] 0.375	1.44 [0.64; 3.25] 0.376	0.04 [-0.05; 0.14] 0.375
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	3 (5.9)	3 (6.1)	0.96 [0.18; 4.99] 0.960	0.96 [0.20; 4.53] 0.960	-0.00 [-0.10; 0.09] 0.960

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	5 (11.6)	2 (5.0)	2.50 [0.46; 13.69] 0.291	2.33 [0.48; 11.32] 0.296	0.07 [-0.05; 0.18] 0.268
Pooled Analysis					
Interaction Test:	p = 0.317				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	28 (13.7)	27 (13.4)	1.13 [0.63; 2.04] 0.681	1.01 [0.62; 1.65] 0.959	0.00 [-0.06; 0.07] 0.959
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	6 (7.4)	12 (13.6)	0.52 [0.18; 1.47] 0.215	0.58 [0.23; 1.49] 0.249	-0.05 [-0.14; 0.04] 0.239
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	10 (12.2)	7 (9.0)	1.50 [0.54; 4.21] 0.439	1.37 [0.55; 3.42] 0.503	0.03 [-0.06; 0.13] 0.499
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.461				
≤ 3 months					
N'/N	120 / 120	110 / 110			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	20 (16.7)	23 (20.9)	0.76 [0.39; 1.47] 0.411	0.80 [0.46; 1.37] 0.411	-0.04 [-0.14; 0.06] 0.411

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 3 - < 12 months					
N'/N	30 / 30	39 / 39			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	3 (10.0)	10 (25.6)	0.32 [0.08; 1.30] 0.111	0.39 [0.12; 1.29] 0.124	-0.16 [-0.33; 0.02] 0.078
≥ 12 months					
N'/N	39 / 39	38 / 38			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	7 (17.9)	7 (18.4)	0.97 [0.30; 3.08] 0.957	0.97 [0.38; 2.51] 0.957	-0.00 [-0.18; 0.17] 0.957
KITE					
Interaction Test:	p = 0.962				
≤ 3 months					
N'/N	85 / 85	92 / 92			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	14 (16.5)	12 (13.0)	1.31 [0.57; 3.03] 0.521	1.26 [0.62; 2.57] 0.521	0.03 [-0.07; 0.14] 0.521
> 3 - < 12 months					
N'/N	51 / 51	49 / 49			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	5 (9.8)	3 (6.1)	1.67 [0.38; 7.38] 0.501	1.60 [0.40; 6.34] 0.503	0.04 [-0.07; 0.14] 0.495
≥ 12 months					
N'/N	43 / 43	40 / 40			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	6 (14.0)	4 (10.0)	1.46 [0.38; 5.61] 0.582	1.40 [0.42; 4.58] 0.583	0.04 [-0.10; 0.18] 0.578
Pooled Analysis					
Interaction Test:	p = 0.607				
≤ 3 months					
N'/N	205 / 205	202 / 202			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	34 (16.6)	35 (17.3)	1.02 [0.60; 1.75] 0.928	0.95 [0.62; 1.45] 0.808	-0.01 [-0.08; 0.06] 0.808

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by duration of DME (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
> 3 - < 12 months					
N'/N	81 / 81	88 / 88			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	8 (9.9)	13 (14.8)	0.64 [0.25; 1.65] 0.359	0.71 [0.30; 1.65] 0.414	-0.04 [-0.14; 0.06] 0.407
≥ 12 months					
N'/N	82 / 82	78 / 78			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	13 (15.9)	11 (14.1)	1.20 [0.50; 2.89] 0.684	1.13 [0.54; 2.37] 0.748	0.02 [-0.09; 0.13] 0.746

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + duration of DME + treatment * duration of DME.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + duration of DME + treatment * duration of DME.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-3.9 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by DME type (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.121				
focal					
N'/N	59 / 59	48 / 48			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	6 (10.2)	12 (25.0)	0.34 [0.12; 0.99] 0.047 *	0.41 [0.16; 1.00] 0.051	-0.15 [-0.29; -0.00] 0.045 *
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	17 (13.4)	19 (14.2)	0.94 [0.46; 1.89] 0.853	0.94 [0.51; 1.73] 0.853	-0.01 [-0.09; 0.08] 0.853
KITE					
Interaction Test:	p = 0.506				
focal					
N'/N	63 / 63	66 / 66			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	6 (9.5)	6 (9.1)	1.05 [0.32; 3.45] 0.933	1.05 [0.36; 3.08] 0.933	0.00 [-0.10; 0.10] 0.933
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	14 (12.2)	8 (7.3)	1.75 [0.70; 4.35] 0.229	1.66 [0.72; 3.80] 0.231	0.05 [-0.03; 0.13] 0.220

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.092				
focal					
N'/N	122 / 122	114 / 114			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	12 (9.8)	18 (15.8)	0.58 [0.26; 1.27] 0.170	0.60 [0.31; 1.18] 0.137	-0.06 [-0.15; 0.02] 0.141
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	31 (12.8)	27 (11.1)	1.32 [0.75; 2.34] 0.339	1.16 [0.72; 1.89] 0.540	0.02 [-0.04; 0.08] 0.539
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 100 Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.201				
focal					
N'/N	59 / 59	48 / 48			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	8 (13.6)	13 (27.1)	0.42 [0.16; 1.13] 0.085	0.50 [0.23; 1.11] 0.088	-0.14 [-0.29; 0.02] 0.083
diffuse					
N'/N	127 / 127	134 / 134			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	21 (16.5)	24 (17.9)	0.91 [0.48; 1.73] 0.769	0.92 [0.54; 1.57] 0.769	-0.01 [-0.11; 0.08] 0.769
KITE					
Interaction Test:	p = 0.380				
focal					
N'/N	63 / 63	66 / 66			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	7 (11.1)	8 (12.1)	0.91 [0.31; 2.67] 0.858	0.92 [0.35; 2.38] 0.858	-0.01 [-0.12; 0.10] 0.858

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse					
N'/N	115 / 115	109 / 109			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	18 (15.7)	11 (10.1)	1.65 [0.74; 3.68] 0.218	1.55 [0.77; 3.13] 0.221	0.06 [-0.03; 0.14] 0.211
Pooled Analysis					
Interaction Test:	p = 0.113				
focal					
N'/N	122 / 122	114 / 114			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	15 (12.3)	21 (18.4)	0.61 [0.30; 1.25] 0.178	0.65 [0.35; 1.18] 0.155	-0.07 [-0.16; 0.03] 0.157
diffuse					
N'/N	242 / 242	243 / 243			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	39 (16.1)	35 (14.4)	1.24 [0.75; 2.07] 0.404	1.13 [0.74; 1.72] 0.576	0.02 [-0.05; 0.08] 0.575

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
*: $p < 0.05$
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + DME type + treatment * DME type.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + DME type + treatment * DME type.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-3.10 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by CSFT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.930				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	15 (14.0)	17 (17.7)	0.76 [0.36; 1.61] 0.472	0.79 [0.42; 1.50] 0.472	-0.04 [-0.14; 0.06] 0.473
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	8 (11.4)	12 (16.9)	0.63 [0.24; 1.66] 0.354	0.68 [0.29; 1.55] 0.356	-0.05 [-0.17; 0.06] 0.350
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	1 (8.3)	3 (15.0)	0.52 [0.05; 5.60] 0.586	0.56 [0.06; 4.76] 0.592	-0.07 [-0.29; 0.15] 0.555
KITE					
Interaction Test:	p = 0.970				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	10 (11.8)	7 (8.5)	1.43 [0.52; 3.95] 0.492	1.38 [0.55; 3.45] 0.493	0.03 [-0.06; 0.12] 0.489
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	8 (10.8)	6 (7.6)	1.47 [0.49; 4.47] 0.493	1.42 [0.52; 3.91] 0.493	0.03 [-0.06; 0.12] 0.492

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	2 (10.0)	1 (5.3)	2.00 [0.17; 24.07] 0.585	1.90 [0.19; 19.27] 0.587	0.05 [-0.12; 0.21] 0.575
Pooled Analysis					
Interaction Test:	p = 0.981				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	25 (13.0)	24 (13.5)	1.05 [0.57; 1.95] 0.876	0.96 [0.57; 1.61] 0.873	-0.01 [-0.07; 0.06] 0.873
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	16 (11.1)	18 (12.0)	0.96 [0.46; 1.98] 0.907	0.92 [0.49; 1.73] 0.798	-0.01 [-0.08; 0.06] 0.798
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	3 (9.4)	4 (10.3)	1.00 [0.20; 4.87] 0.995	0.98 [0.22; 4.39] 0.975	-0.00 [-0.14; 0.14] 0.975
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.916				
< 450 µm					
N'/N	107 / 107	96 / 96			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	17 (15.9)	22 (22.9)	0.64 [0.31; 1.28] 0.206	0.69 [0.39; 1.23] 0.208	-0.07 [-0.18; 0.04] 0.206

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 450 - < 650 µm					
N'/N	70 / 70	71 / 71			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	12 (17.1)	15 (21.1)	0.77 [0.33; 1.79] 0.548	0.81 [0.41; 1.61] 0.549	-0.04 [-0.17; 0.09] 0.547
≥ 650 µm					
N'/N	12 / 12	20 / 20			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	1 (8.3)	3 (15.0)	0.52 [0.05; 5.60] 0.586	0.56 [0.06; 4.76] 0.592	-0.07 [-0.29; 0.15] 0.555
KITE					
Interaction Test:	p = 0.508				
< 450 µm					
N'/N	85 / 85	82 / 82			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	12 (14.1)	11 (13.4)	1.06 [0.44; 2.56] 0.895	1.05 [0.49; 2.25] 0.895	0.01 [-0.10; 0.11] 0.895
≥ 450 - < 650 µm					
N'/N	74 / 74	79 / 79			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	9 (12.2)	7 (8.9)	1.42 [0.50; 4.04] 0.506	1.37 [0.54; 3.50] 0.507	0.03 [-0.06; 0.13] 0.506
≥ 650 µm					
N'/N	20 / 20	19 / 19			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	4 (20.0)	1 (5.3)	4.50 [0.45; 44.52] 0.199	3.80 [0.47; 31.01] 0.213	0.15 [-0.05; 0.35] 0.153
Pooled Analysis					
Interaction Test:	p = 0.609				
< 450 µm					
N'/N	192 / 192	178 / 178			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	29 (15.1)	33 (18.5)	0.84 [0.48; 1.46] 0.532	0.81 [0.51; 1.28] 0.363	-0.04 [-0.11; 0.04] 0.364

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by CSFT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
≥ 450 - < 650 µm					
N'/N	144 / 144	150 / 150			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	21 (14.6)	22 (14.7)	1.02 [0.53; 1.97] 0.941	0.99 [0.57; 1.71] 0.962	-0.00 [-0.08; 0.08] 0.962
≥ 650 µm					
N'/N	32 / 32	39 / 39			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	5 (15.6)	4 (10.3)	1.77 [0.43; 7.30] 0.430	1.57 [0.41; 6.04] 0.504	0.05 [-0.10; 0.21] 0.499

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + CSFT + treatment * CSFT.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + CSFT + treatment * CSFT.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-3.11 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by status of SRF (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.869				
presence					
N'/N	62 / 62	61 / 61			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	8 (12.9)	10 (16.4)	0.76 [0.28; 2.06] 0.585	0.79 [0.33; 1.86] 0.585	-0.03 [-0.16; 0.09] 0.584
absence					
N'/N	127 / 127	126 / 126			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	16 (12.6)	22 (17.5)	0.68 [0.34; 1.37] 0.281	0.72 [0.40; 1.31] 0.282	-0.05 [-0.14; 0.04] 0.278
KITE					
Interaction Test:	p = 0.718				
presence					
N'/N	56 / 56	67 / 67			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	5 (8.9)	5 (7.5)	1.22 [0.33; 4.43] 0.767	1.20 [0.36; 3.92] 0.767	0.01 [-0.08; 0.11] 0.769
absence					
N'/N	123 / 123	114 / 114			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	15 (12.2)	9 (7.9)	1.62 [0.68; 3.86] 0.276	1.54 [0.70; 3.39] 0.278	0.04 [-0.03; 0.12] 0.268

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.893				
presence					
N'/N	118 / 118	128 / 128			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	13 (11.0)	15 (11.7)	0.97 [0.44; 2.16] 0.946	0.91 [0.46; 1.83] 0.801	-0.01 [-0.09; 0.07] 0.800
absence					
N'/N	250 / 250	240 / 240			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	31 (12.4)	31 (12.9)	1.04 [0.60; 1.80] 0.891	0.97 [0.61; 1.54] 0.885	-0.00 [-0.06; 0.05] 0.885
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 100 Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.373				
presence					
N'/N	62 / 62	61 / 61			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	11 (17.7)	11 (18.0)	0.98 [0.39; 2.47] 0.966	0.98 [0.46; 2.10] 0.966	-0.00 [-0.14; 0.13] 0.966
absence					
N'/N	127 / 127	126 / 126			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	19 (15.0)	29 (23.0)	0.59 [0.31; 1.12] 0.104	0.65 [0.39; 1.10] 0.107	-0.08 [-0.18; 0.02] 0.101
KITE					
Interaction Test:	p = 0.576				
presence					
N'/N	56 / 56	67 / 67			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	5 (8.9)	6 (9.0)	1.00 [0.29; 3.46] 0.996	1.00 [0.32; 3.09] 0.996	-0.00 [-0.10; 0.10] 0.996

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by status of SRF (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
absence					
N'/N	123 / 123	114 / 114			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	20 (16.3)	13 (11.4)	1.51 [0.71; 3.19] 0.283	1.43 [0.74; 2.73] 0.285	0.05 [-0.04; 0.14] 0.277
Pooled Analysis					
Interaction Test:	p = 0.779				
presence					
N'/N	118 / 118	128 / 128			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	16 (13.6)	17 (13.3)	1.06 [0.50; 2.22] 0.885	0.99 [0.53; 1.86] 0.971	-0.00 [-0.09; 0.08] 0.971
absence					
N'/N	250 / 250	240 / 240			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	39 (15.6)	42 (17.5)	0.93 [0.57; 1.52] 0.774	0.90 [0.60; 1.34] 0.589	-0.02 [-0.08; 0.05] 0.589

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
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Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + status of SRF + treatment * status of SRF.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + status of SRF + treatment * status of SRF.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-3.12 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by exposure (week 52) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 52					
Test of heterogeneity in main analysis: **p_H=0.106**					
KESTREL					
Interaction Test:	p = 0.774				
Non-exposed					
N'/N	71 / 71	75 / 75			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	10 (14.1)	13 (17.3)	0.78 [0.32; 1.92] 0.591	0.81 [0.38; 1.73] 0.591	-0.03 [-0.15; 0.09] 0.589
Exposed					
N'/N	118 / 118	112 / 112			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	14 (11.9)	19 (17.0)	0.66 [0.31; 1.39] 0.273	0.70 [0.37; 1.33] 0.274	-0.05 [-0.14; 0.04] 0.271
KITE					
Interaction Test:	p = 0.159				
Non-exposed					
N'/N	85 / 85	90 / 90			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	10 (11.8)	4 (4.4)	2.87 [0.86; 9.52] 0.085	2.65 [0.86; 8.12] 0.089	0.07 [-0.01; 0.15] 0.075
Exposed					
N'/N	94 / 94	91 / 91			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	10 (10.6)	10 (11.0)	0.96 [0.38; 2.44] 0.939	0.97 [0.42; 2.22] 0.939	-0.00 [-0.09; 0.09] 0.939

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by exposure (week 52) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.326				
Non-exposed					
N'/N	156 / 156	165 / 165			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	20 (12.8)	17 (10.3)	1.32 [0.66; 2.65] 0.429	1.24 [0.68; 2.28] 0.479	0.03 [-0.04; 0.09] 0.480
Exposed					
N'/N	212 / 212	203 / 203			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	24 (11.3)	29 (14.3)	0.84 [0.46; 1.53] 0.568	0.79 [0.48; 1.31] 0.363	-0.03 [-0.09; 0.03] 0.363

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 52) + treatment * exposure (week 52).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 52) + treatment * exposure (week 52).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-3.13 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by exposure (week 100) (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 100					
Test of heterogeneity in main analysis: **p_H=0.100**					
KESTREL					
Interaction Test:	p = 0.751				
Non-exposed					
N'/N	12 / 12	13 / 13			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	1 (8.3)	1 (7.7)	1.09 [0.06; 19.62] 0.953	1.08 [0.08; 15.46] 0.953	0.01 [-0.21; 0.22] 0.953
Exposed					
N'/N	177 / 177	174 / 174			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	29 (16.4)	39 (22.4)	0.68 [0.40; 1.16] 0.154	0.73 [0.47; 1.13] 0.156	-0.06 [-0.14; 0.02] 0.152
KITE					
Interaction Test:	p = 0.617				
Non-exposed					
N'/N	17 / 17	12 / 12			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	1 (5.9)	1 (8.3)	0.69 [0.04; 12.20] 0.799	0.71 [0.05; 10.21] 0.798	-0.02 [-0.22; 0.17] 0.803
Exposed					
N'/N	162 / 162	169 / 169			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	24 (14.8)	18 (10.7)	1.46 [0.76; 2.80] 0.257	1.39 [0.79; 2.46] 0.258	0.04 [-0.03; 0.11] 0.256

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by exposure (week 100) (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis					
Interaction Test:	p = 0.963				
Non-exposed					
N'/N	29 / 29	25 / 25			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	2 (6.9)	2 (8.0)	0.93 [0.12; 7.23] 0.948	0.88 [0.13; 5.70] 0.892	-0.01 [-0.15; 0.13] 0.891
Exposed					
N'/N	339 / 339	343 / 343			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	53 (15.6)	57 (16.6)	0.98 [0.65; 1.49] 0.931	0.94 [0.66; 1.32] 0.700	-0.01 [-0.07; 0.04] 0.700

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + exposure (week 100) + treatment * exposure (week 100).
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study + exposure (week 100) + treatment * exposure (week 100).
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-4.1 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, n (%)	1 (0.5)	0 (0.0)	N.E.	2.97 [0.12; 72.41] 0.504	0.01 [-0.01; 0.02] 0.316
KITE, N'/N	179 / 179	181 / 181			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, n (%)	1 (0.3)	0 (0.0)	N.E.	2.97 [0.12; 72.41] 0.484	0.00 [-0.00; 0.01] 0.318
p_H=N.E.					
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, n (%)	1 (0.5)	0 (0.0)	N.E.	2.97 [0.12; 72.41] 0.504	0.01 [-0.01; 0.02] 0.316
KITE, N'/N	179 / 179	181 / 181			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular AE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, n (%)	1 (0.3)	0 (0.0)	N.E.	2.97 [0.12; 72.41] 0.484	0.00 [-0.00; 0.01] 0.318
p_H=N.E.					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-4.2 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-4.3 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-4.4 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-4.5 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-4.6 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-4.7 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-4.8 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-4.9 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-4.10 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-4.11 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-4.12 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-4.13 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-5.1 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any non-ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (0.5)	0 (0.0)	N.E.	2.97 [0.12; 72.41] 0.504	0.01 [-0.01; 0.02] 0.316
KITE, N'/N	179 / 179	181 / 181			
Any non-ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (0.6)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.496	0.01 [-0.01; 0.02] 0.316
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any non-ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	2 (0.5)	0 (0.0)	N.E.	3.00 [0.31; 28.71] 0.317	0.01 [-0.00; 0.01] 0.156
p_H=N.E.					
Any non-ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any non-ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	2 (1.1)	0 (0.0)	N.E.	4.95 [0.24; 102.36] 0.301	0.01 [-0.00; 0.03] 0.155
KITE, N'/N	179 / 179	181 / 181			
Any non-ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (0.6)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.496	0.01 [-0.01; 0.02] 0.316

	Treatment Groups		Comparison		
Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any non-ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	3 (0.8)	0 (0.0)	N.E.	4.00 [0.45; 35.63] 0.179	0.01 [-0.00; 0.02] 0.082
p_H=N.E.					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 21-5.2 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-5.3 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-5.4 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-5.5 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-5.6 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-5.7 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-5.8 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-5.9 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-5.10 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-5.11 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-5.12 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 21-5.13 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

22 Safety analysis: Any serious adverse event of potential relevance to intravitreal anti-VEGF injection

Table 22-1.1 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious adverse event of potential relevance to intravitreal anti-VEGF injection (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any SAE of potential relevance to intravitreal anti-VEGF injection, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any SAE of potential relevance to intravitreal anti-VEGF injection, n (%)	0 (0.0)	3 (1.6)	N.E.	0.14 [0.01; 2.72] 0.195	-0.02 [-0.03; 0.00] 0.081
KITE, N'/N	179 / 179	181 / 181			
Any SAE of potential relevance to intravitreal anti-VEGF injection, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any SAE of potential relevance to intravitreal anti-VEGF injection, n (%)	0 (0.0)	3 (0.8)	N.E.	0.14 [0.01; 2.72] 0.129	-0.01 [-0.02; 0.00] 0.081
p_H=N.E.					
Any SAE of potential relevance to intravitreal anti-VEGF injection, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any SAE of potential relevance to intravitreal anti-VEGF injection, n (%)	0 (0.0)	3 (1.6)	N.E.	0.14 [0.01; 2.72] 0.195	-0.02 [-0.03; 0.00] 0.081
KITE, N'/N	179 / 179	181 / 181			
Any SAE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (0.6)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.496	0.01 [-0.01; 0.02] 0.316

	Treatment Groups		Comparison		
Any serious adverse event of potential relevance to intravitreal anti-VEGF injection (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any SAE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (0.3)	3 (0.8)	N.E.	0.50 [0.09; 2.70] 0.410	-0.01 [-0.02; 0.01] 0.315
p_H=N.E.					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 22-1.2 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-1.3 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-1.4 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-1.5 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-1.6 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-1.7 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-1.8 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-1.9 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-1.10 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-1.11 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-1.12 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-1.13 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-2.1 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection, n (%)	0 (0.0)	3 (1.6)	N.E.	0.14 [0.01; 2.72] 0.195	-0.02 [-0.03; 0.00] 0.081
KITE, N'/N	179 / 179	181 / 181			
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection, n (%)	0 (0.0)	3 (0.8)	N.E.	0.14 [0.01; 2.72] 0.129	-0.01 [-0.02; 0.00] 0.081
p_H=N.E.					
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection, n (%)	0 (0.0)	3 (1.6)	N.E.	0.14 [0.01; 2.72] 0.195	-0.02 [-0.03; 0.00] 0.081
KITE, N'/N	179 / 179	181 / 181			
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (0.6)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.496	0.01 [-0.01; 0.02] 0.316

	Treatment Groups		Comparison		
Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (0.3)	3 (0.8)	N.E.	0.50 [0.09; 2.70] 0.410	-0.01 [-0.02; 0.01] 0.315
p_H=N.E.					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 22-2.2 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-2.3 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-2.4 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-2.5 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-2.6 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-2.7 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-2.8 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-2.9 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-2.10 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-2.11 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-2.12 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-2.13 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-3.1 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	0 (0.0)	3 (1.6)	N.E.	0.14 [0.01; 2.72] 0.195	-0.02 [-0.03; 0.00] 0.081
KITE, N'/N	179 / 179	181 / 181			
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	0 (0.0)	3 (0.8)	N.E.	0.14 [0.01; 2.72] 0.129	-0.01 [-0.02; 0.00] 0.081
p_H=N.E.					
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	0 (0.0)	3 (1.6)	N.E.	0.14 [0.01; 2.72] 0.195	-0.02 [-0.03; 0.00] 0.081
KITE, N'/N	179 / 179	181 / 181			
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	1 (0.6)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.496	0.01 [-0.01; 0.02] 0.316

	Treatment Groups		Comparison		
Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	1 (0.3)	3 (0.8)	N.E.	0.50 [0.09; 2.70] 0.410	-0.01 [-0.02; 0.01] 0.315
p_H=N.E.					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 22-3.2 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-3.3 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-3.4 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-3.5 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-3.6 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-3.7 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-3.8 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-3.9 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-3.10 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-3.11 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-3.12 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-3.13 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-4.1 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, N'/N	179 / 179	181 / 181			
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
p_H=N.E.					
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, N'/N	179 / 179	181 / 181			
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular SAE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
p_H=N.E.					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 22-4.2 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-4.3 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-4.4 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-4.5 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-4.6 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-4.7 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-4.8 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-4.9 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-4.10 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-4.11 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-4.12 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-4.13 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-5.1 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any non-ocular SAE of potential relevance intravitreal anti-VEGF injection, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any non-ocular SAE of potential relevance intravitreal anti-VEGF injection, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, N'/N	179 / 179	181 / 181			
Any non-ocular SAE of potential relevance intravitreal anti-VEGF injection, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any non-ocular SAE of potential relevance intravitreal anti-VEGF injection, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
p_H=N.E.					
Any non-ocular SAE of potential relevance intravitreal anti-VEGF injection, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any non-ocular SAE of potential relevance intravitreal anti-VEGF injection, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, N'/N	179 / 179	181 / 181			
Any non-ocular SAE of potential relevance intravitreal anti-VEGF injection, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any non-ocular SAE of potential relevance intravitreal anti-VEGF injection, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
p_H=N.E.					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 22-5.2 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-5.3 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-5.4 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-5.5 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-5.6 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-5.7 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-5.8 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-5.9 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-5.10 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-5.11 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-5.12 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 22-5.13 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

23 Safety analysis: Any severe adverse event of potential relevance to intravitreal anti-VEGF injection

Table 23-1.1 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe adverse event of potential relevance to intravitreal anti-VEGF injection (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any severe AE of potential relevance to intravitreal anti-VEGF injection, n (%)	0 (0.0)	3 (1.6)	N.E.	0.14 [0.01; 2.72] 0.195	-0.02 [-0.03; 0.00] 0.081
KITE, N'/N	179 / 179	181 / 181			
Any severe AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (0.6)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.496	0.01 [-0.01; 0.02] 0.316
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any severe AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (0.3)	3 (0.8)	N.E.	0.50 [0.09; 2.70] 0.410	-0.01 [-0.02; 0.01] 0.315
p_H=N.E.					
Any severe AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any severe AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (0.5)	3 (1.6)	0.33 [0.03; 3.17] 0.334	0.33 [0.03; 3.14] 0.335	-0.01 [-0.03; 0.01] 0.310
KITE, N'/N	179 / 179	181 / 181			
Any severe AE of potential relevance to intravitreal anti-VEGF injection, n (%)	2 (1.1)	0 (0.0)	N.E.	5.06 [0.24; 104.57] 0.294	0.01 [-0.00; 0.03] 0.155

	Treatment Groups		Comparison		
Any severe adverse event of potential relevance to intravitreal anti-VEGF injection (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any severe AE of potential relevance to intravitreal anti-VEGF injection, n (%)	3 (0.8)	3 (0.8)	N.E.	1.00 [0.23; 4.35] 0.999	-0.00 [-0.01; 0.01] 0.997
p_H=N.E.					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 23-1.2 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-1.3 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-1.4 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-1.5 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-1.6 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-1.7 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-1.8 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-1.9 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-1.10 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-1.11 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-1.12 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-1.13 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-2.1 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	0 (0.0)	3 (1.6)	N.E.	0.14 [0.01; 2.72] 0.195	-0.02 [-0.03; 0.00] 0.081
KITE, N'/N	179 / 179	181 / 181			
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (0.6)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.496	0.01 [-0.01; 0.02] 0.316
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (0.3)	3 (0.8)	N.E.	0.50 [0.09; 2.70] 0.410	-0.01 [-0.02; 0.01] 0.315
p_H=N.E.					
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	0 (0.0)	3 (1.6)	N.E.	0.14 [0.01; 2.72] 0.195	-0.02 [-0.03; 0.00] 0.081
KITE, N'/N	179 / 179	181 / 181			
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	2 (1.1)	0 (0.0)	N.E.	5.06 [0.24; 104.57] 0.294	0.01 [-0.00; 0.03] 0.155

	Treatment Groups		Comparison		
Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	2 (0.5)	3 (0.8)	N.E.	0.75 [0.17; 3.32] 0.703	-0.00 [-0.01; 0.01] 0.654
p_H=N.E.					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 23-2.2 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-2.3 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-2.4 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-2.5 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-2.6 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-2.7 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-2.8 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-2.9 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-2.10 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-2.11 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-2.12 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-2.13 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-3.1 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	0 (0.0)	3 (1.6)	N.E.	0.14 [0.01; 2.72] 0.195	-0.02 [-0.03; 0.00] 0.081
KITE, N'/N	179 / 179	181 / 181			
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	1 (0.6)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.496	0.01 [-0.01; 0.02] 0.316
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	1 (0.3)	3 (0.8)	N.E.	0.50 [0.09; 2.70] 0.410	-0.01 [-0.02; 0.01] 0.315
p_H=N.E.					
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	0 (0.0)	3 (1.6)	N.E.	0.14 [0.01; 2.72] 0.195	-0.02 [-0.03; 0.00] 0.081
KITE, N'/N	179 / 179	181 / 181			
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	2 (1.1)	0 (0.0)	N.E.	5.06 [0.24; 104.57] 0.294	0.01 [-0.00; 0.03] 0.155

	Treatment Groups		Comparison		
Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection at the study eye, n (%)	2 (0.5)	3 (0.8)	N.E.	0.75 [0.17; 3.32] 0.703	-0.00 [-0.01; 0.01] 0.654
p_H=N.E.					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 23-3.2 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-3.3 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-3.4 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-3.5 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-3.6 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-3.7 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-3.8 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-3.9 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-3.10 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-3.11 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-3.12 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-3.13 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-4.1 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, N'/N	179 / 179	181 / 181			
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
p_H=N.E.					
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, N'/N	179 / 179	181 / 181			
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any severe ocular AE of potential relevance to intravitreal anti-VEGF injection at the fellow eye, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
p_H=N.E.					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 23-4.2 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-4.3 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-4.4 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-4.5 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-4.6 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-4.7 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-4.8 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-4.9 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-4.10 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-4.11 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-4.12 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-4.13 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-5.1 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Any severe non-ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 52					
KESTREL, N'/N	189 / 189	187 / 187			
Any severe non-ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
KITE, N'/N	179 / 179	181 / 181			
Any severe non-ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any severe non-ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
p_H=N.E.					
Any severe non-ocular AE of potential relevance to intravitreal anti-VEGF injection, Week 100					
KESTREL, N'/N	189 / 189	187 / 187			
Any severe non-ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (0.5)	0 (0.0)	N.E.	2.97 [0.12; 72.41] 0.504	0.01 [-0.01; 0.02] 0.316
KITE, N'/N	179 / 179	181 / 181			
Any severe non-ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	Treatment Groups		Comparison		
Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any severe non-ocular AE of potential relevance to intravitreal anti-VEGF injection, n (%)	1 (0.3)	0 (0.0)	N.E.	2.97 [0.12; 72.41] 0.484	0.00 [-0.00; 0.01] 0.318
p_H=N.E.					

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
N.E.: Not estimable
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 23-5.2 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-5.3 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-5.4 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-5.5 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-5.6 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-5.7 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-5.8 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-5.9 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-5.10 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-5.11 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-5.12 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 52) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 23-5.13 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

24 Safety analysis: Any adverse event of potential relevance to intravitreal anti-VEGF injection by SOC and PT

Table 24-1.1 Any adverse event of potential relevance to intravitreal anti-VEGF injection by SOC and PT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any adverse event of potential relevance to intravitreal anti-VEGF injection by SOC and PT, week 100					
Eye disorders					
KESTREL, n (%)	24 (12.7)	36 (19.3)	0.61 [0.35; 1.07] 0.085	0.66 [0.41; 1.06] 0.086	-0.07 [-0.14; 0.01] 0.082
KITE, n (%)	20 (11.2)	18 (9.9)	1.14 [0.58; 2.23] 0.705	1.12 [0.62; 2.05] 0.705	0.01 [-0.05; 0.08] 0.705
Pooled Analysis, n (%) p_H=0.163	44 (12.0)	54 (14.7)	0.83 [0.54; 1.28] 0.398	0.81 [0.56; 1.18] 0.272	-0.03 [-0.08; 0.02] 0.272
Conjunctival haemorrhage					
KESTREL, n (%)	11 (5.8)	18 (9.6)	0.58 [0.27; 1.26] 0.171	0.60 [0.29; 1.25] 0.172	-0.04 [-0.09; 0.02] 0.166
KITE, n (%)	7 (3.9)	4 (2.2)	1.80 [0.52; 6.26] 0.355	1.77 [0.53; 5.94] 0.356	0.02 [-0.02; 0.05] 0.349
Pooled Analysis, n (%) p_H=0.131	18 (4.9)	22 (6.0)	1.01 [0.49; 2.09] 0.977	0.81 [0.45; 1.49] 0.504	-0.01 [-0.04; 0.02] 0.504
Investigations					
KESTREL, n (%)	7 (3.7)	2 (1.1)	3.56 [0.73; 17.34] 0.117	3.46 [0.73; 16.45] 0.118	0.03 [-0.00; 0.06] 0.093
KITE, n (%)	4 (2.2)	3 (1.7)	1.36 [0.30; 6.15] 0.693	1.35 [0.31; 5.94] 0.693	0.01 [-0.02; 0.03] 0.692
Pooled Analysis, n (%) p_H=0.388	11 (3.0)	5 (1.4)	2.22 [0.74; 6.64] 0.154	2.20 [0.77; 6.28] 0.130	0.02 [-0.00; 0.04] 0.129

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Intraocular pressure increased					
KESTREL, n (%)	7 (3.7)	2 (1.1)	3.56 [0.73; 17.34] 0.117	3.46 [0.73; 16.45] 0.118	0.03 [-0.00; 0.06] 0.093
KITE, n (%)	4 (2.2)	3 (1.7)	1.36 [0.30; 6.15] 0.693	1.35 [0.31; 5.94] 0.693	0.01 [-0.02; 0.03] 0.692
Pooled Analysis, n (%) p_H=0.388	11 (3.0)	5 (1.4)	2.22 [0.74; 6.64] 0.154	2.20 [0.77; 6.28] 0.130	0.02 [-0.00; 0.04] 0.129

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 24-1.2 Any adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-1.3 Any adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-1.4 Any adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-1.5 Any adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-1.6 Any adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-1.7 Any adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-1.8 Any adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-1.9 Any adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-1.10 Any adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-1.11 Any adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-1.13 Any adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-2.1 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC and PT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC and PT, week 100					
Eye disorders					
KESTREL, n (%)	24 (12.7)	36 (19.3)	0.61 [0.35; 1.07] 0.085	0.66 [0.41; 1.06] 0.086	-0.07 [-0.14; 0.01] 0.082
KITE, n (%)	20 (11.2)	18 (9.9)	1.14 [0.58; 2.23] 0.705	1.12 [0.62; 2.05] 0.705	0.01 [-0.05; 0.08] 0.705
Pooled Analysis, n (%) p_H=0.163	44 (12.0)	54 (14.7)	0.83 [0.54; 1.28] 0.398	0.81 [0.56; 1.18] 0.272	-0.03 [-0.08; 0.02] 0.272
Conjunctival haemorrhage					
KESTREL, n (%)	11 (5.8)	18 (9.6)	0.58 [0.27; 1.26] 0.171	0.60 [0.29; 1.25] 0.172	-0.04 [-0.09; 0.02] 0.166
KITE, n (%)	7 (3.9)	4 (2.2)	1.80 [0.52; 6.26] 0.355	1.77 [0.53; 5.94] 0.356	0.02 [-0.02; 0.05] 0.349
Pooled Analysis, n (%) p_H=0.131	18 (4.9)	22 (6.0)	1.01 [0.49; 2.09] 0.977	0.81 [0.45; 1.49] 0.504	-0.01 [-0.04; 0.02] 0.504
Investigations					
KESTREL, n (%)	7 (3.7)	2 (1.1)	3.56 [0.73; 17.34] 0.117	3.46 [0.73; 16.45] 0.118	0.03 [-0.00; 0.06] 0.093
KITE, n (%)	4 (2.2)	3 (1.7)	1.36 [0.30; 6.15] 0.693	1.35 [0.31; 5.94] 0.693	0.01 [-0.02; 0.03] 0.692
Pooled Analysis, n (%) p_H=0.388	11 (3.0)	5 (1.4)	2.22 [0.74; 6.64] 0.154	2.20 [0.77; 6.28] 0.130	0.02 [-0.00; 0.04] 0.129
Intraocular pressure increased					
KESTREL, n (%)	7 (3.7)	2 (1.1)	3.56 [0.73; 17.34] 0.117	3.46 [0.73; 16.45] 0.118	0.03 [-0.00; 0.06] 0.093

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE, n (%)	4 (2.2)	3 (1.7)	1.36 [0.30; 6.15] 0.693	1.35 [0.31; 5.94] 0.693	0.01 [-0.02; 0.03] 0.692
Pooled Analysis, n (%) p_H=0.388	11 (3.0)	5 (1.4)	2.22 [0.74; 6.64] 0.154	2.20 [0.77; 6.28] 0.130	0.02 [-0.00; 0.04] 0.129

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 24-2.2 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-2.3 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-2.4 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-2.5 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-2.6 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-2.7 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-2.8 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-2.9 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-2.10 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-2.11 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-2.13 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-3.1 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC and PT (SAF), binary analysis, week 100

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KESTREL, N'/N	189 / 189	187 / 187			
KITE, N'/N	179 / 179	181 / 181			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC and PT, week 100					
Eye disorders					
KESTREL, n (%)	24 (12.7)	36 (19.3)	0.61 [0.35; 1.07] 0.085	0.66 [0.41; 1.06] 0.086	-0.07 [-0.14; 0.01] 0.082
KITE, n (%)	20 (11.2)	18 (9.9)	1.14 [0.58; 2.23] 0.705	1.12 [0.62; 2.05] 0.705	0.01 [-0.05; 0.08] 0.705
Pooled Analysis, n (%) p_H=0.163	44 (12.0)	54 (14.7)	0.83 [0.54; 1.28] 0.398	0.81 [0.56; 1.18] 0.272	-0.03 [-0.08; 0.02] 0.272
Conjunctival haemorrhage					
KESTREL, n (%)	11 (5.8)	18 (9.6)	0.58 [0.27; 1.26] 0.171	0.60 [0.29; 1.25] 0.172	-0.04 [-0.09; 0.02] 0.166
KITE, n (%)	7 (3.9)	4 (2.2)	1.80 [0.52; 6.26] 0.355	1.77 [0.53; 5.94] 0.356	0.02 [-0.02; 0.05] 0.349
Pooled Analysis, n (%) p_H=0.131	18 (4.9)	22 (6.0)	1.01 [0.49; 2.09] 0.977	0.81 [0.45; 1.49] 0.504	-0.01 [-0.04; 0.02] 0.504
Investigations					
KESTREL, n (%)	7 (3.7)	2 (1.1)	3.56 [0.73; 17.34] 0.117	3.46 [0.73; 16.45] 0.118	0.03 [-0.00; 0.06] 0.093
KITE, n (%)	4 (2.2)	3 (1.7)	1.36 [0.30; 6.15] 0.693	1.35 [0.31; 5.94] 0.693	0.01 [-0.02; 0.03] 0.692
Pooled Analysis, n (%) p_H=0.388	11 (3.0)	5 (1.4)	2.22 [0.74; 6.64] 0.154	2.20 [0.77; 6.28] 0.130	0.02 [-0.00; 0.04] 0.129
Intraocular pressure increased					
KESTREL, n (%)	7 (3.7)	2 (1.1)	3.56 [0.73; 17.34] 0.117	3.46 [0.73; 16.45] 0.118	0.03 [-0.00; 0.06] 0.093

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC and PT (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
KITE, n (%)	4 (2.2)	3 (1.7)	1.36 [0.30; 6.15] 0.693	1.35 [0.31; 5.94] 0.693	0.01 [-0.02; 0.03] 0.692
Pooled Analysis, n (%) p_H=0.388	11 (3.0)	5 (1.4)	2.22 [0.74; 6.64] 0.154	2.20 [0.77; 6.28] 0.130	0.02 [-0.00; 0.04] 0.129

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
CI: Confidence interval
OR: Odds ratio
RR: Relative risk
RD: Risk difference
p_H: p-value of test of heterogeneity based on study*treatment in the pooled analysis
.....

Imputation Method: None

Analysis method for KESTREL and KITE:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment.
RR and RD calculated directly (with Wald CI and p-value).

Analysis method for pooled analysis:
OR (with Wald CI and p-value) obtained from logistic regression model: logit(proportion) = treatment + study + treatment * study.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

Table 24-3.2 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-3.3 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-3.4 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-3.5 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-3.6 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-3.7 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-3.8 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-3.9 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-3.10 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-3.11 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-3.13 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-4.1 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC and PT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-4.2 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-4.3 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-4.4 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-4.5 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-4.6 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-4.7 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-4.8 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-4.9 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-4.10 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-4.11 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-4.13 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-5.1 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC and PT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-5.2 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-5.3 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-5.4 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-5.5 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-5.6 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-5.7 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-5.8 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-5.9 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-5.10 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-5.11 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 24-5.13 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

25 Safety analysis: Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by SOC and PT

Table 25-1.1 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by SOC and PT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-1.2 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-1.3 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-1.4 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-1.5 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-1.6 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-1.7 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-1.8 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-1.9 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-1.10 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-1.11 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-1.13 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-2.1 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC and PT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-2.2 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-2.3 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-2.4 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-2.5 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-2.6 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-2.7 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-2.8 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-2.9 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-2.10 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-2.11 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-2.13 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-3.1 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC and PT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-3.2 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-3.3 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-3.4 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-3.5 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-3.6 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-3.7 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-3.8 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-3.9 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-3.10 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-3.11 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-3.13 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-4.1 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC and PT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-4.2 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-4.3 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-4.4 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-4.5 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-4.6 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-4.7 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-4.8 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-4.9 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-4.10 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-4.11 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-4.13 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-5.1 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC and PT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-5.2 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-5.3 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-5.4 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-5.5 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-5.6 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-5.7 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-5.8 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-5.9 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-5.10 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-5.11 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 25-5.13 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

26 Safety analysis: Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by SOC and PT

Table 26-1.1 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by SOC and PT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-1.2 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-1.3 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-1.4 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-1.5 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-1.6 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-1.7 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-1.8 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-1.9 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-1.10 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and CSFT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-1.11 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-1.13 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-2.1 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC and PT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-2.2 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-2.3 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-2.4 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-2.5 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-2.6 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-2.7 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and HbA1c (SAF), binary analysis, week 100

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Table 26-2.8 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-2.9 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

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Table 26-2.11 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-2.13 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-3.1 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC and PT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-3.2 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-3.3 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-3.4 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and BCVA (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-3.5 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and region (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-3.6 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and diabetes type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-3.7 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and HbA1c (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-3.8 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and duration of DME (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-3.9 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and DME type (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-3.10 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and CSFT (SAF), binary analysis, week 100

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Table 26-3.11 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and status of SRF (SAF), binary analysis, week 100

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Table 26-4.1 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC and PT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-4.2 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-4.3 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and gender (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-4.4 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and BCVA (SAF), binary analysis, week 100

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Table 26-4.5 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and region (SAF), binary analysis, week 100

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Table 26-4.6 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and diabetes type (SAF), binary analysis, week 100

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Table 26-4.7 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and HbA1c (SAF), binary analysis, week 100

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Table 26-4.10 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and CSFT (SAF), binary analysis, week 100

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Table 26-4.13 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

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Table 26-5.1 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC and PT (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-5.2 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and age (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Table 26-5.3 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and gender (SAF), binary analysis, week 100

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Table 26-5.4 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and BCVA (SAF), binary analysis, week 100

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Table 26-5.5 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and region (SAF), binary analysis, week 100

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Table 26-5.10 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and CSFT (SAF), binary analysis, week 100

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Table 26-5.11 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and status of SRF (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

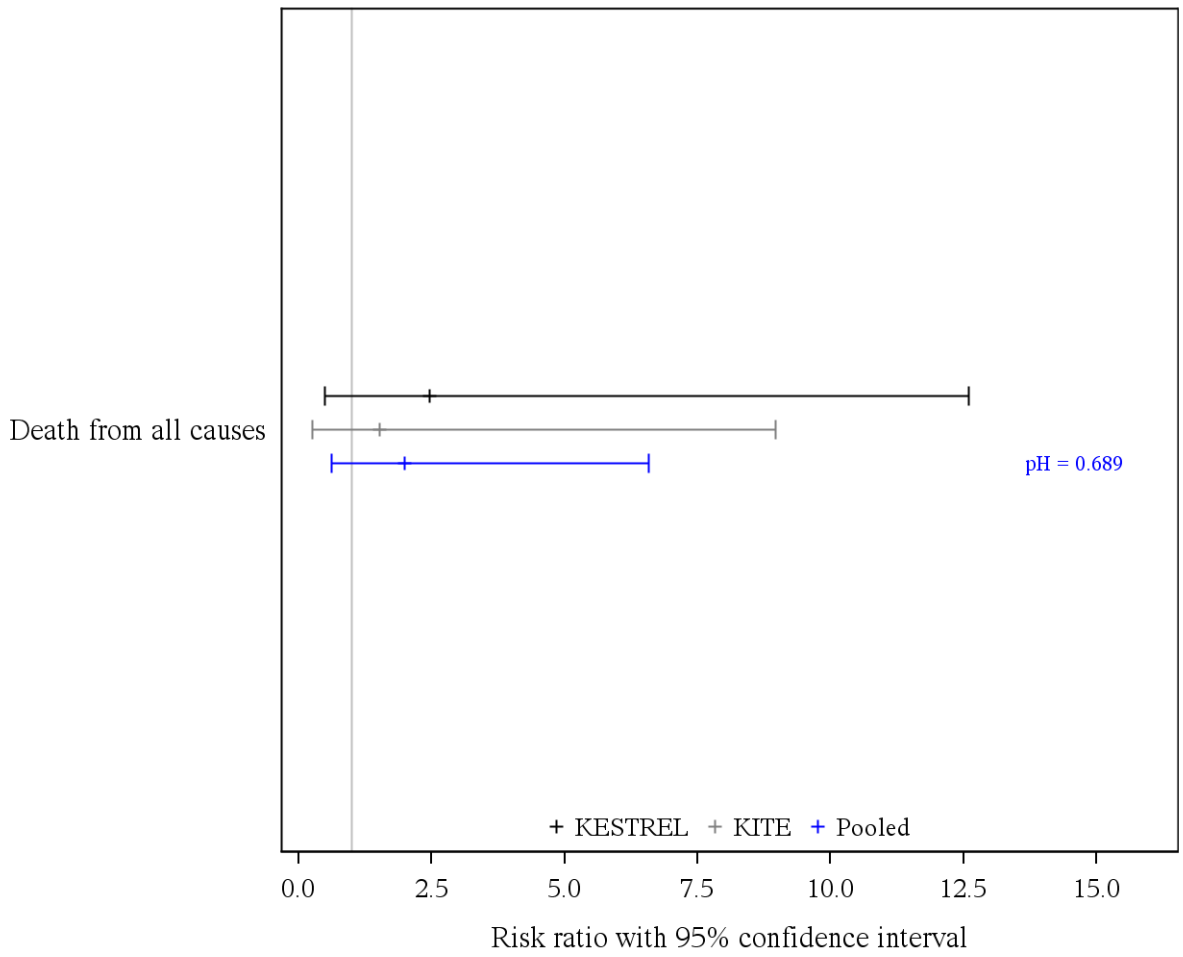
Table 26-5.13 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and exposure (week 100) (SAF), binary analysis, week 100

There is no data meeting the display criteria for this table.

Figures

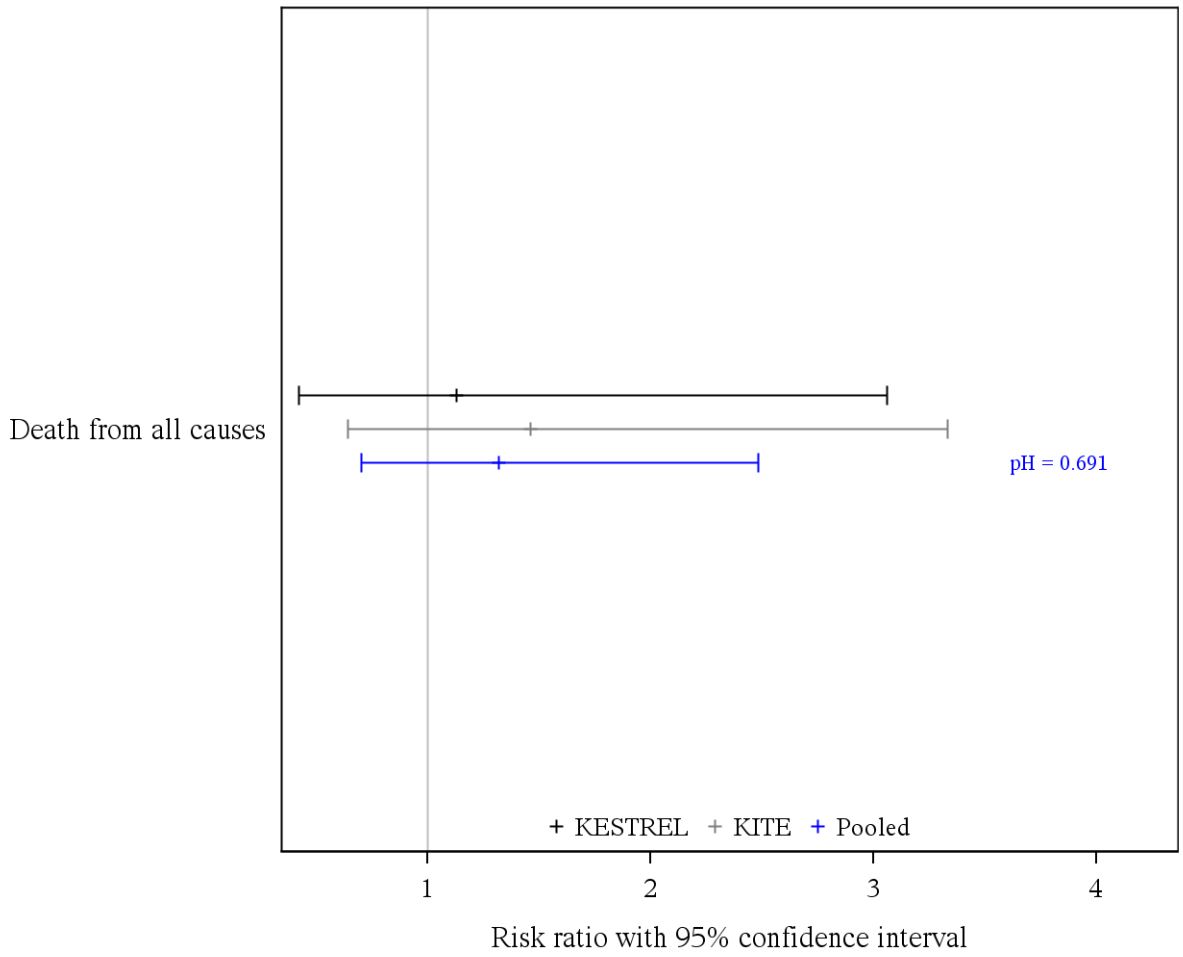
2 Mortality

Figure 2.1.1 All-cause mortality (FAS), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

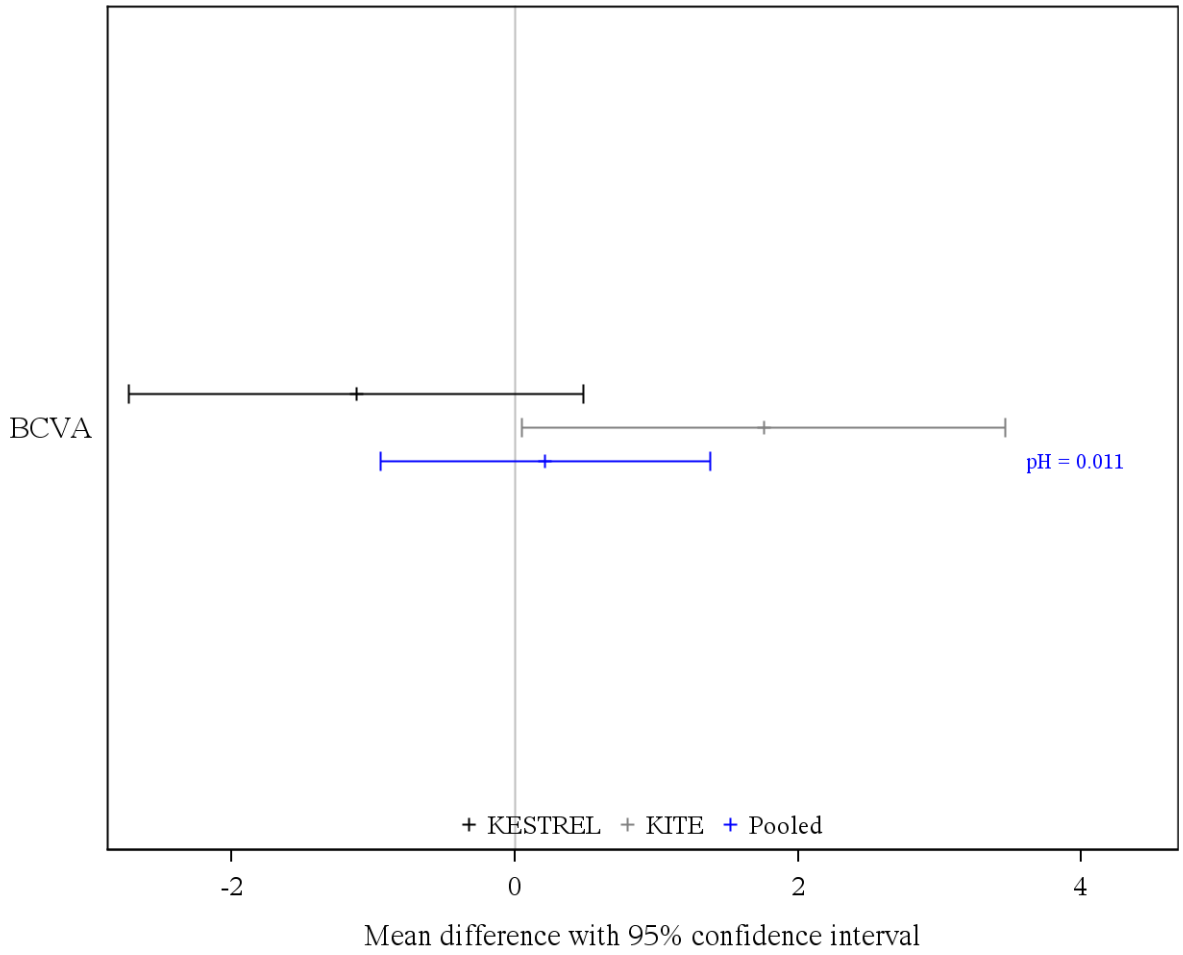
Figure 2.2.1 All-cause mortality (FAS), forest plot, week 100



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

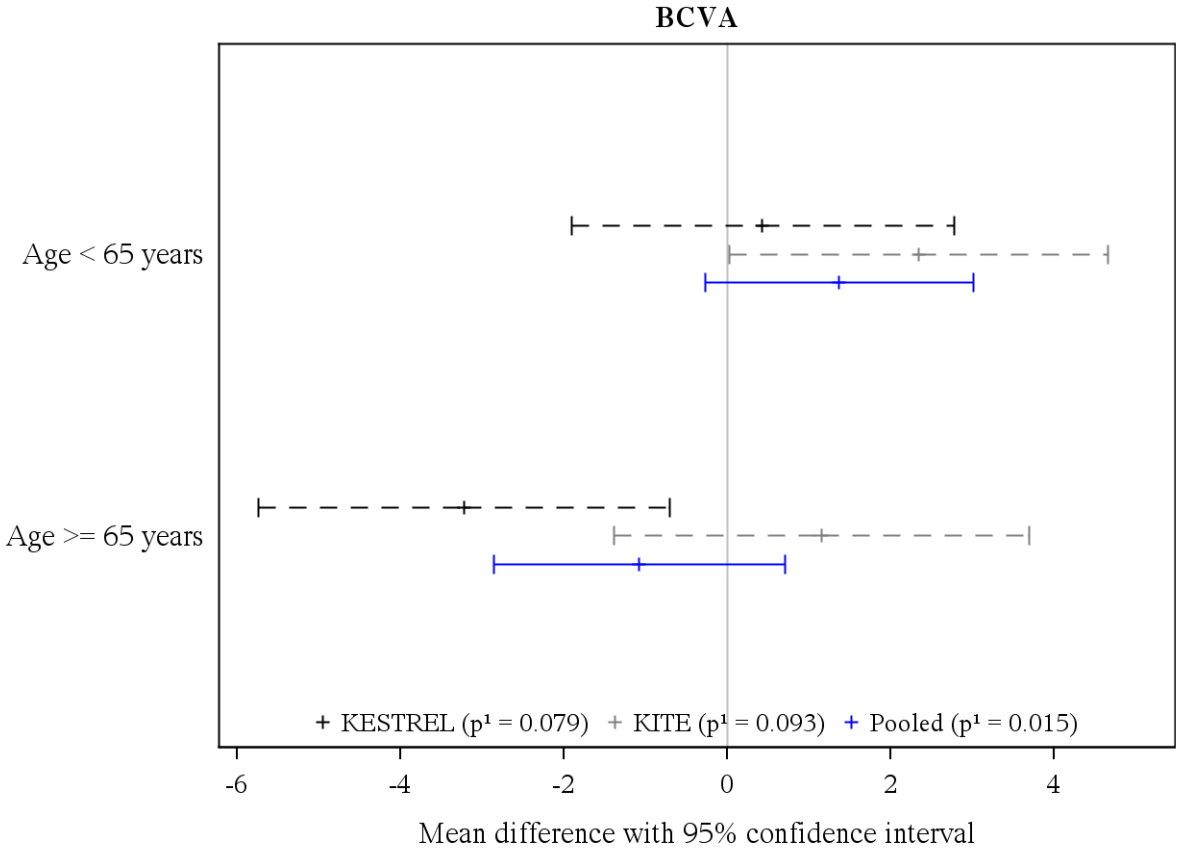
3 BCVA: Continuous analysis

Figure 3.1.1 BCVA (FAS), forest plot, week 52



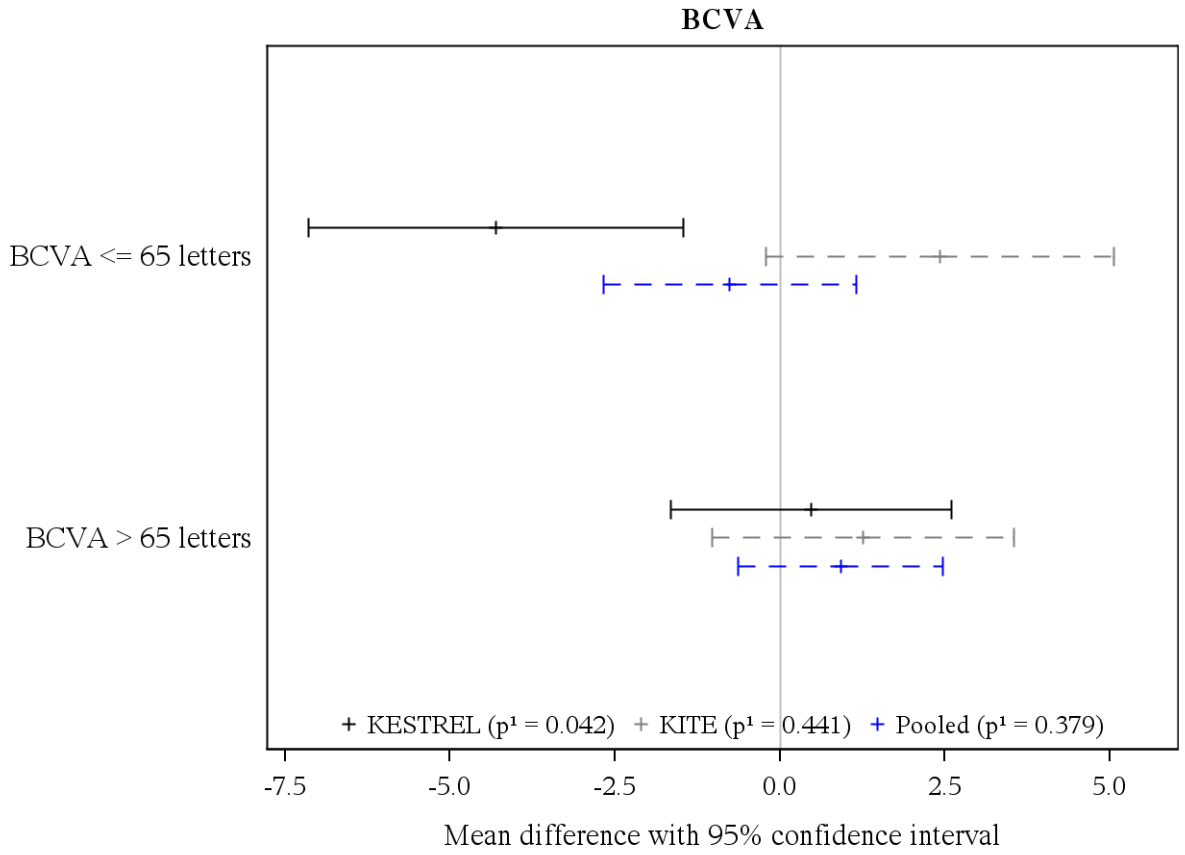
p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 3.1.2 BCVA by age (FAS), forest plot, week 52



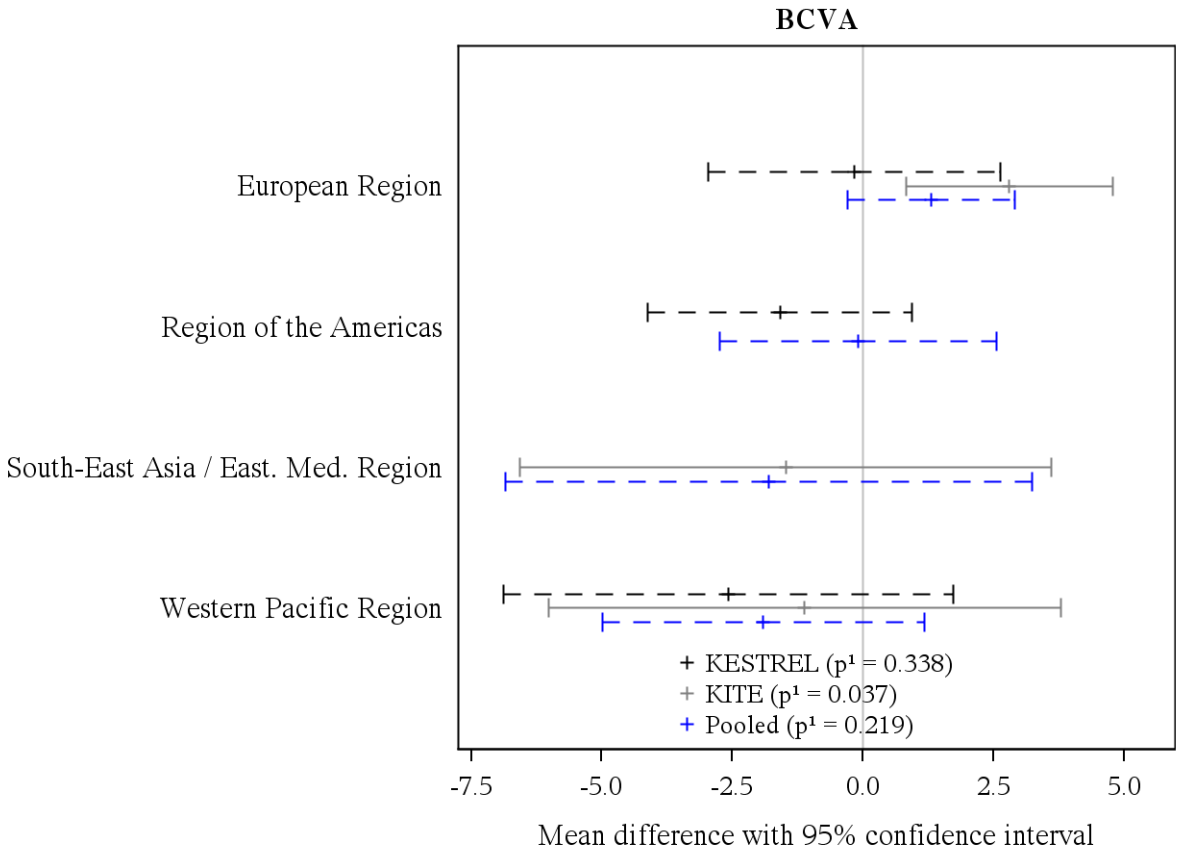
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.011$

Figure 3.1.4 BCVA by BCVA (FAS), forest plot, week 52



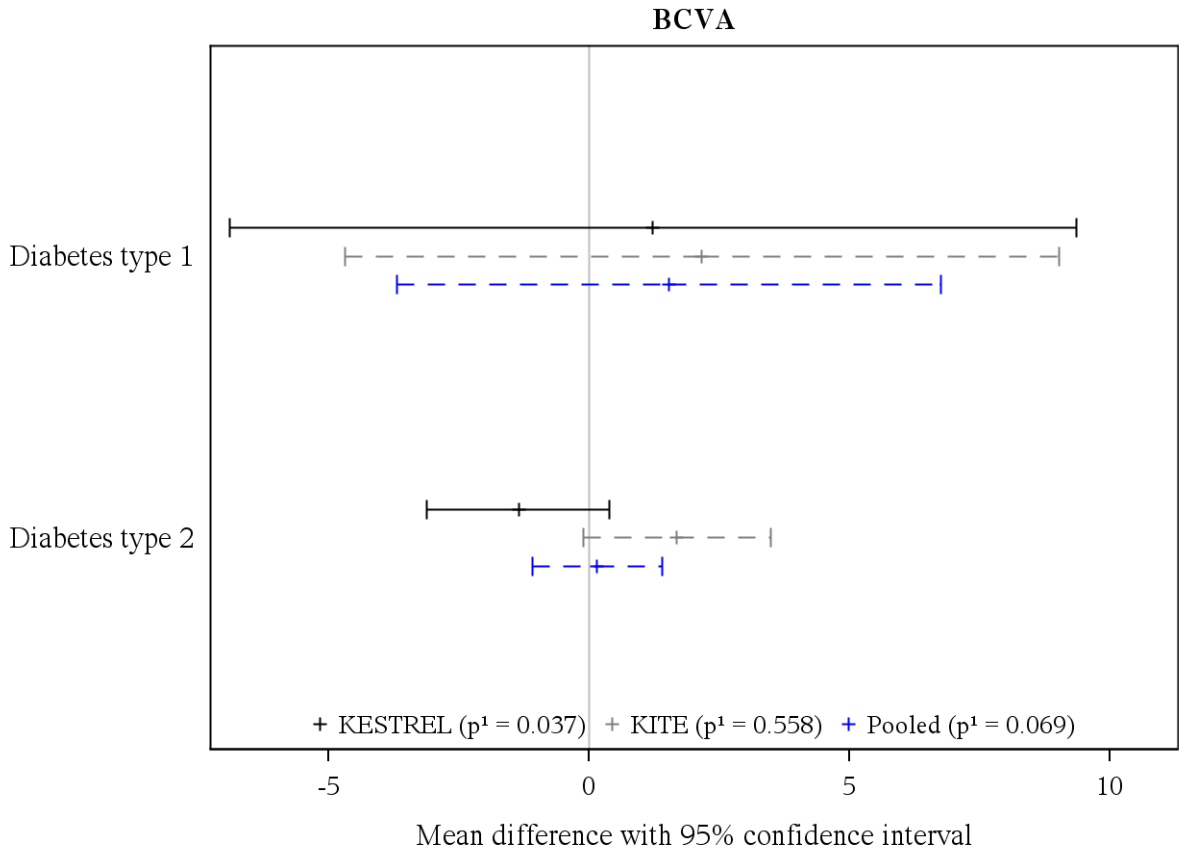
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.011$

Figure 3.1.5 BCVA by region (FAS), forest plot, week 52



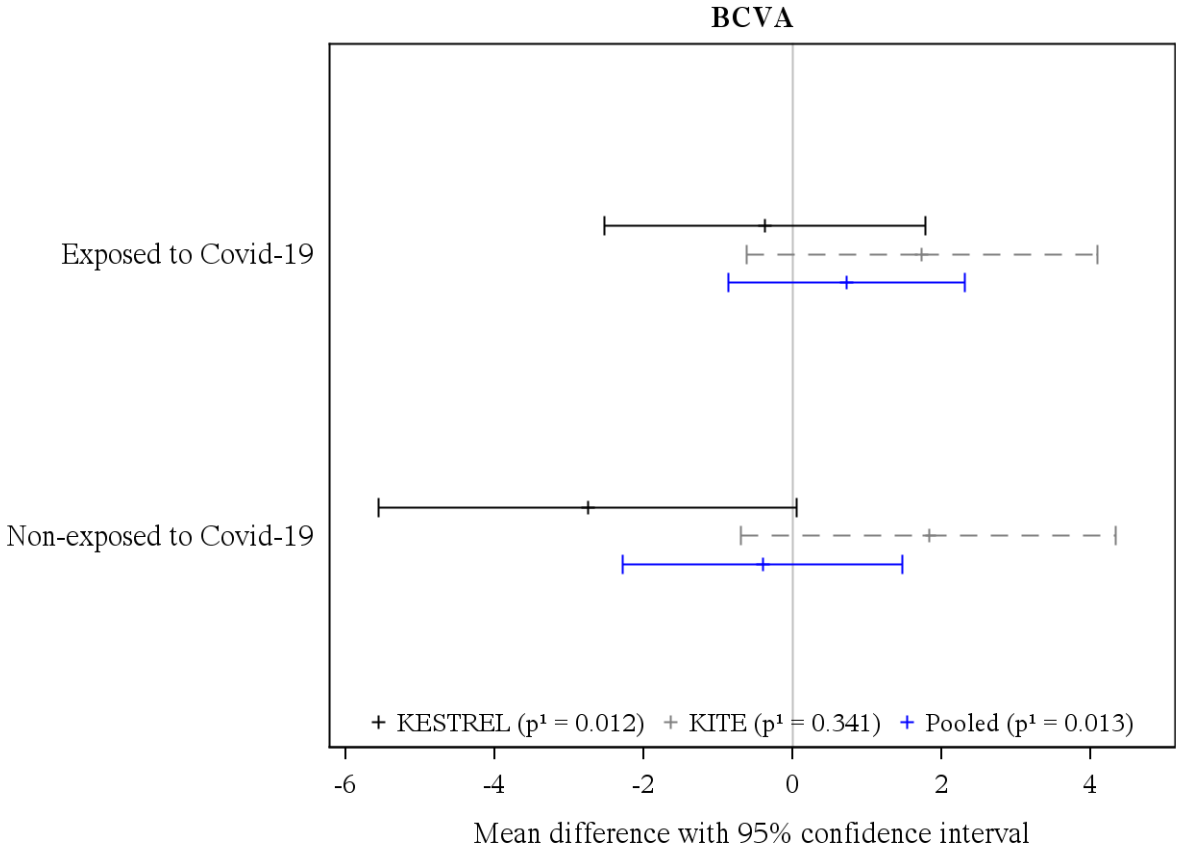
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.011$

Figure 3.1.6 BCVA by diabetes type (FAS), forest plot, week 52



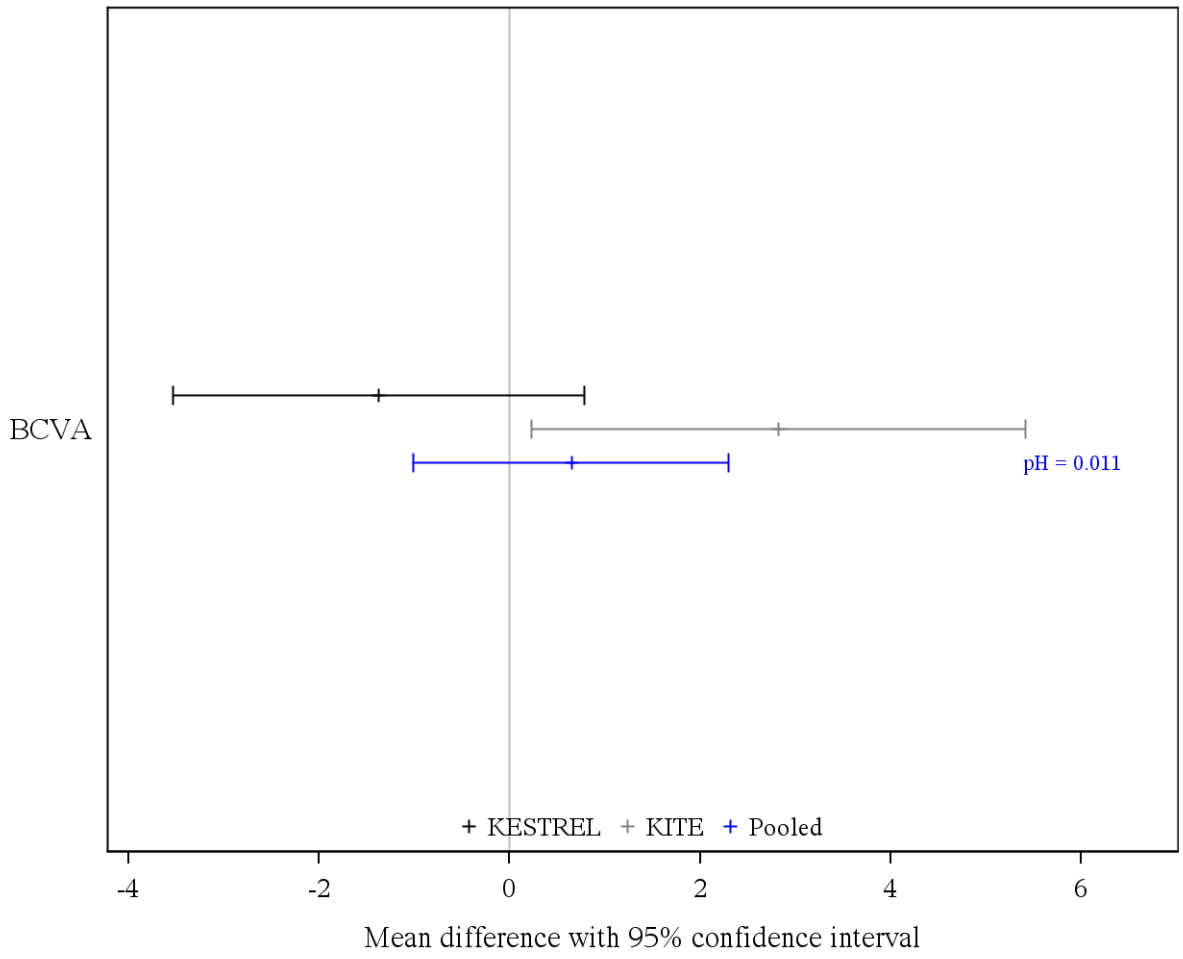
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.011$

Figure 3.1.12 BCVA by exposure (week 52) (FAS), forest plot, week 52



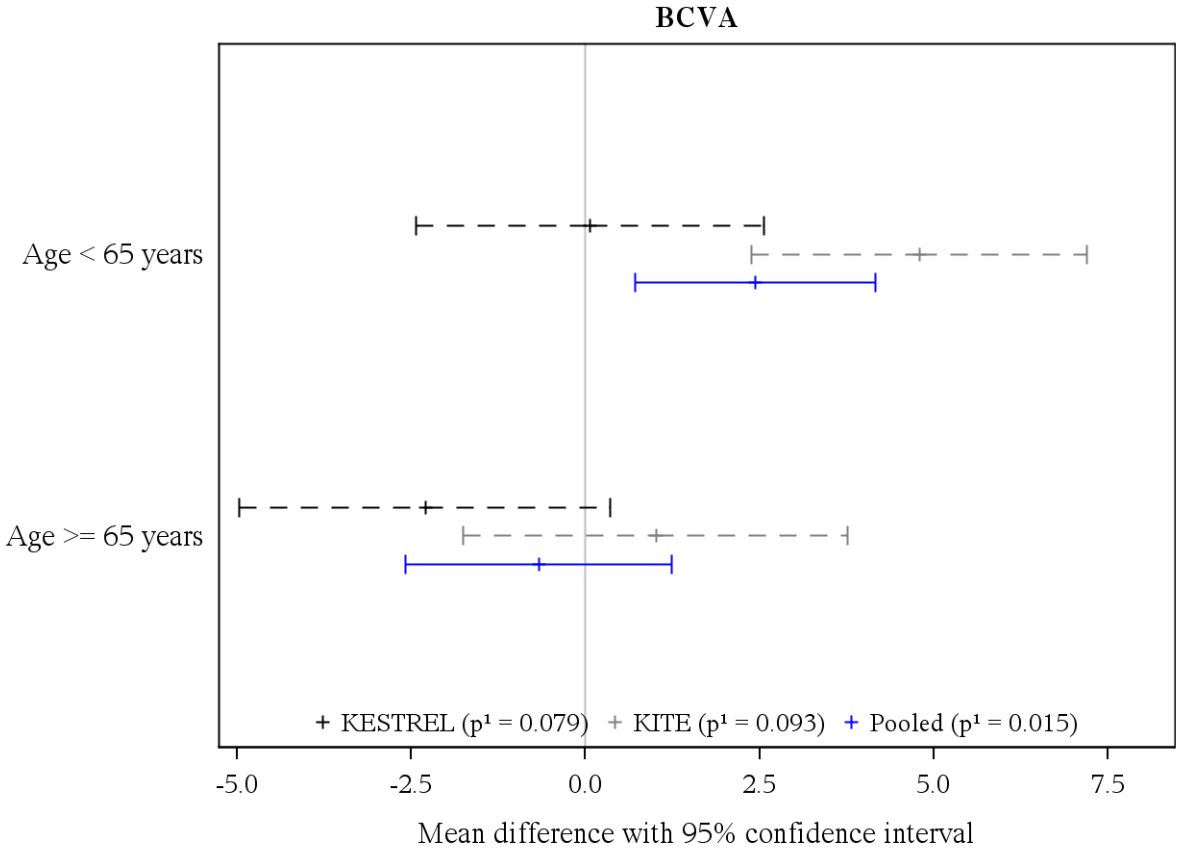
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.011$

Figure 3.2.1 BCVA (FAS), forest plot, week 100



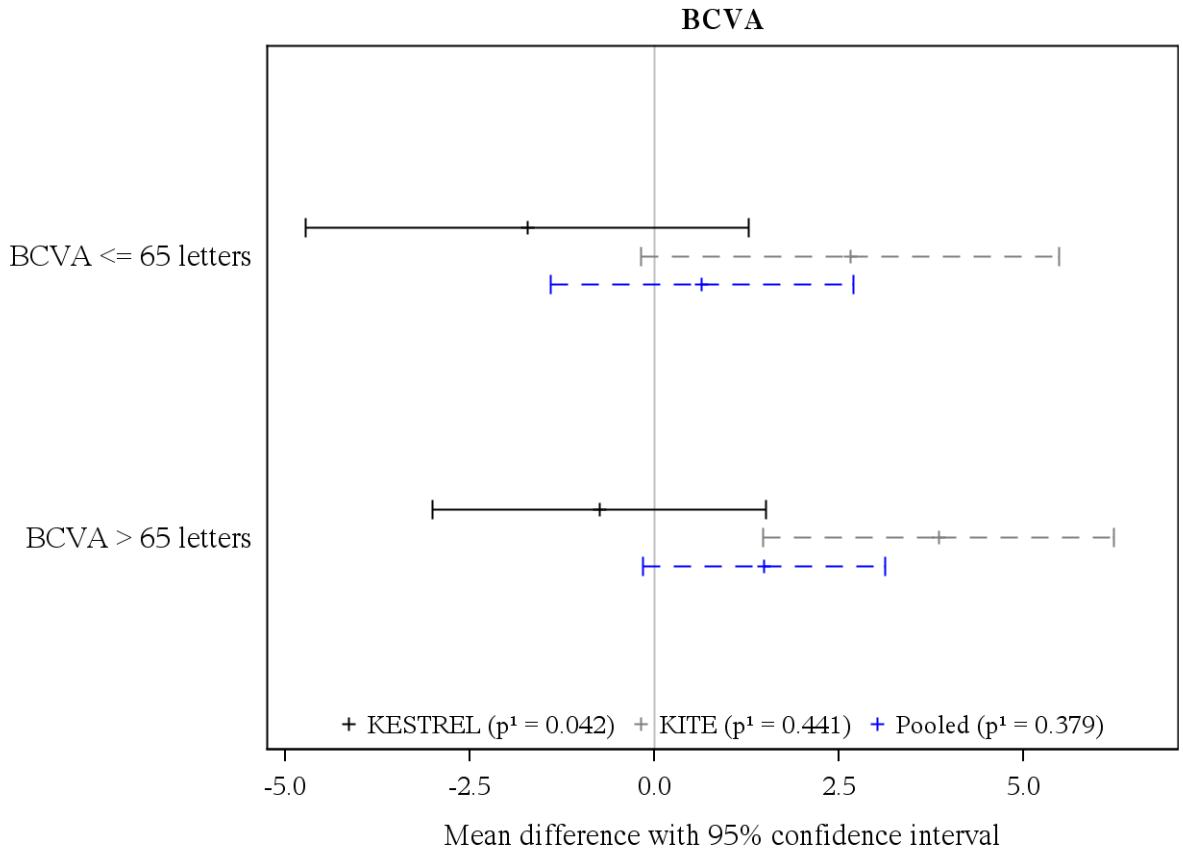
p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 3.2.2 BCVA by age (FAS), forest plot, week 100



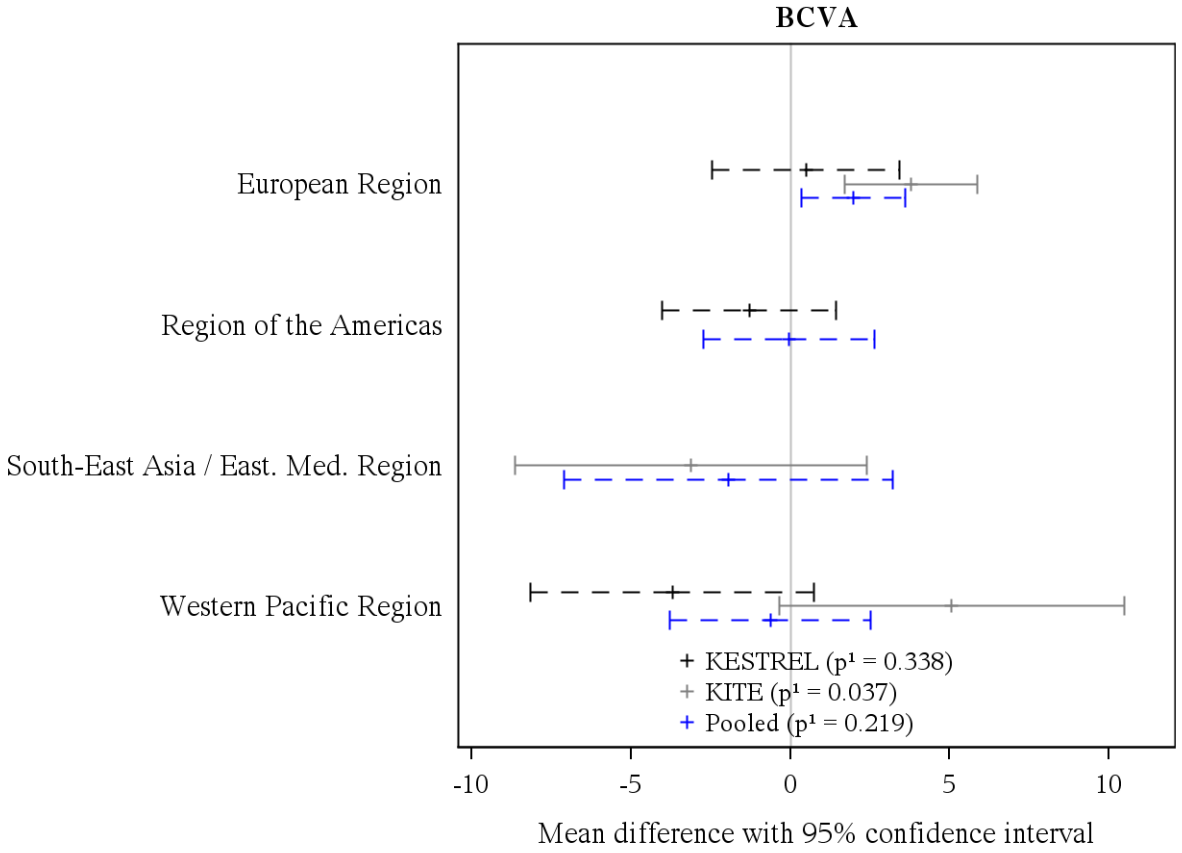
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.011$

Figure 3.2.4 BCVA by BCVA (FAS), forest plot, week 100



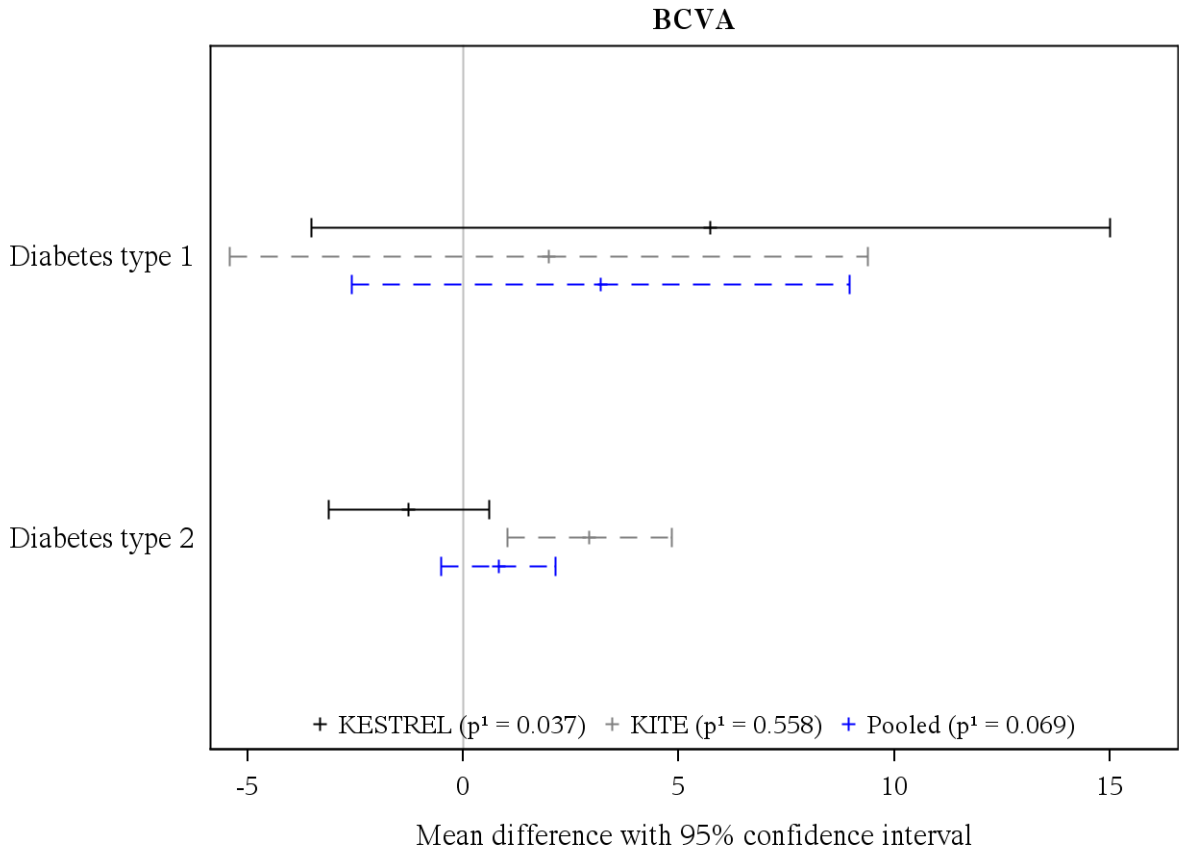
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.011$

Figure 3.2.5 BCVA by region (FAS), forest plot, week 100



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.011$

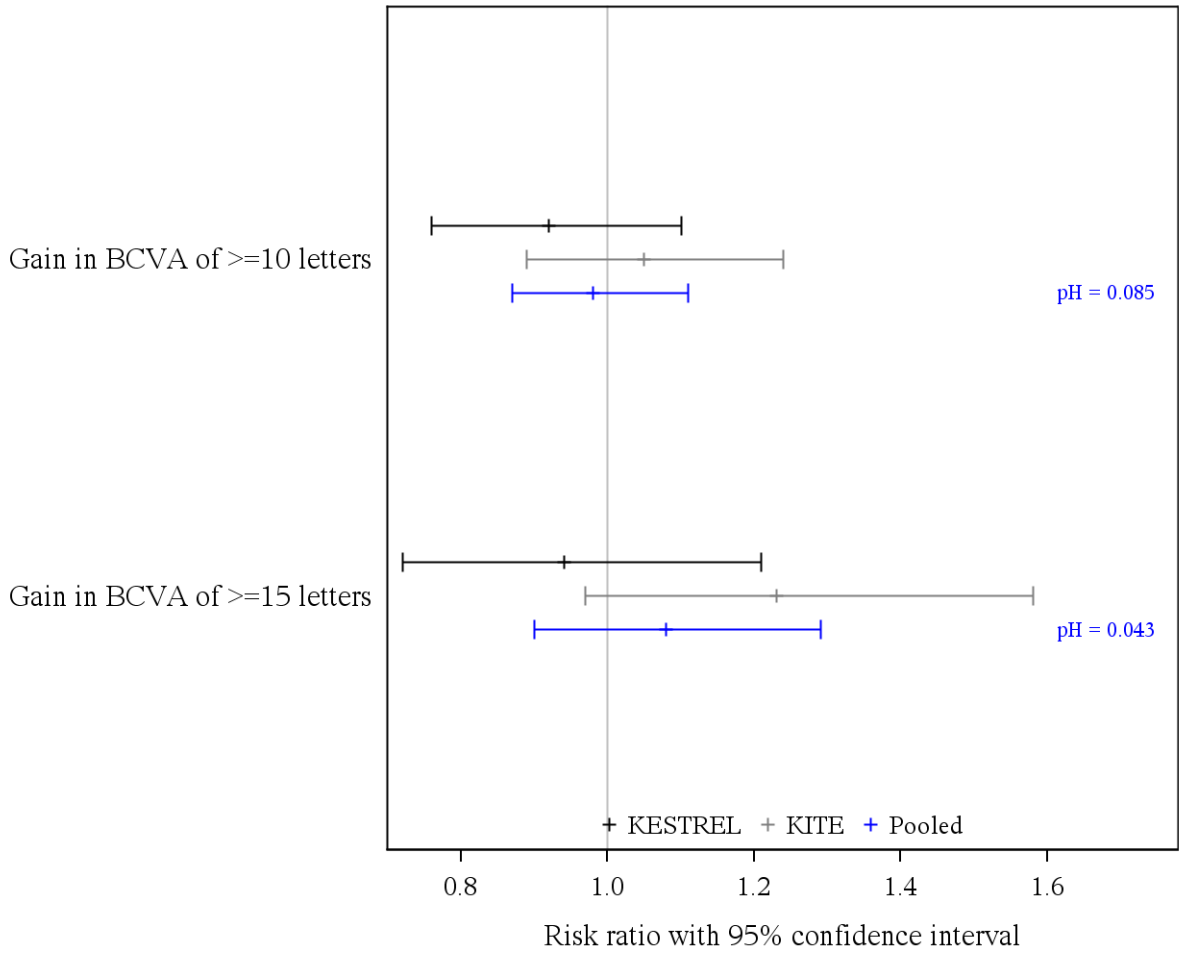
Figure 3.2.6 BCVA by diabetes type (FAS), forest plot, week 100



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.011$

4 BCVA: Binary analysis (Gain)

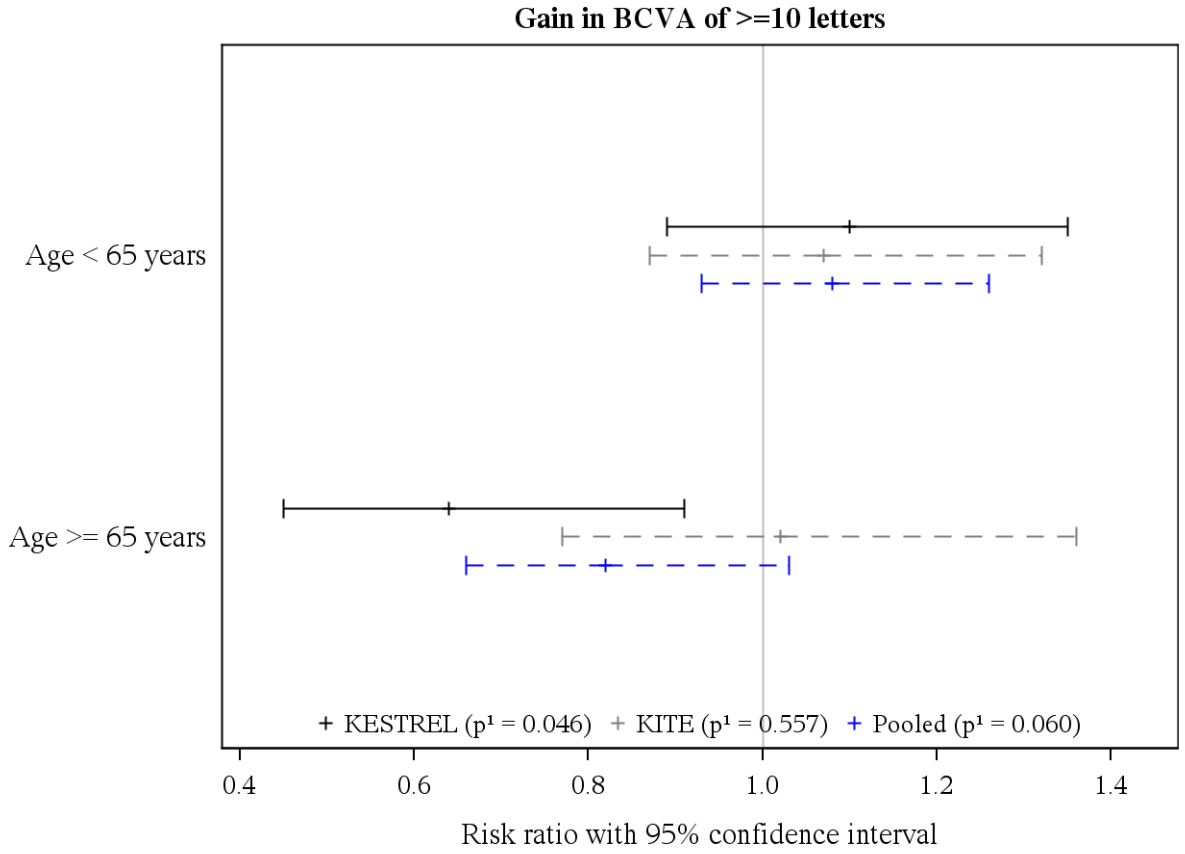
Figure 4.1.1 BCVA - Gain of 10 respectively 15 letters (FAS), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 4.1.2 BCVA - Gain of 10 respectively 15 letters by age (FAS), forest plot, week 52

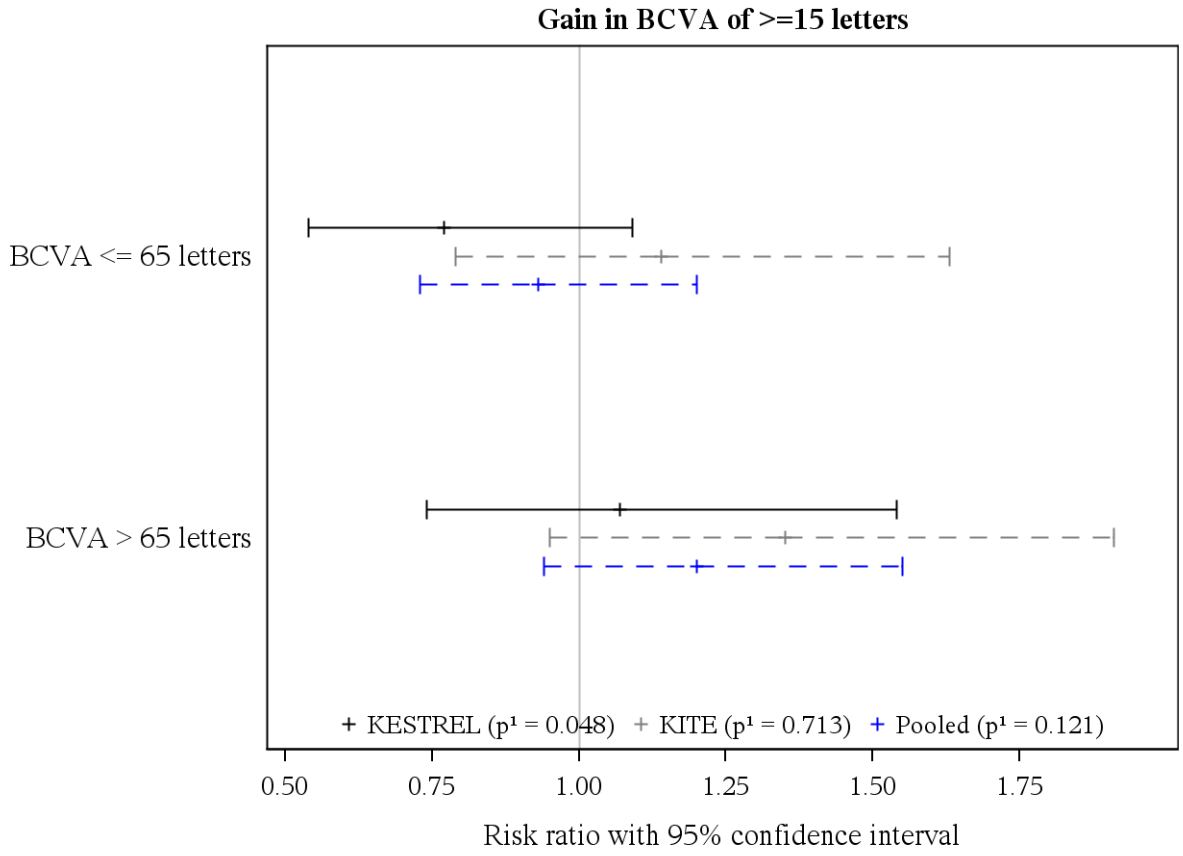
Figure 4.1.2.1 BCVA - Gain of 10 respectively 15 letters by age (FAS), forest plot, week 52, gain of >=10 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: p_H = 0.085

Figure 4.1.4 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), forest plot, week 52

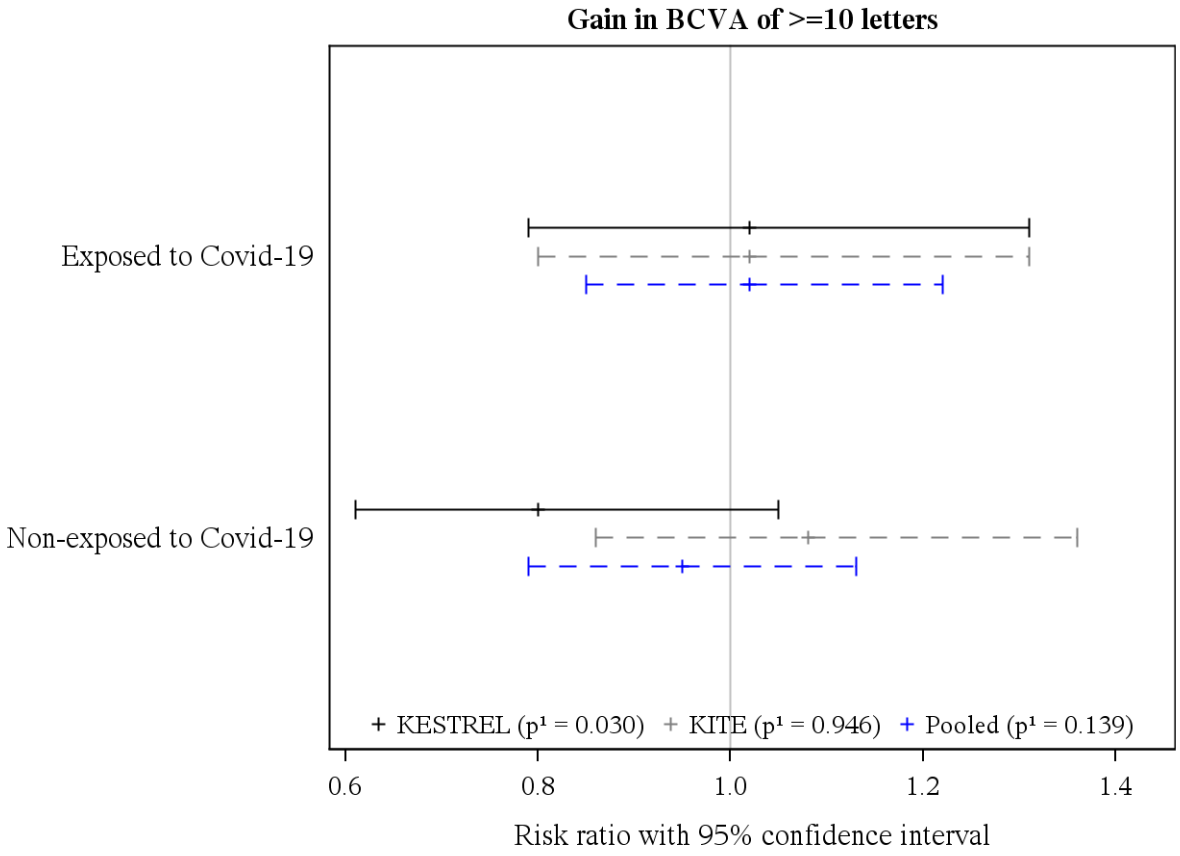
Figure 4.1.4.1 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), forest plot, week 52, gain of >=15 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.043$

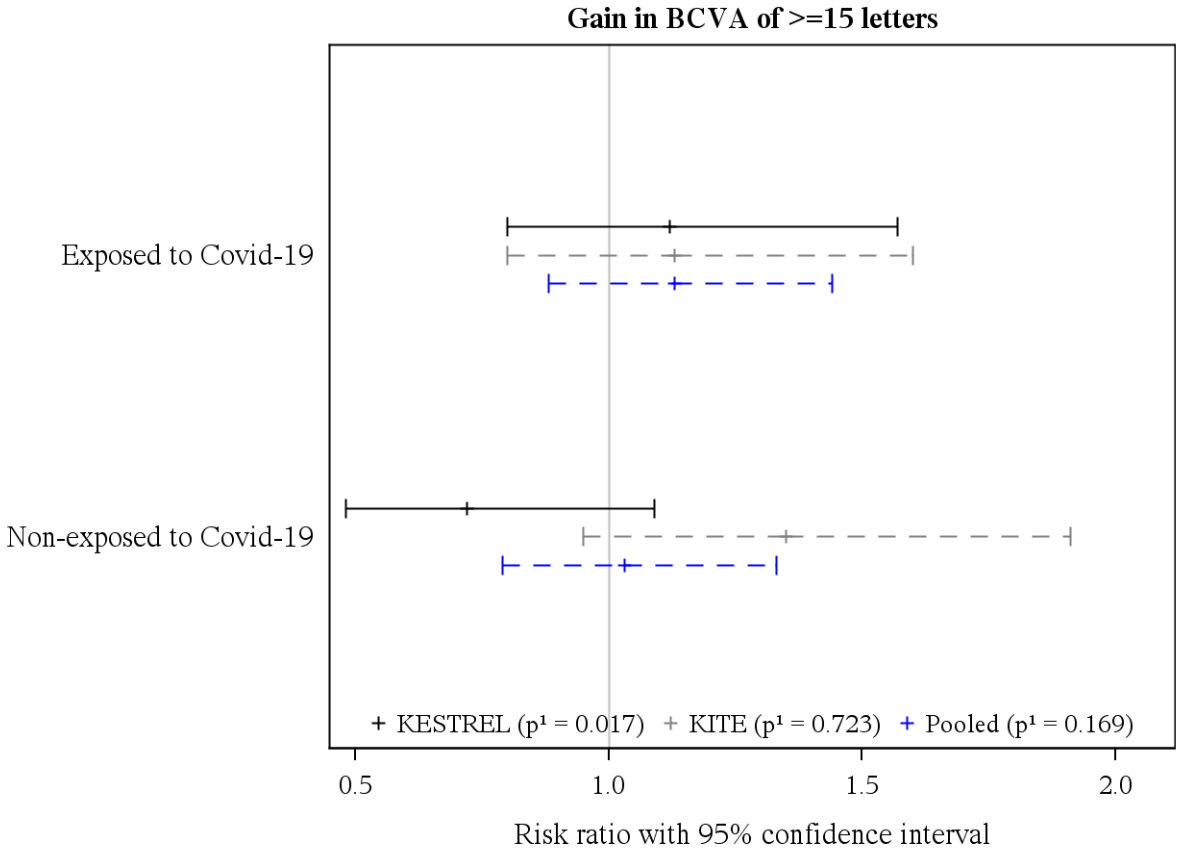
Figure 4.1.12 BCVA - Gain of 10 respectively 15 letters by exposure (week 52) (FAS), forest plot, week 52

Figure 4.1.12.1 BCVA - Gain of 10 respectively 15 letters by exposure (week 52) (FAS), forest plot, week 52, gain of >=10 letters



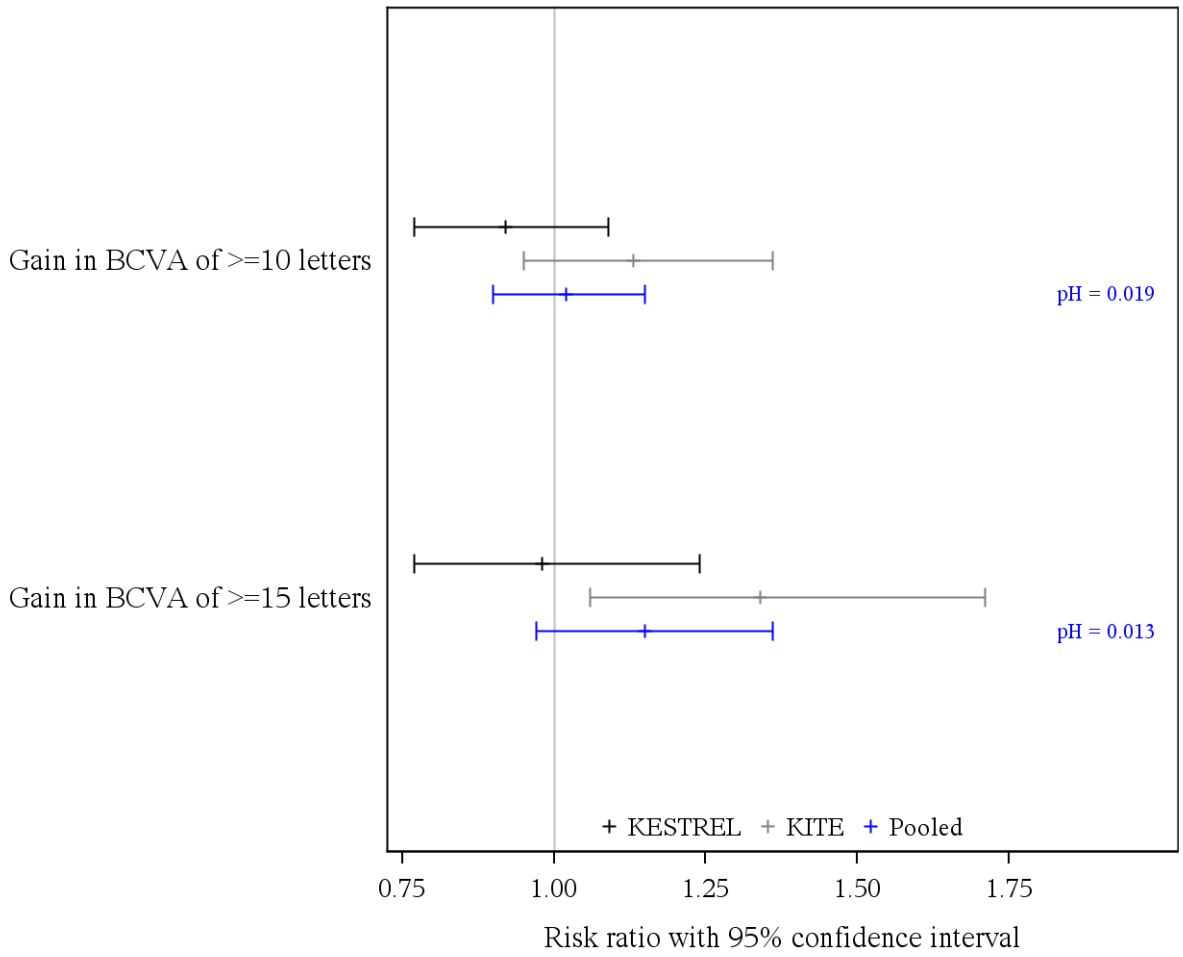
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.085$

Figure 4.1.12.2 BCVA - Gain of 10 respectively 15 letters by exposure (week 52) (FAS), forest plot, week 52, gain of >=15 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.043$

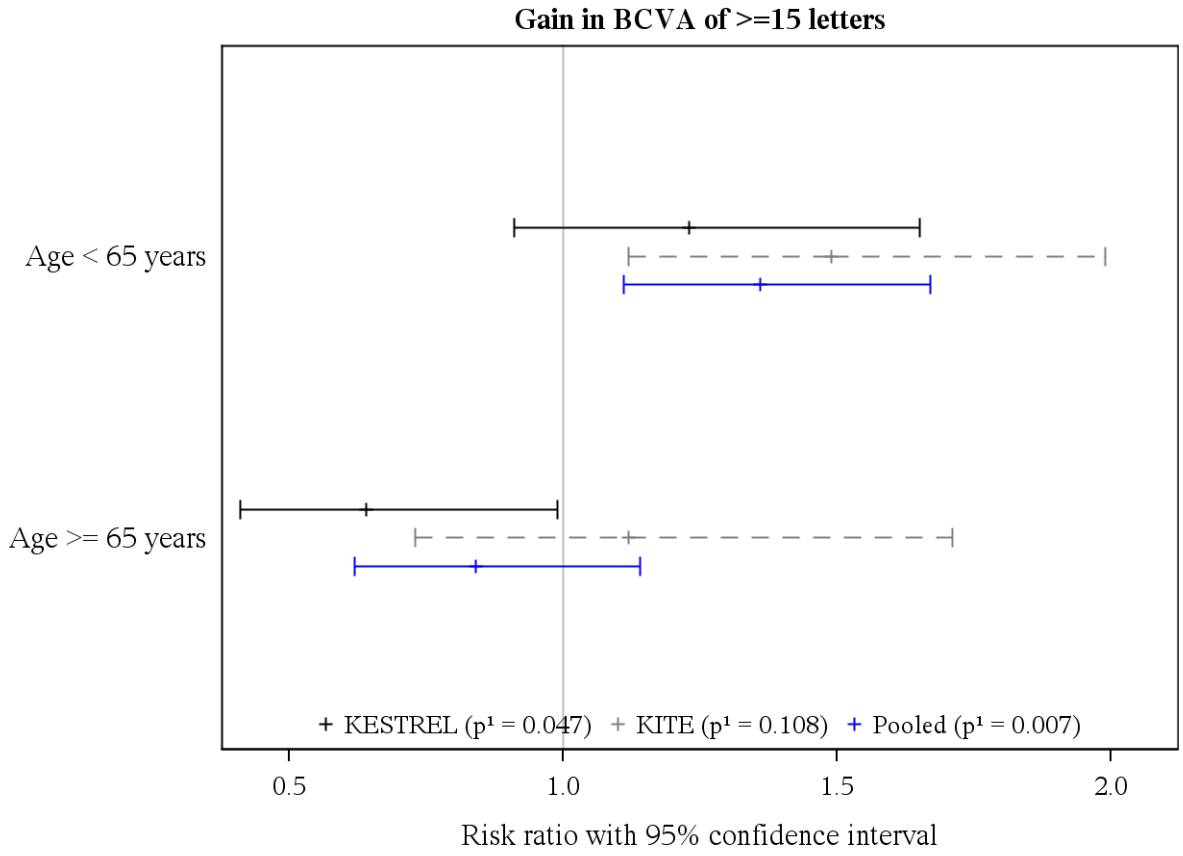
Figure 4.2.1 BCVA - Gain of 10 respectively 15 letters (FAS), forest plot, week 100



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 4.2.2 BCVA - Gain of 10 respectively 15 letters by age (FAS), forest plot, week 100

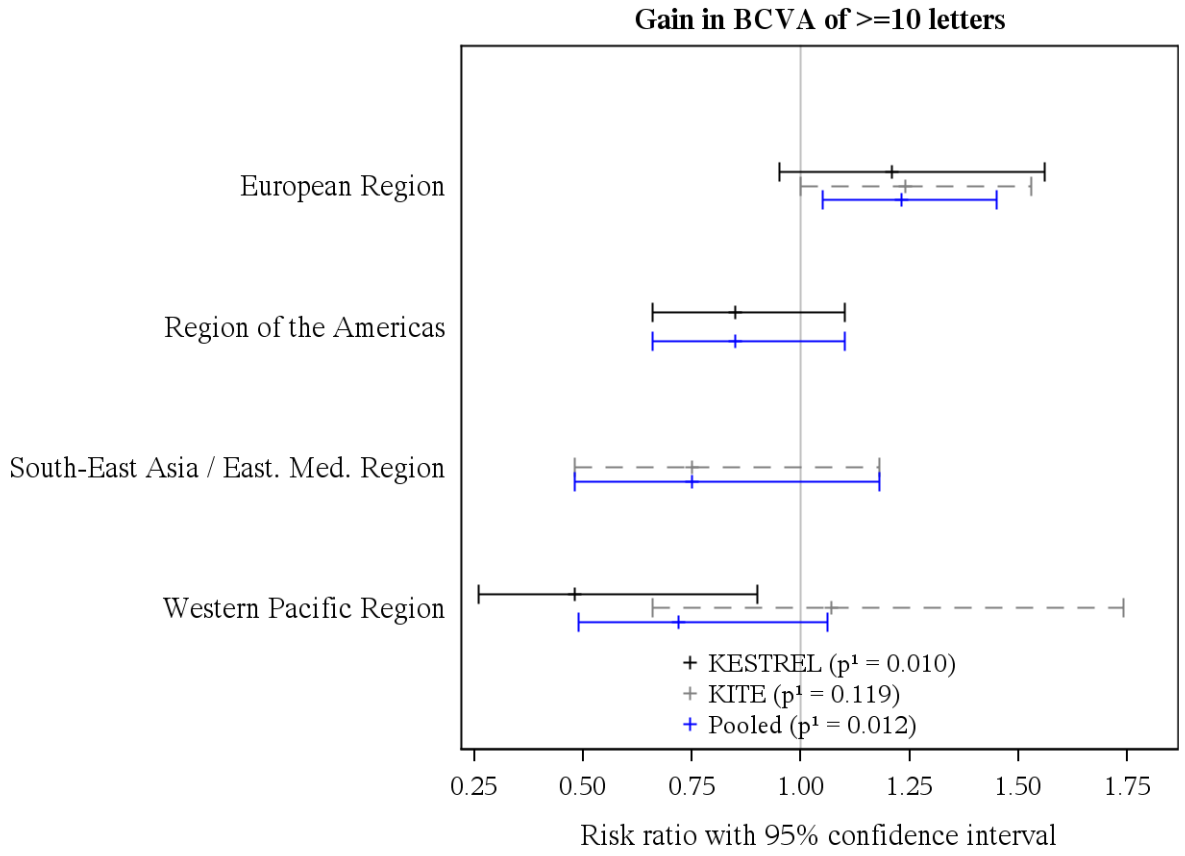
Figure 4.2.2.1 BCVA - Gain of 10 respectively 15 letters by age (FAS), forest plot, week 100, gain of >=15 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.013$

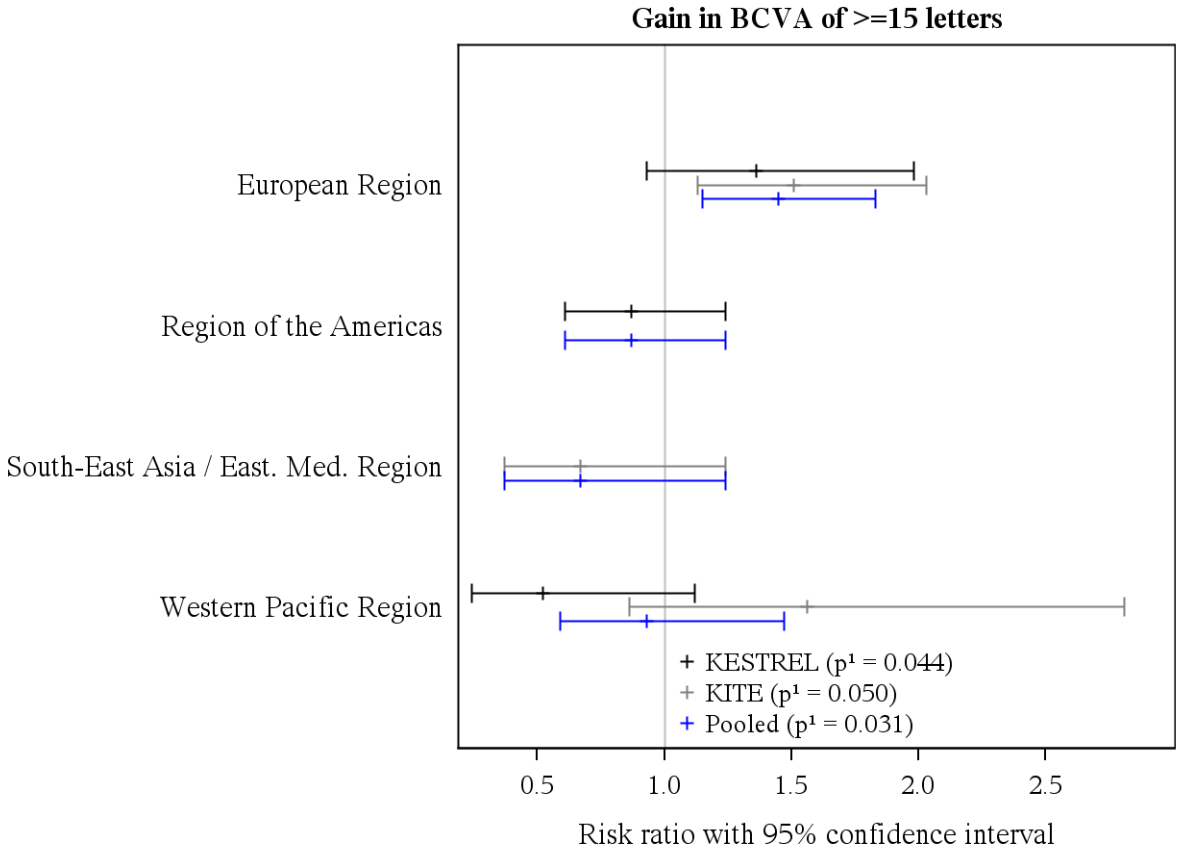
Figure 4.2.5 BCVA - Gain of 10 respectively 15 letters by region (FAS), forest plot, week 100

Figure 4.2.5.1 BCVA - Gain of 10 respectively 15 letters by region (FAS), forest plot, week 100, gain of >=10 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.019$

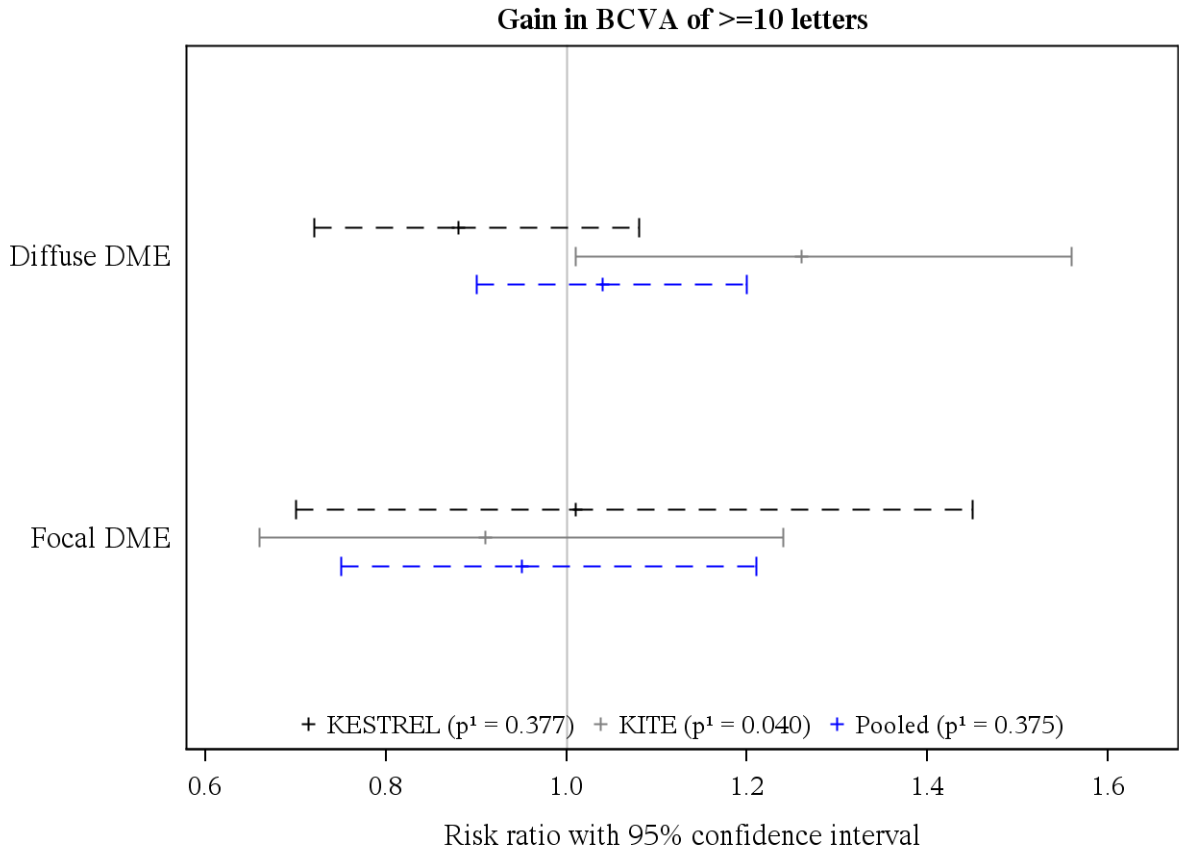
Figure 4.2.5.2 BCVA - Gain of 10 respectively 15 letters by region (FAS), forest plot, week 100, gain of >=15 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.013$

Figure 4.2.9 BCVA - Gain of 10 respectively 15 letters by DME type (FAS), forest plot, week 100

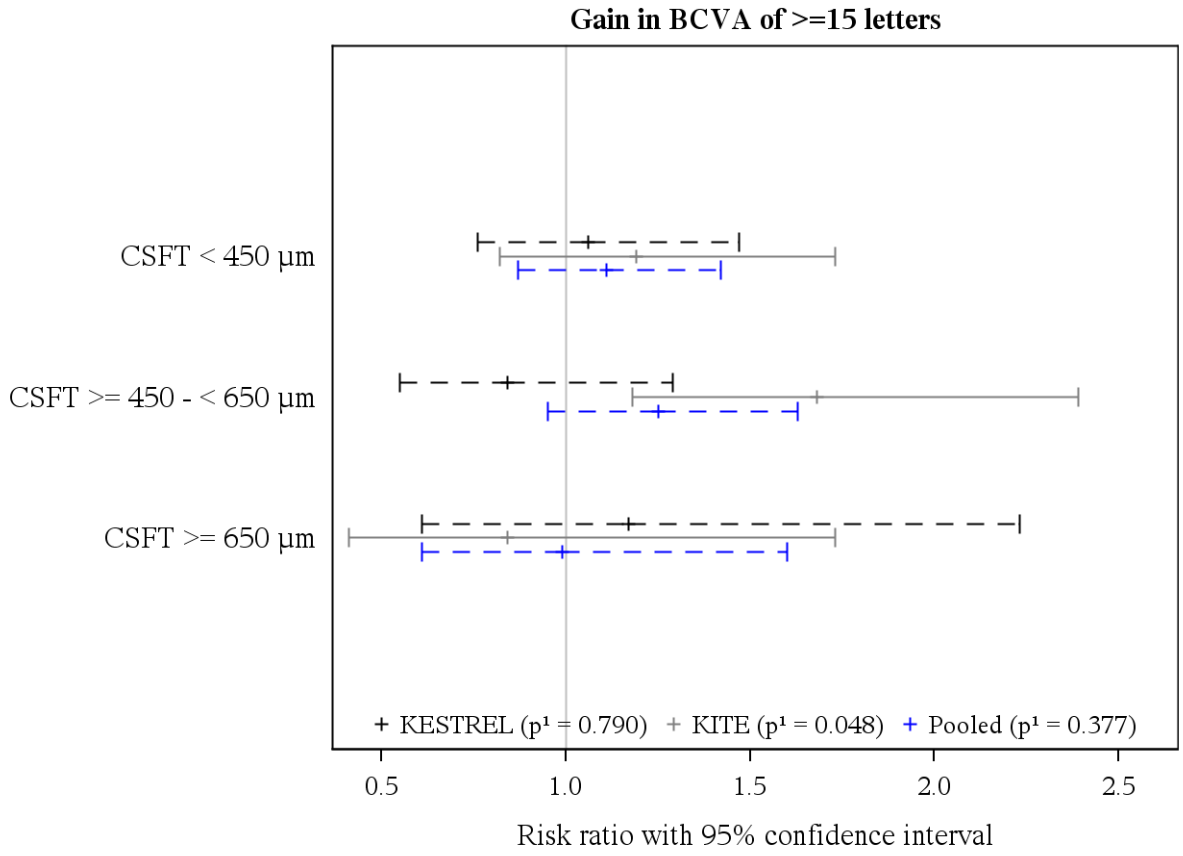
Figure 4.2.9.1 BCVA - Gain of 10 respectively 15 letters by DME type (FAS), forest plot, week 100, gain of >=10 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.019$

Figure 4.2.10 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), forest plot, week 100

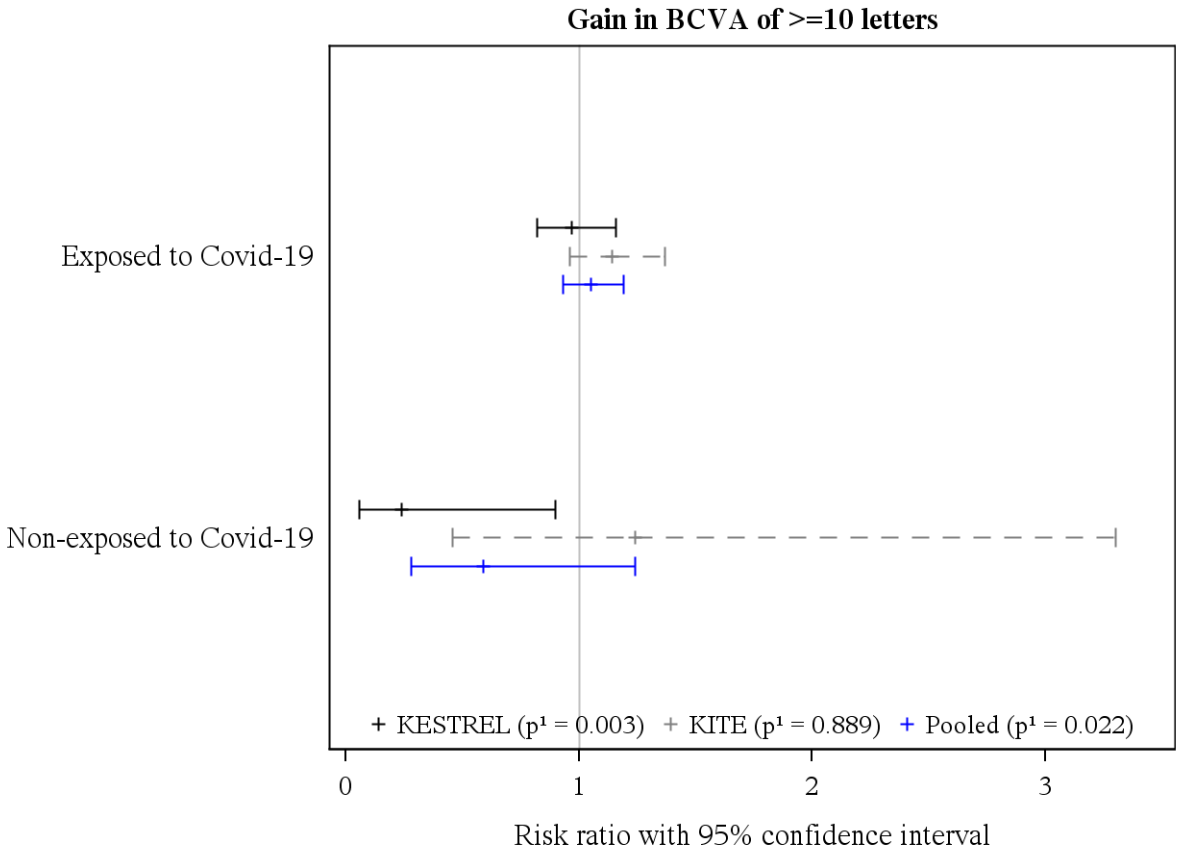
Figure 4.2.10.1 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), forest plot, week 100, gain of >=15 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.013$

Figure 4.2.13 BCVA - Gain of 10 respectively 15 letters by exposure (week 100) (FAS), forest plot, week 100

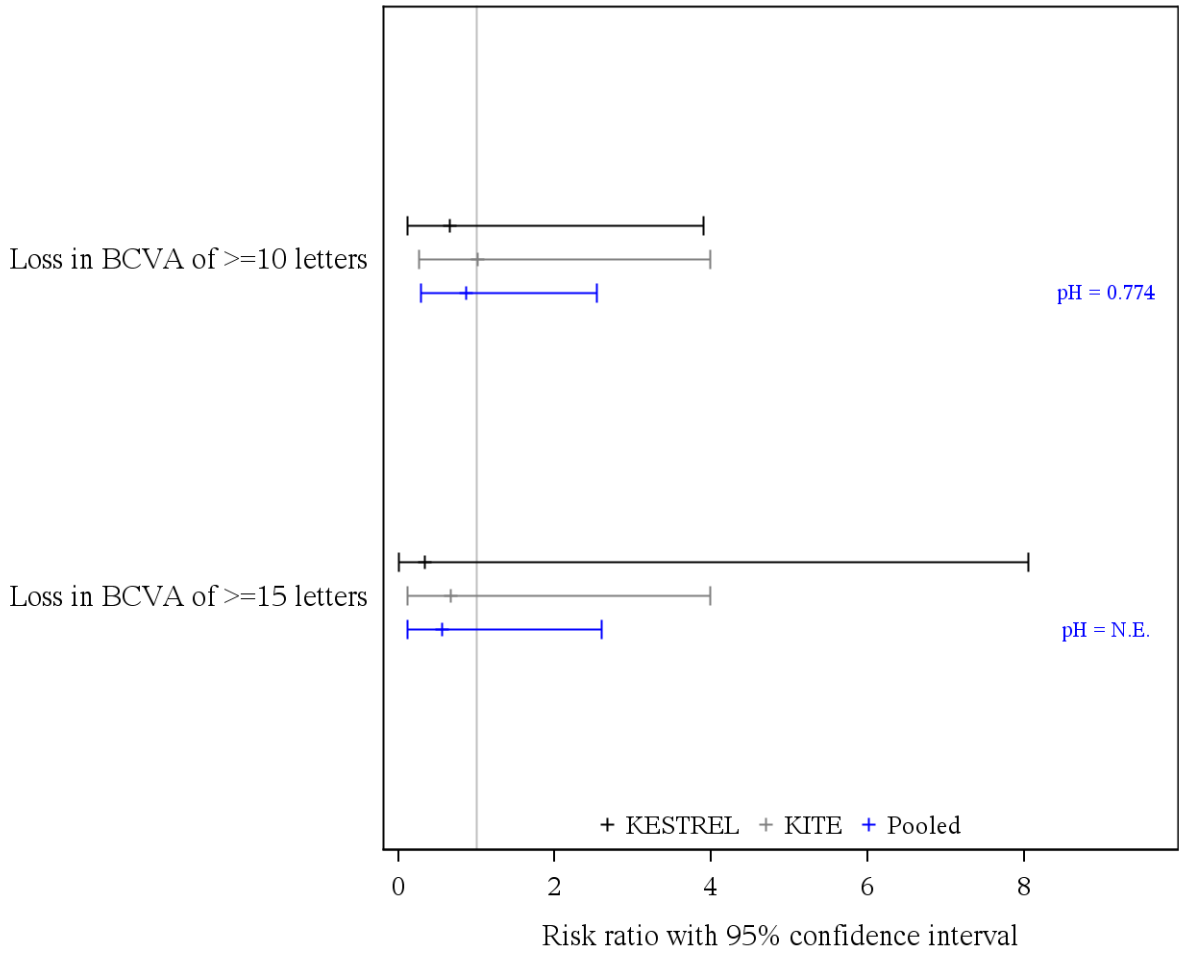
Figure 4.2.13.1 BCVA - Gain of 10 respectively 15 letters by exposure (week 100) (FAS), forest plot, week 100, gain of >=10 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.019$

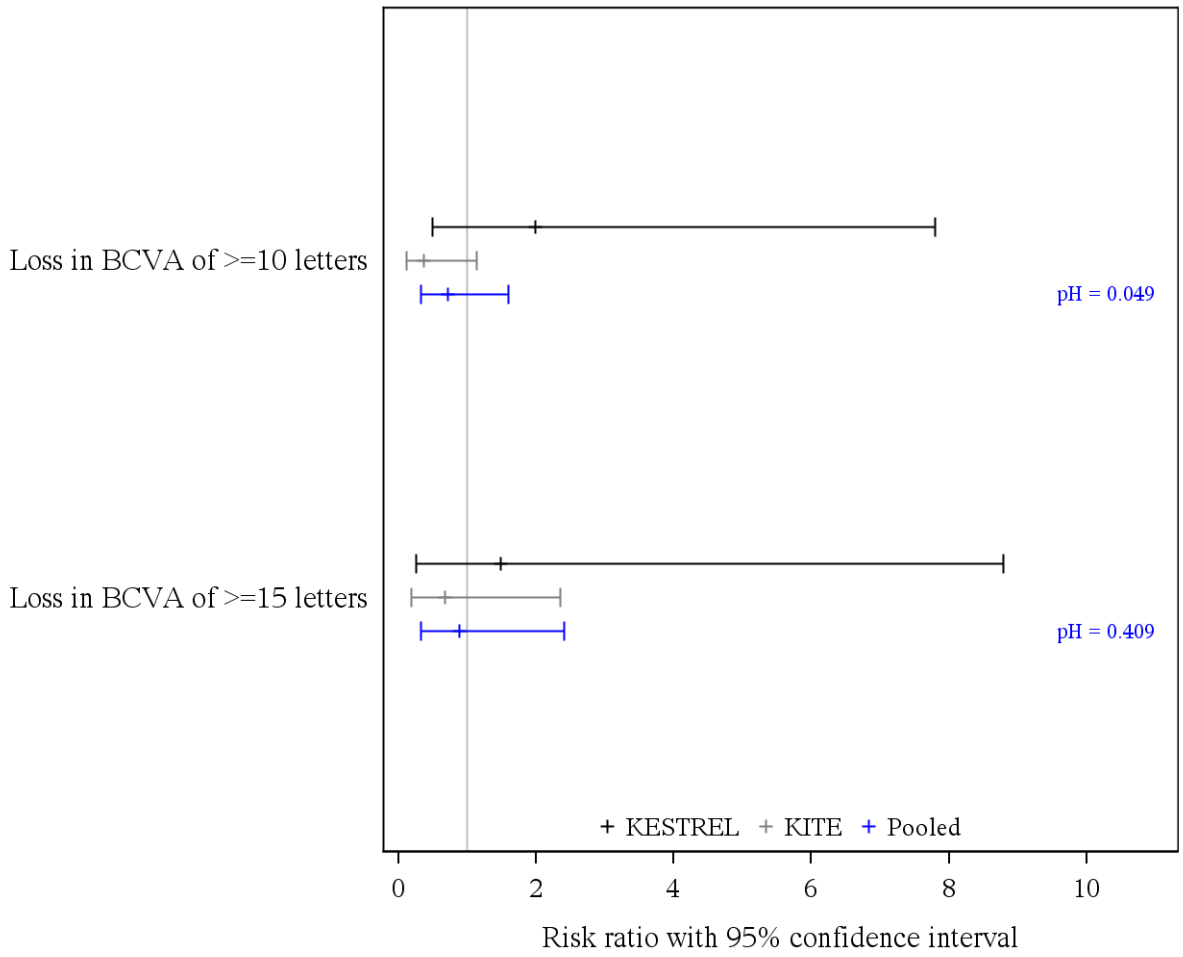
5 BCVA: Binary analysis (Loss)

Figure 5.1.1 BCVA - Loss of 10 respectively 15 letters (FAS), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

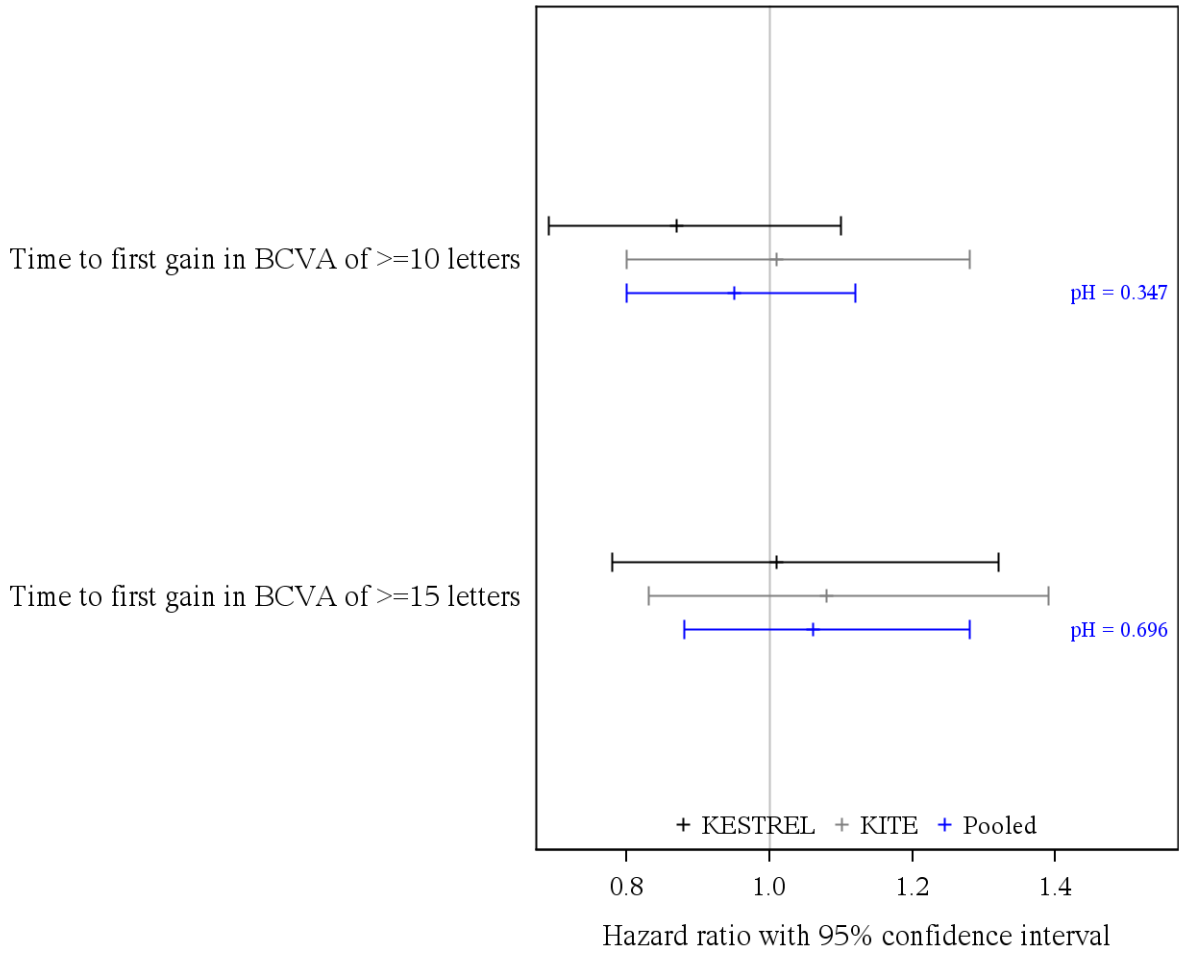
Figure 5.2.1 BCVA - Loss of 10 respectively 15 letters (FAS), forest plot, week 100



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

6 BCVA: Time-to-event analysis (Gain)

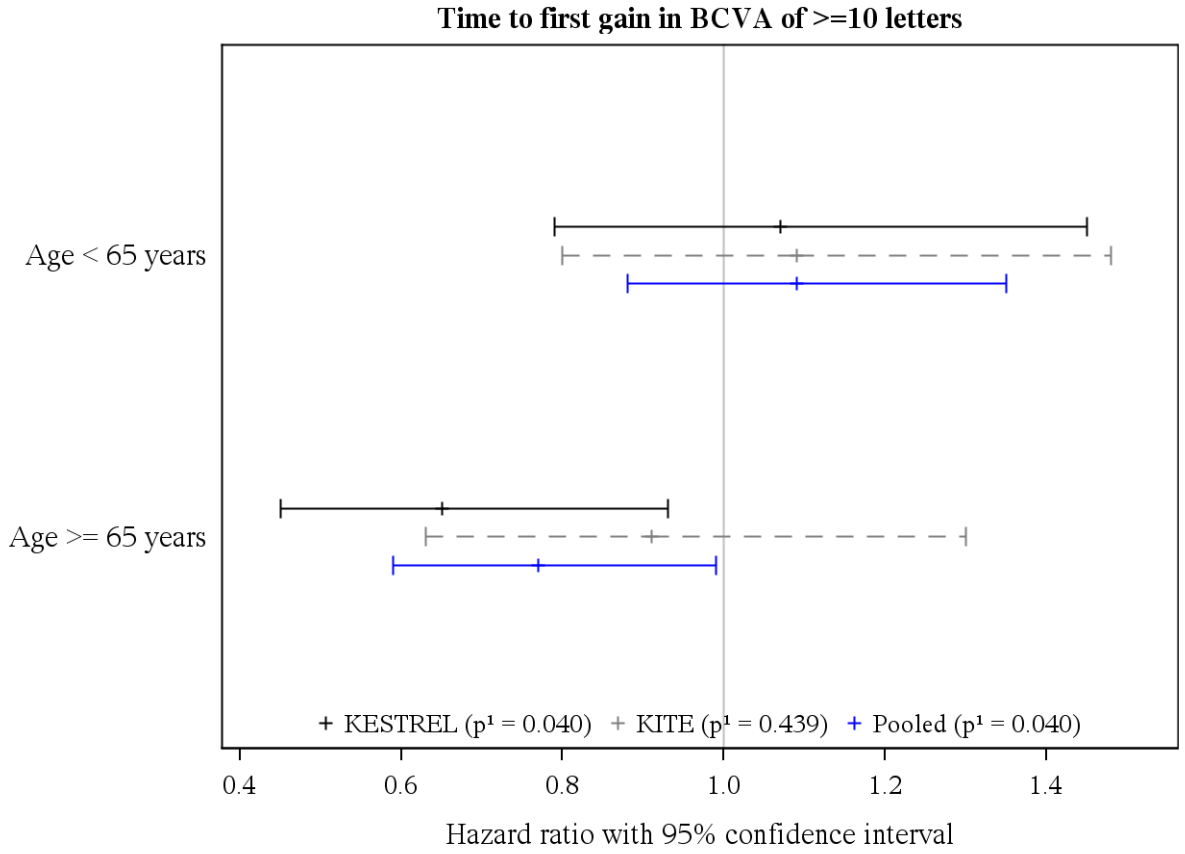
Figure 6.1.1 BCVA - Gain of 10 respectively 15 letters (FAS), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 6.1.2 BCVA - Gain of 10 respectively 15 letters by age (FAS), forest plot, week 52

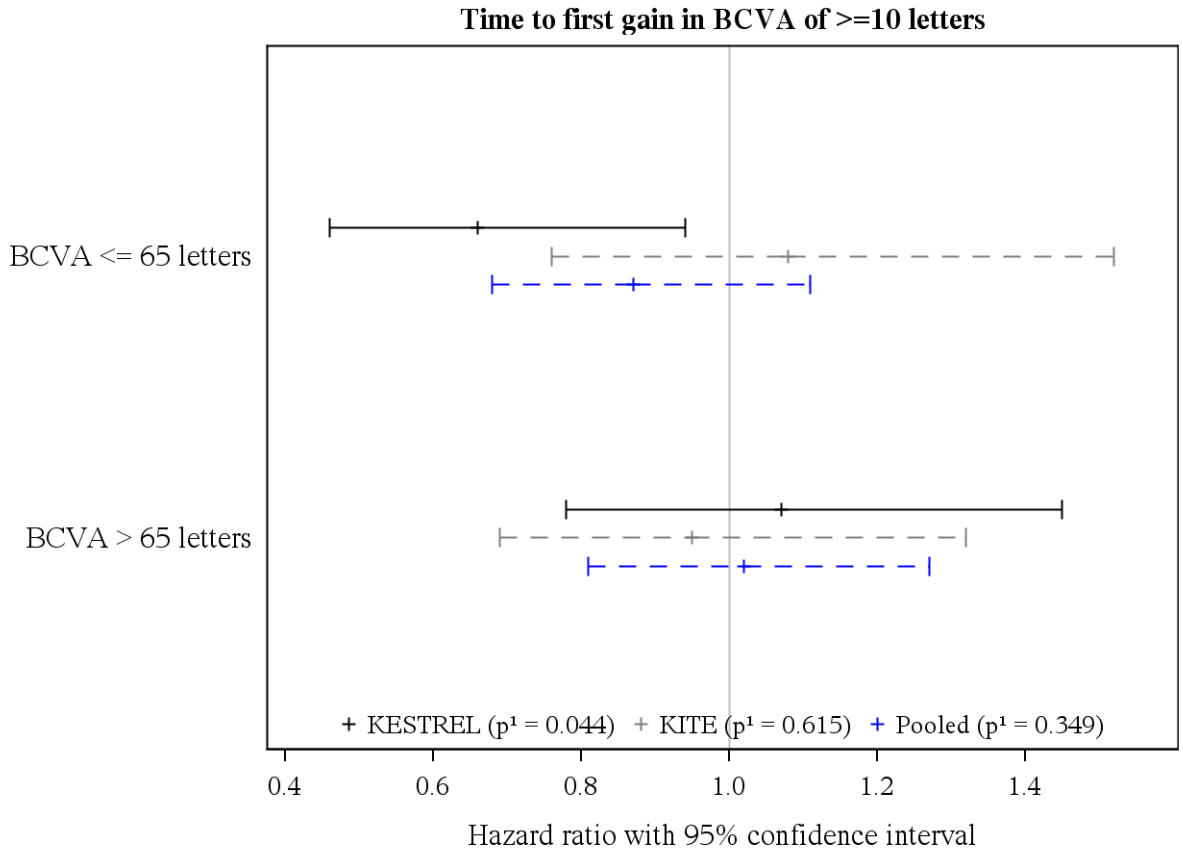
Figure 6.1.2.1 BCVA - Gain of 10 respectively 15 letters by age (FAS), forest plot, week 52, gain of >=10 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.347$

Figure 6.1.4 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), forest plot, week 52

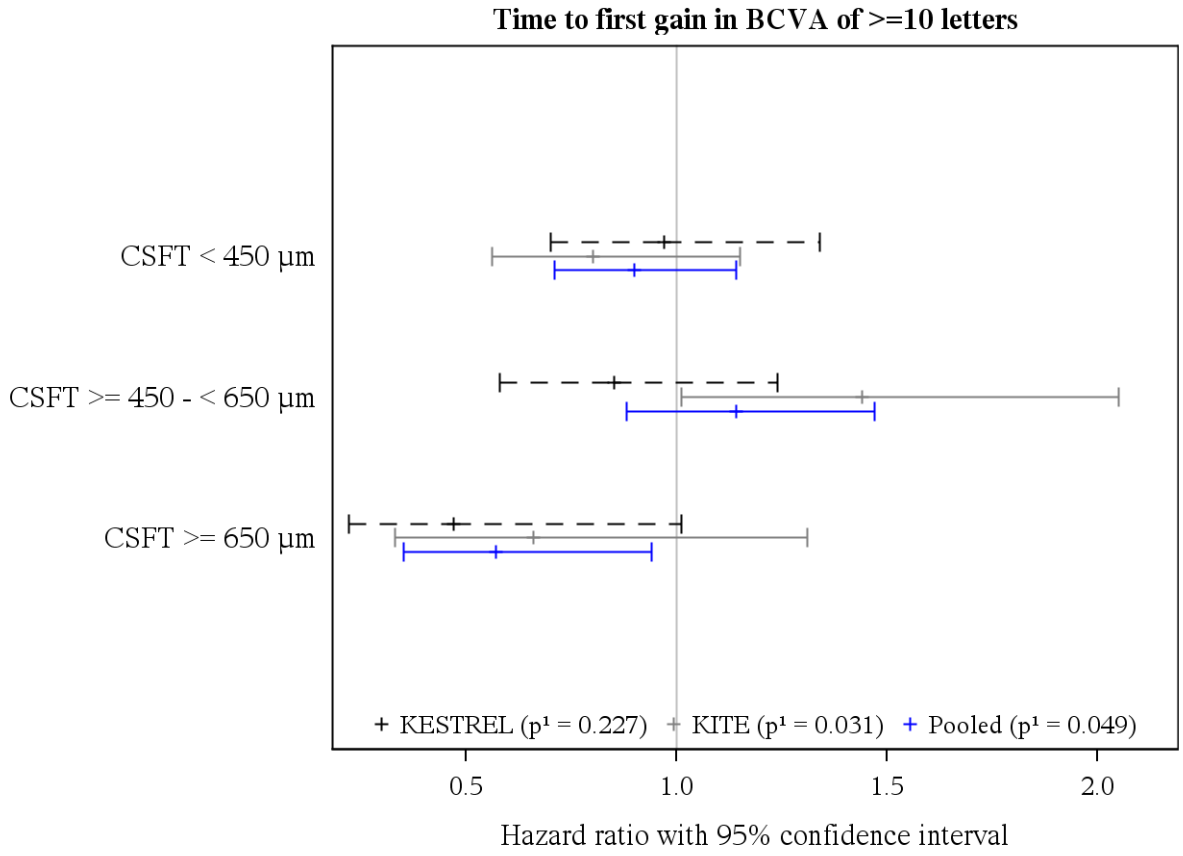
Figure 6.1.4.1 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), forest plot, week 52, gain of >=10 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.347$

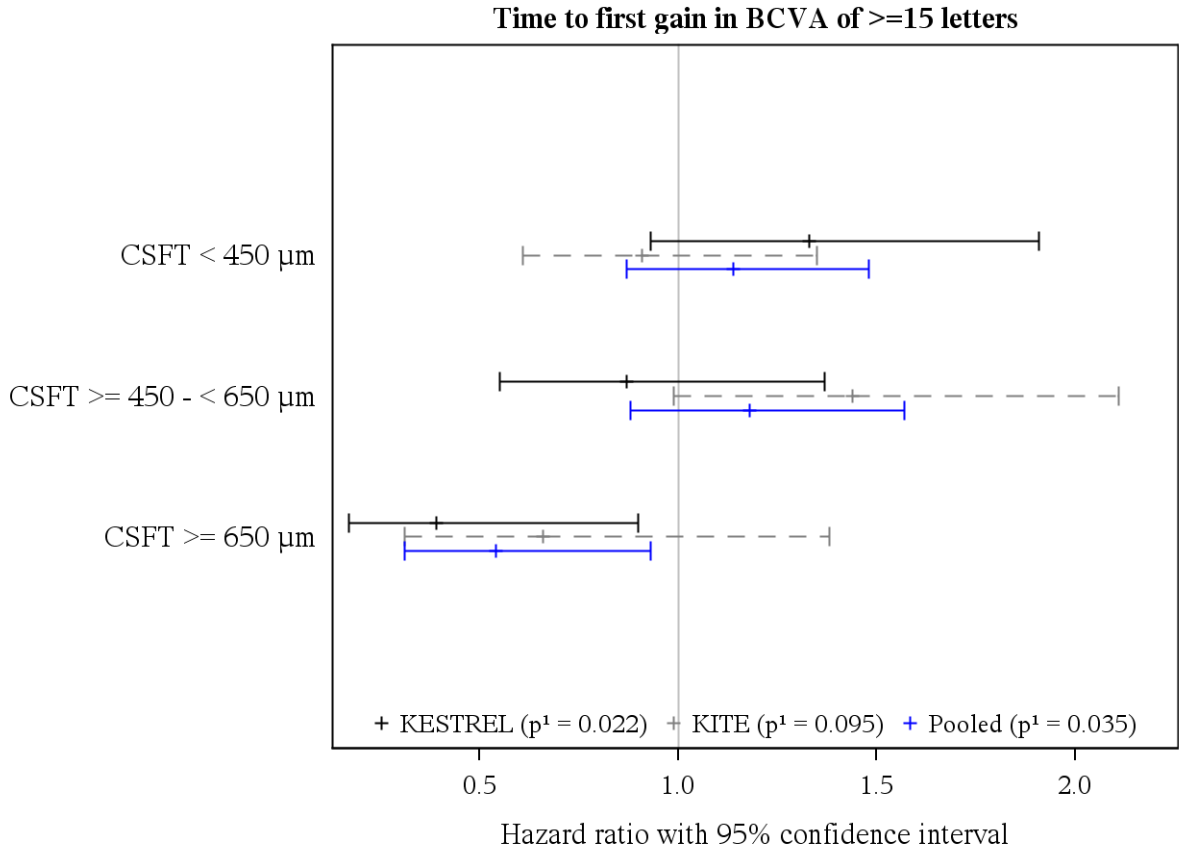
Figure 6.1.10 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), forest plot, week 52

Figure 6.1.10.1 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), forest plot, week 52, gain of >=10 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.347$

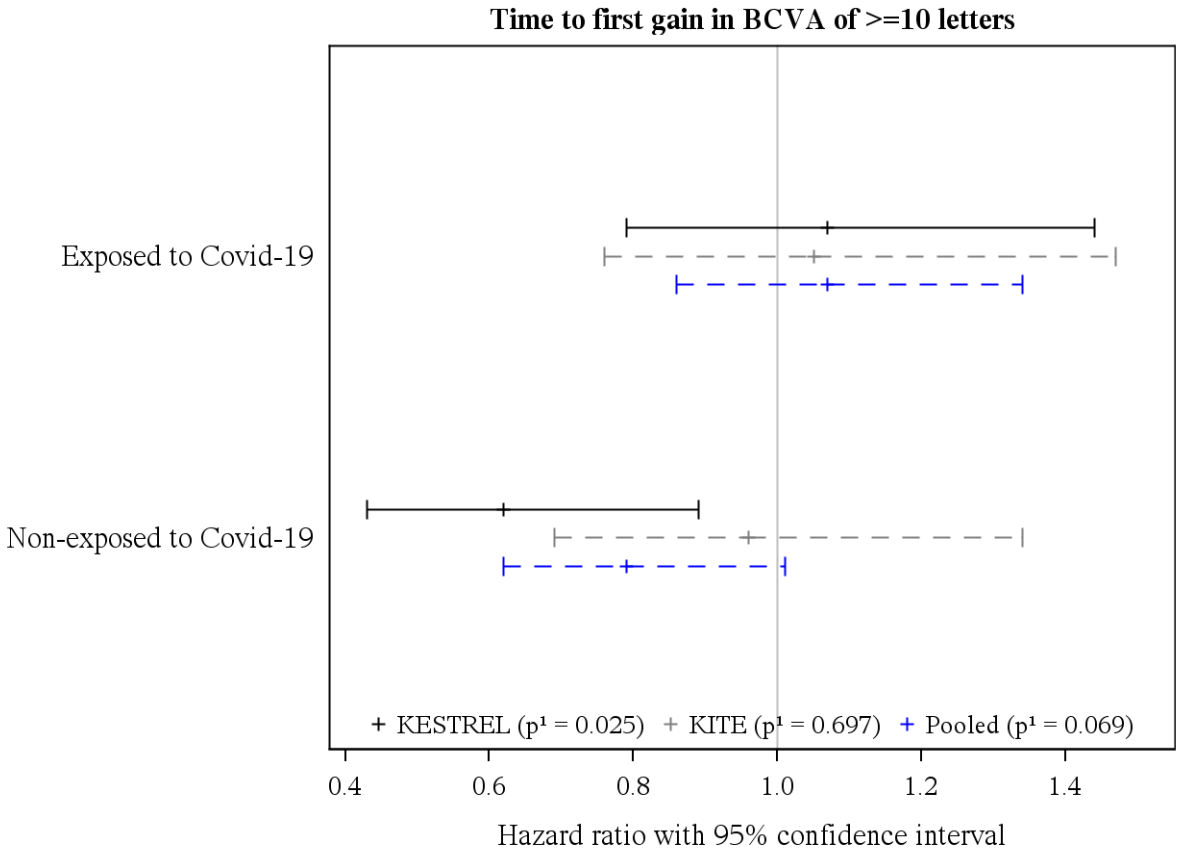
Figure 6.1.10.2 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), forest plot, week 52, gain of >=15 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.696$

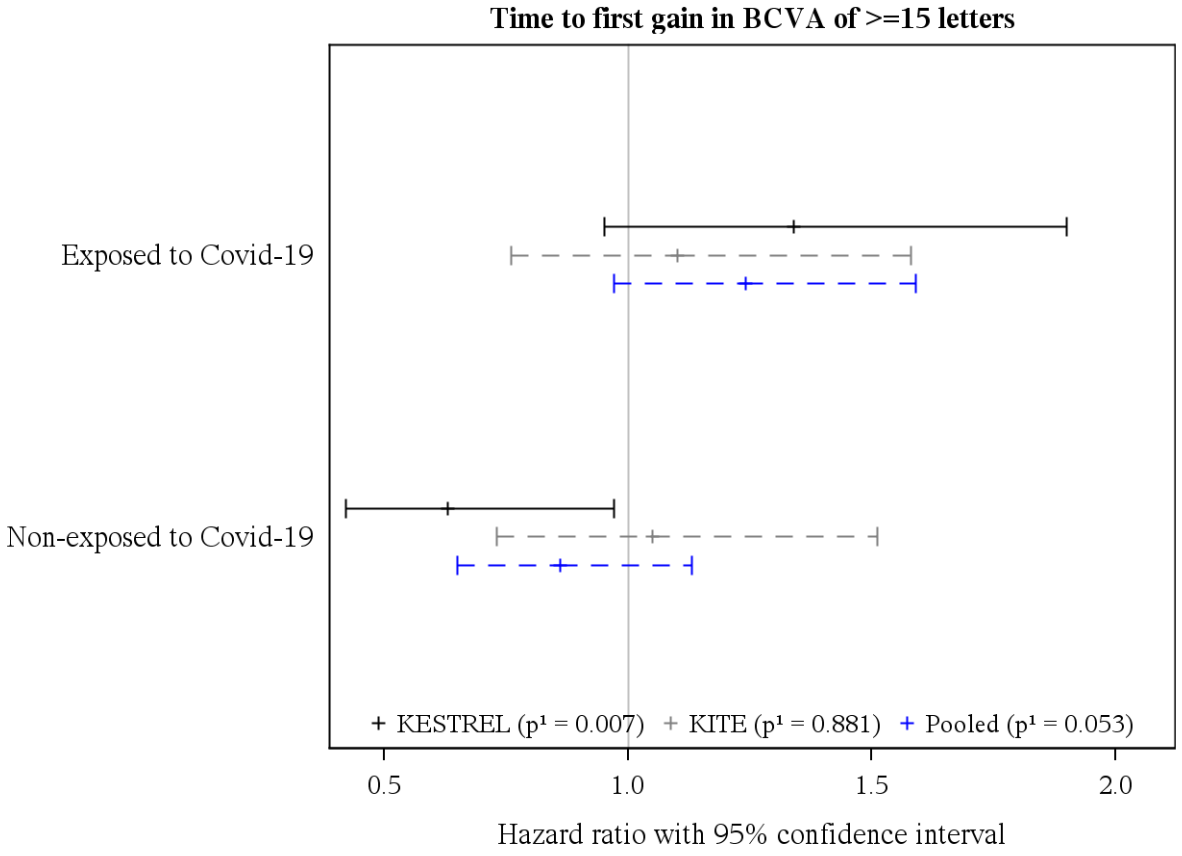
Figure 6.1.12 BCVA - Gain of 10 respectively 15 letters by exposure (week 52) (FAS), forest plot, week 52

Figure 6.1.12.1 BCVA - Gain of 10 respectively 15 letters by exposure (week 52) (FAS), forest plot, week 52, gain of >=10 letters



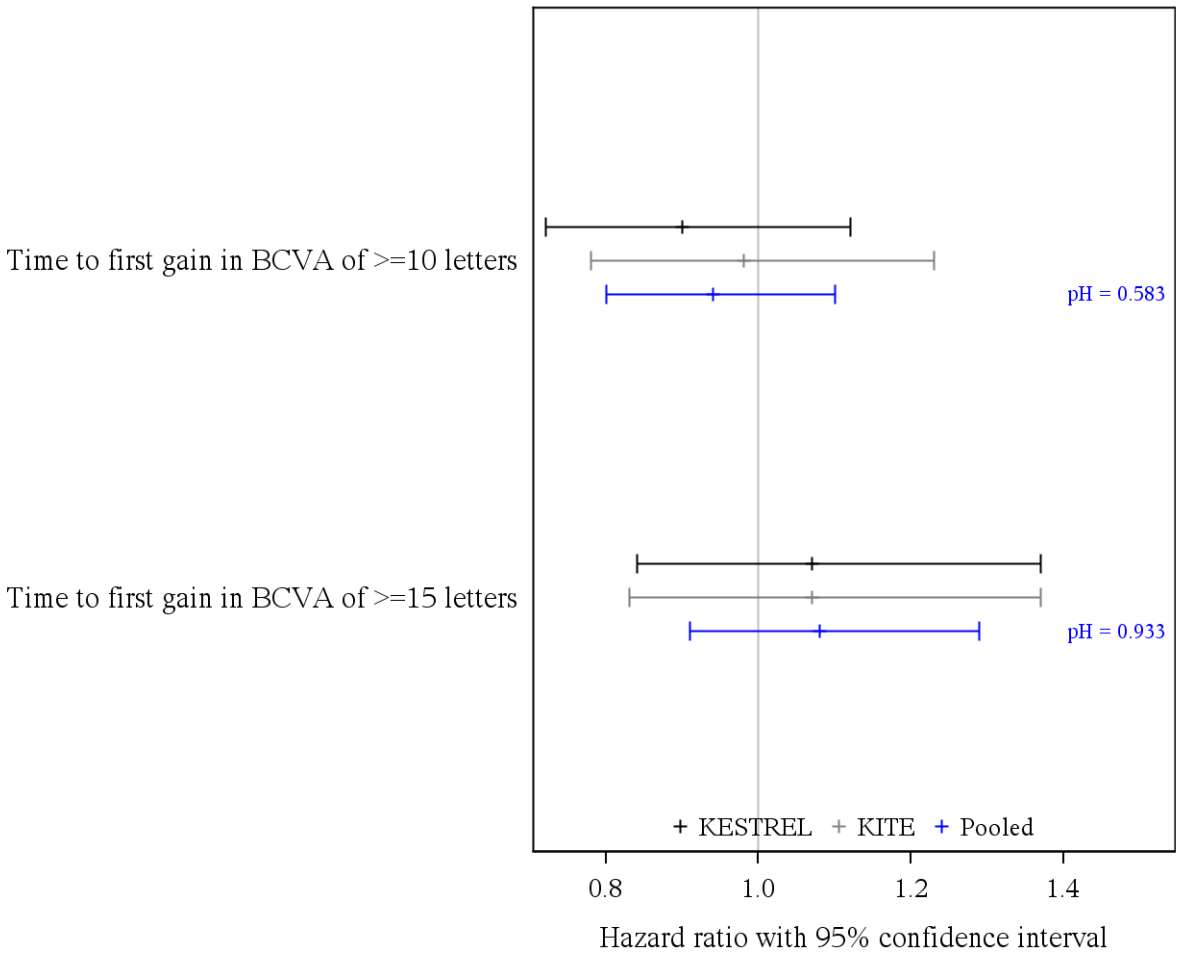
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.347$

Figure 6.1.12.2 BCVA - Gain of 10 respectively 15 letters by exposure (week 52) (FAS), forest plot, week 52, gain of >=15 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.696$

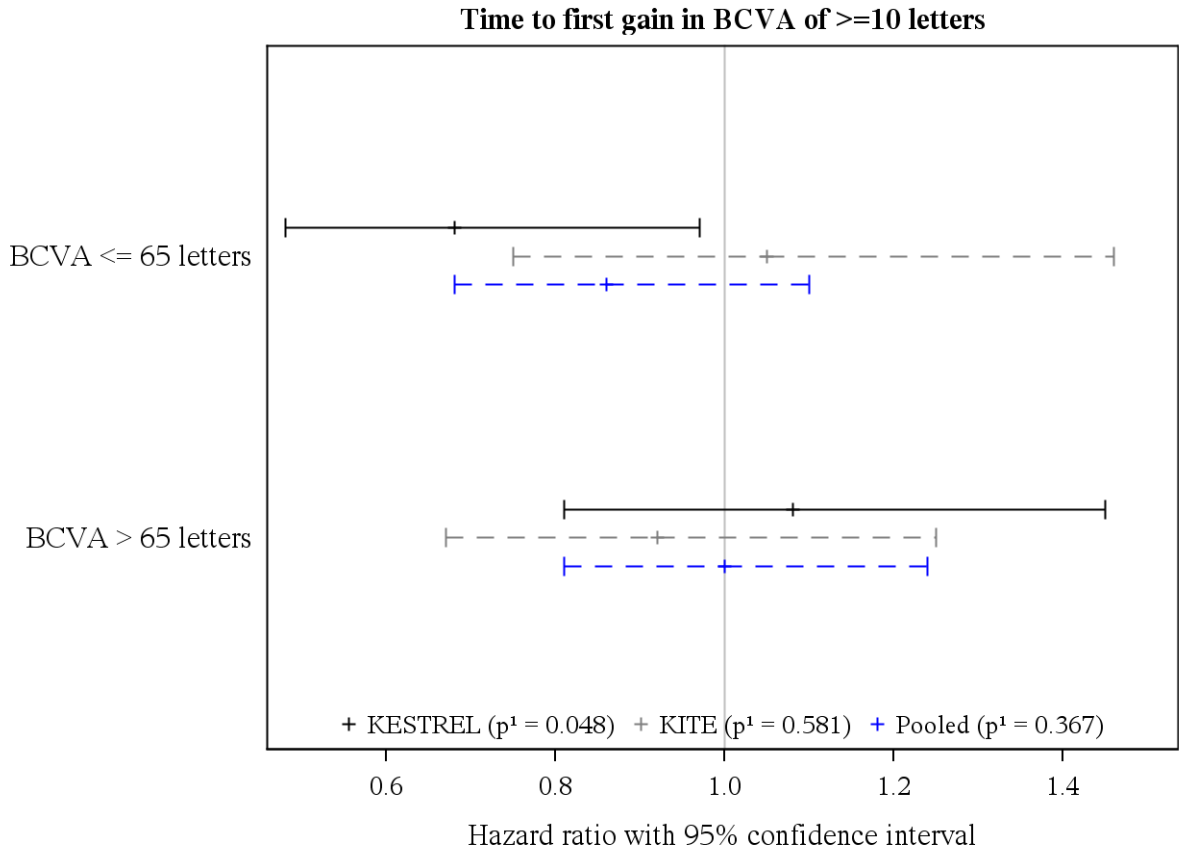
Figure 6.2.1 BCVA - Gain of 10 respectively 15 letters (FAS), forest plot, week 100



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

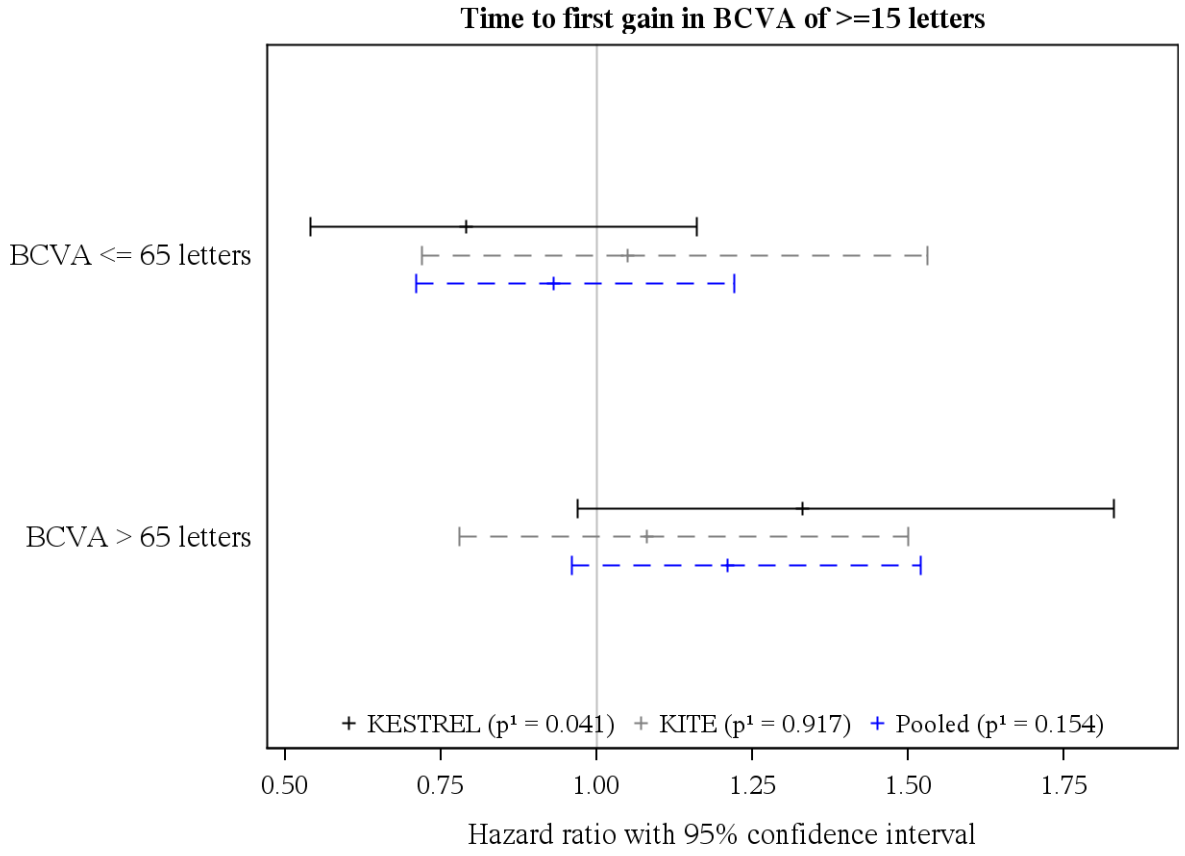
Figure 6.2.4 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), forest plot, week 100

Figure 6.2.4.1 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), forest plot, week 100, gain of >=10 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.583$

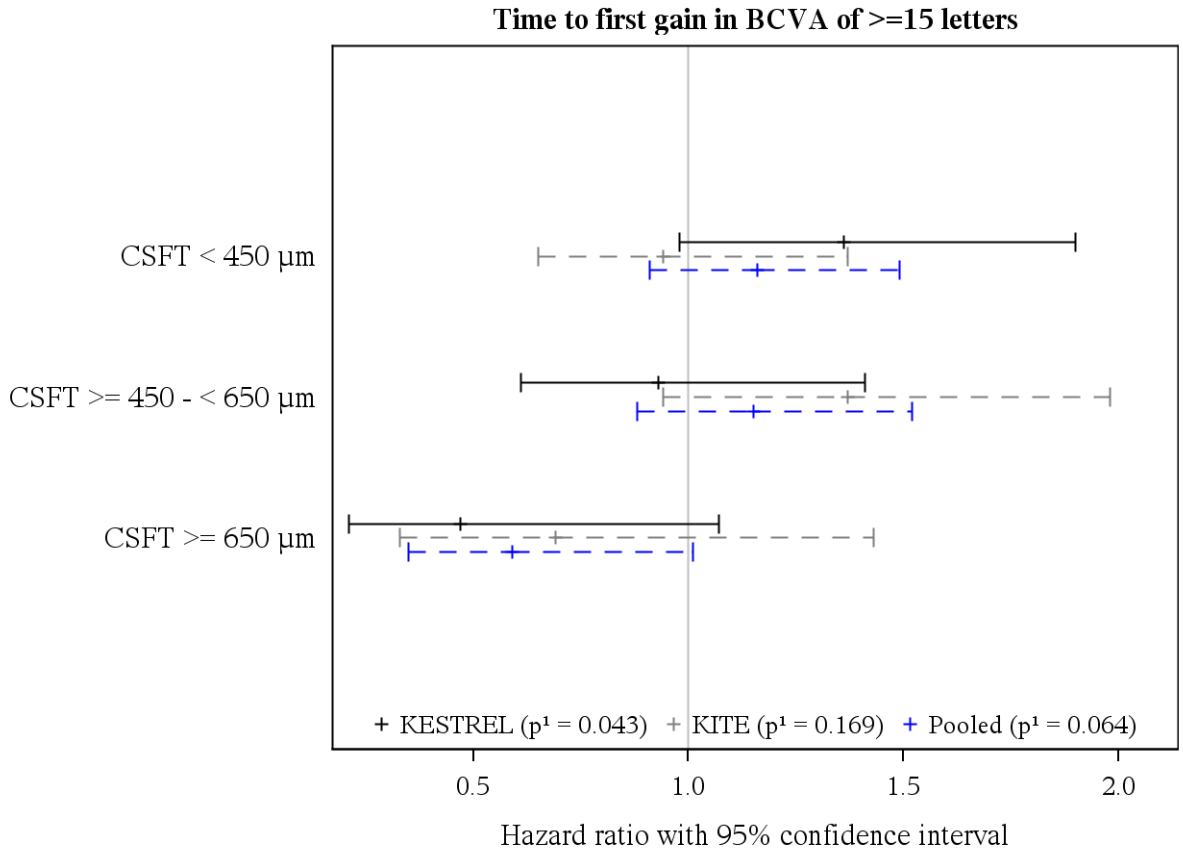
Figure 6.2.4.2 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), forest plot, week 100, gain of >=15 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.933$

Figure 6.2.10 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), forest plot, week 100

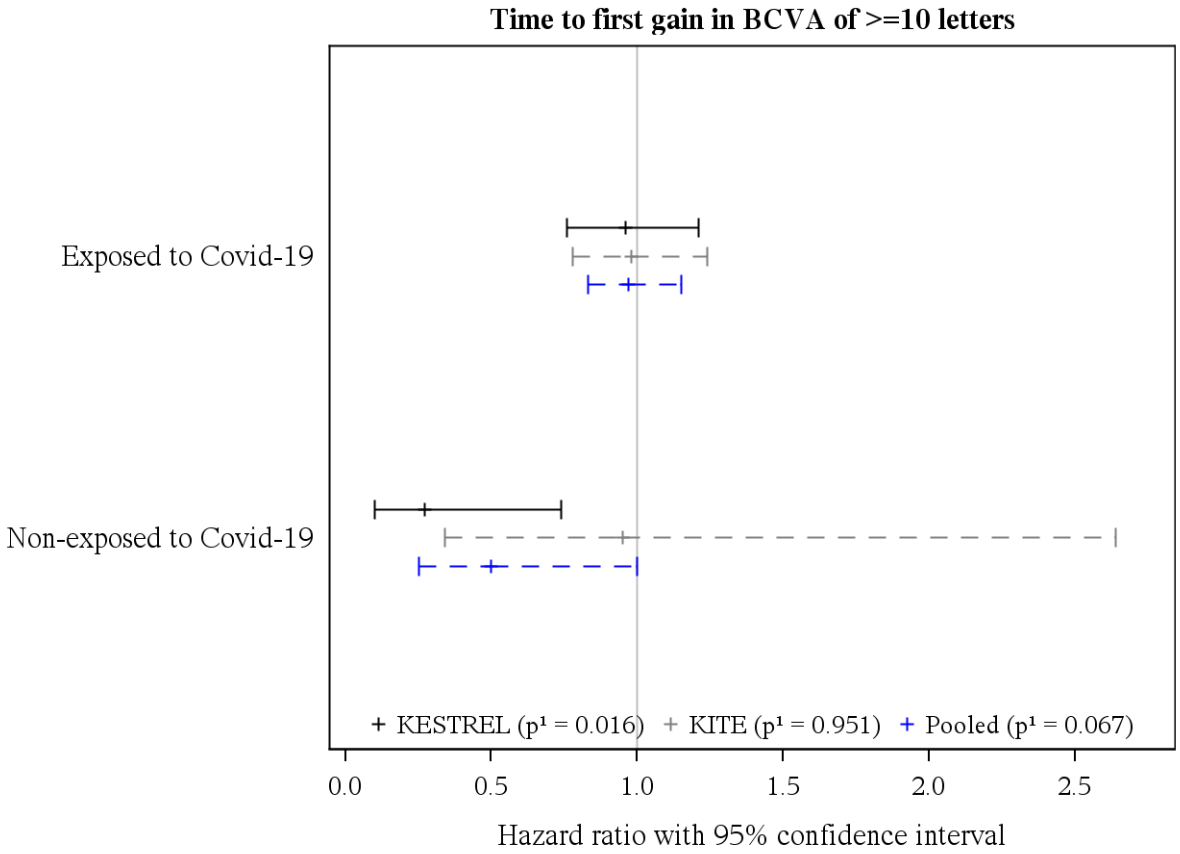
Figure 6.2.10.1 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), forest plot, week 100, gain of >=15 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.933$

Figure 6.2.13 BCVA - Gain of 10 respectively 15 letters by exposure (week 100) (FAS), forest plot, week 100

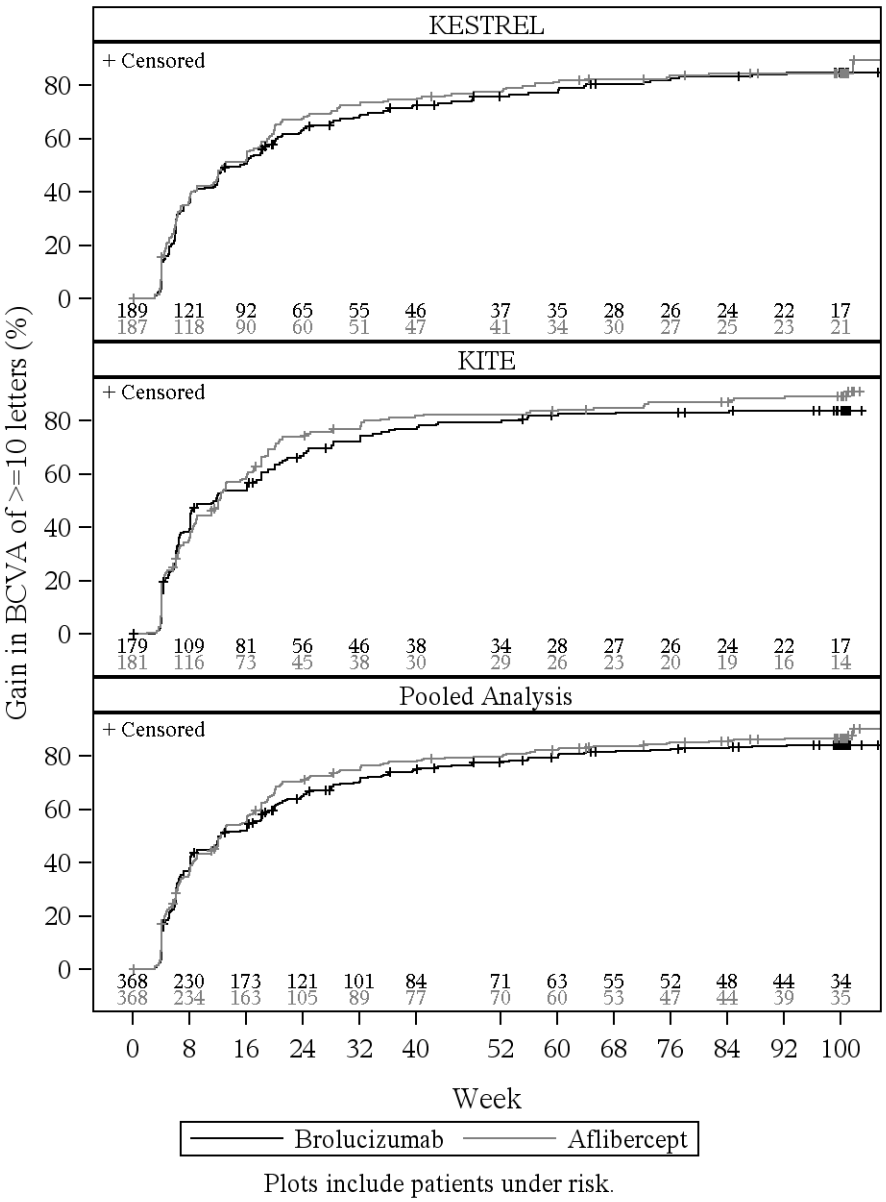
Figure 6.2.13.1 BCVA - Gain of 10 respectively 15 letters by exposure (week 100) (FAS), forest plot, week 100, gain of >=10 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.583$

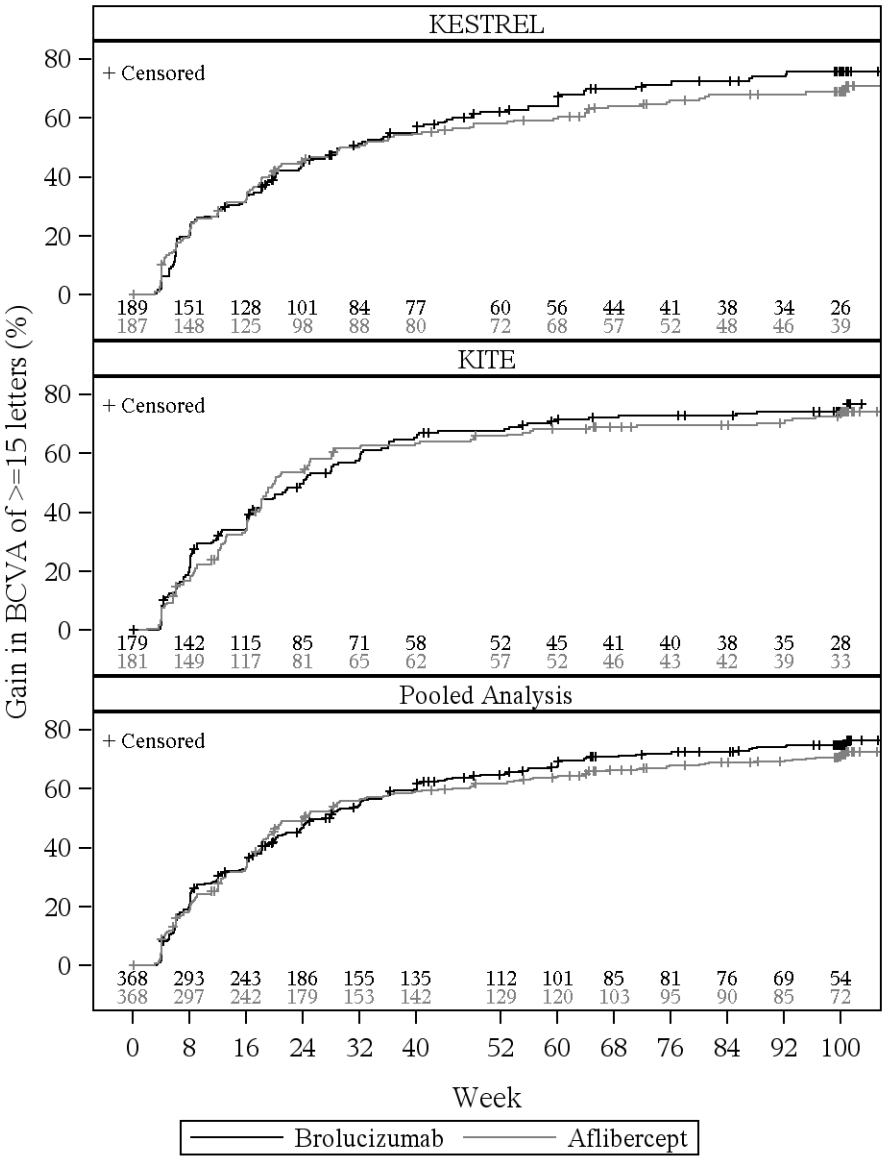
Figure 6.3.1 BCVA - Gain of 10 respectively 15 letters (FAS), Kaplan-Meier plot, week 100

Figure 6.3.1.1 BCVA - Gain of 10 respectively 15 letters (FAS), Kaplan-Meier plot, week 100, gain of >=10 letters



Plots include patients under risk.

Figure 6.3.1.2 BCVA - Gain of 10 respectively 15 letters (FAS), Kaplan-Meier plot, week 100, gain of >=15 letters

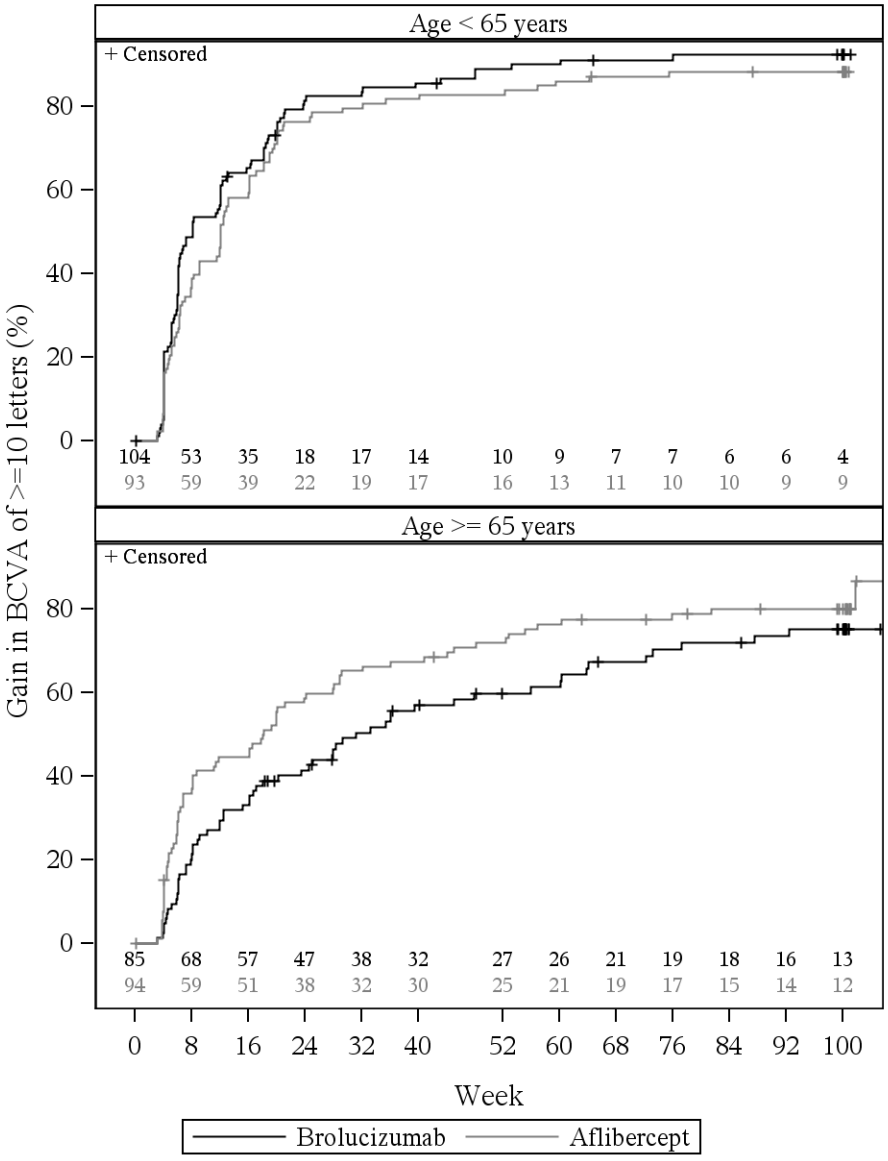


Plots include patients under risk.

Figure 6.3.2 BCVA - Gain of 10 respectively 15 letters by age (FAS), Kaplan-Meier plot, week 100

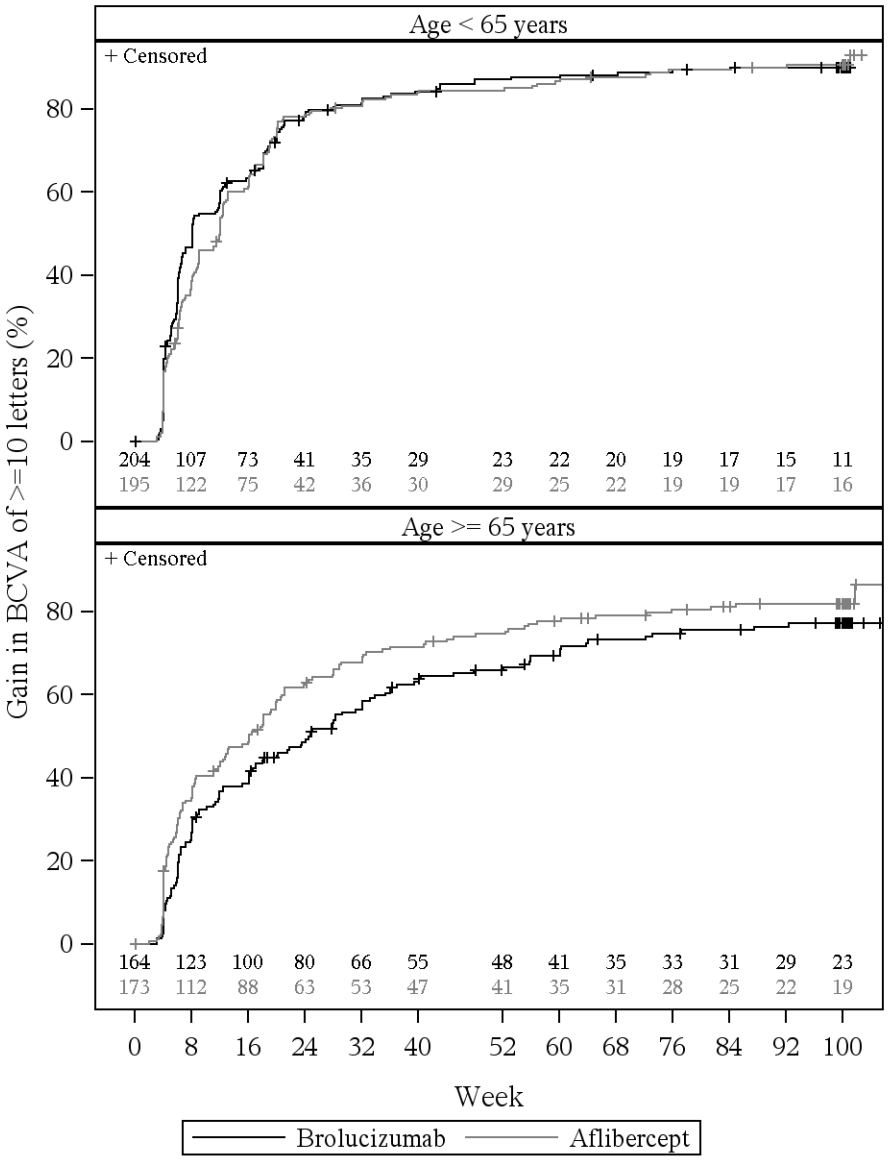
Figure 6.3.2.1 BCVA - Gain of 10 respectively 15 letters by age (FAS), Kaplan-Meier plot, week 100, gain of >=10 letters

Figure 6.3.2.1.1 BCVA - Gain of 10 respectively 15 letters by age (FAS), Kaplan-Meier plot, week 100, gain of >=10 letters for Kestrel



Plots include patients under risk.

Figure 6.3.2.1.3 BCVA - Gain of 10 respectively 15 letters by age (FAS), Kaplan-Meier plot, week 100, gain of >=10 letters for Pooled Analysis

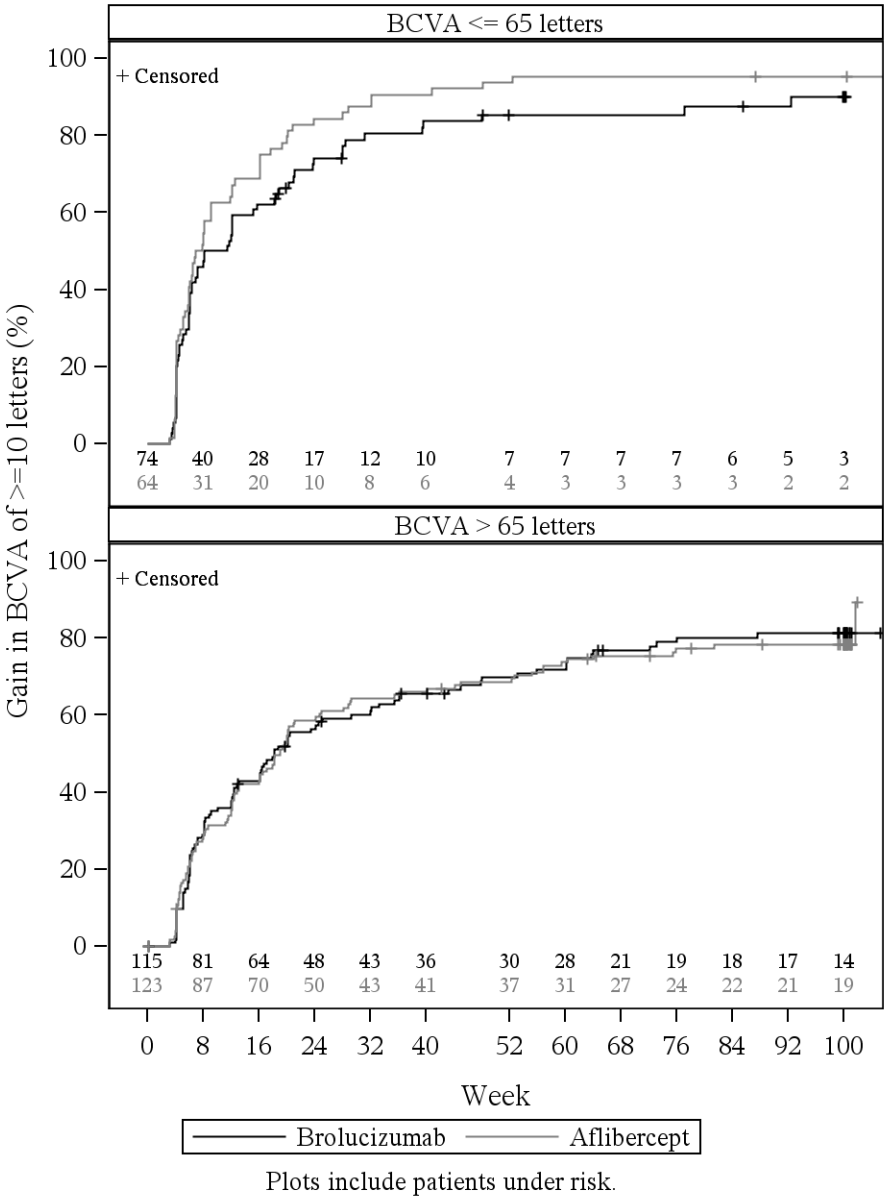


Plots include patients under risk.

Figure 6.3.4 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), Kaplan-Meier plot, week 100

Figure 6.3.4.1 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), Kaplan-Meier plot, week 100, gain of >=10 letters

Figure 6.3.4.1.1 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), Kaplan-Meier plot, week 100, gain of >=10 letters for Kestrel



Plots include patients under risk.

Figure 6.3.4.2 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), Kaplan-Meier plot, week 100, gain of >=15 letters

Figure 6.3.4.2.1 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), Kaplan-Meier plot, week 100, gain of >=15 letters for Kestrel

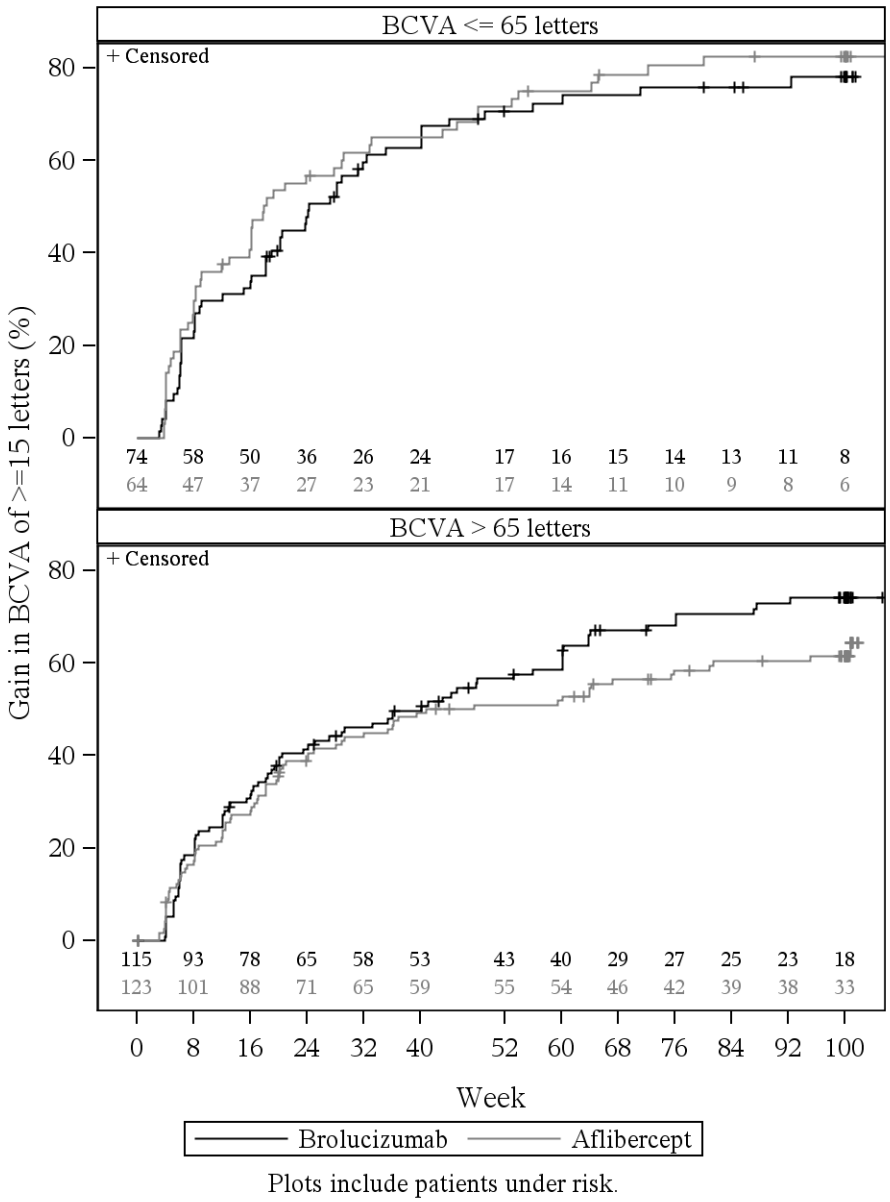
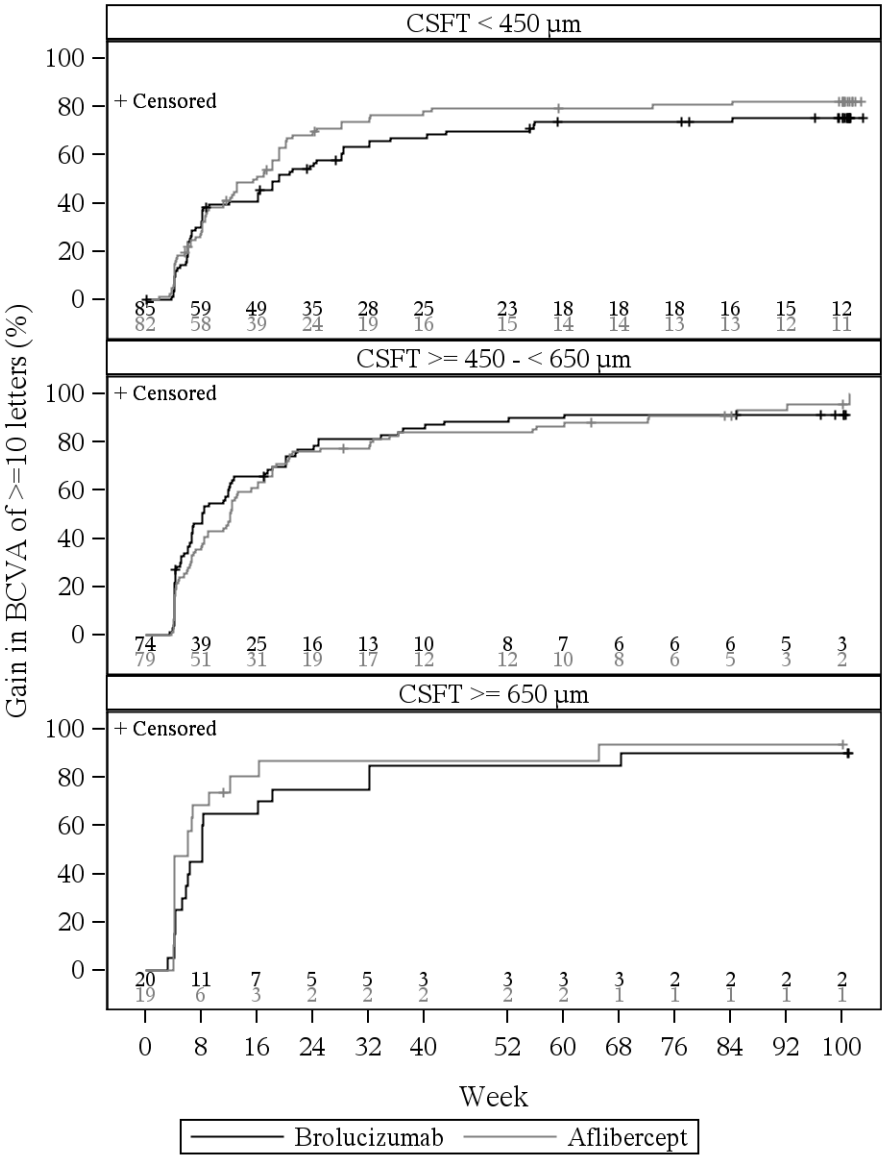


Figure 6.3.10 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), Kaplan-Meier plot, week 100

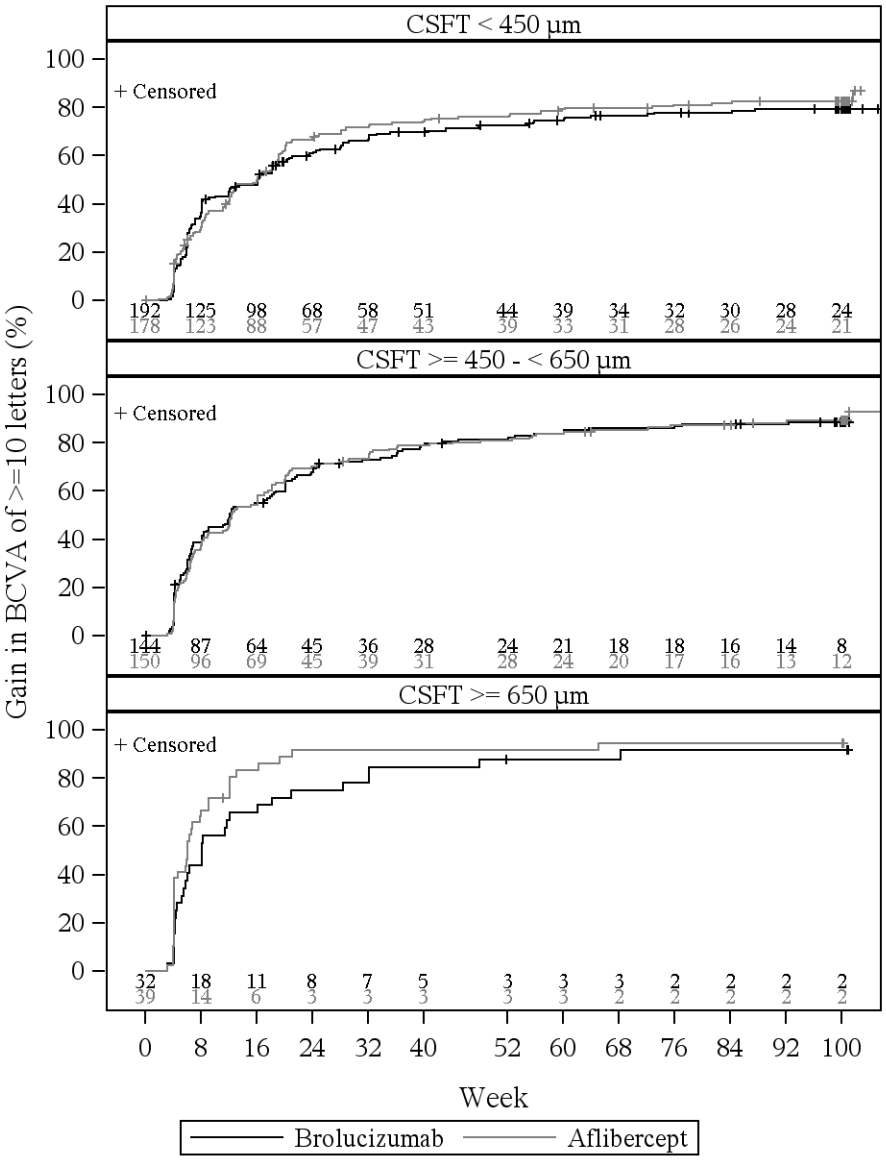
Figure 6.3.10.1 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), Kaplan-Meier plot, week 100, gain of >=10 letters

Figure 6.3.10.1.2 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), Kaplan-Meier plot, week 100, gain of >=10 letters for Kite



Plots include patients under risk.

Figure 6.3.10.1.3 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), Kaplan-Meier plot, week 100, gain of >=10 letters for Pooled Analysis



Plots include patients under risk.

Figure 6.3.10.2 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), Kaplan-Meier plot, week 100, gain of >=15 letters

Figure 6.3.10.2.1 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), Kaplan-Meier plot, week 100, gain of >=15 letters for Kestrel

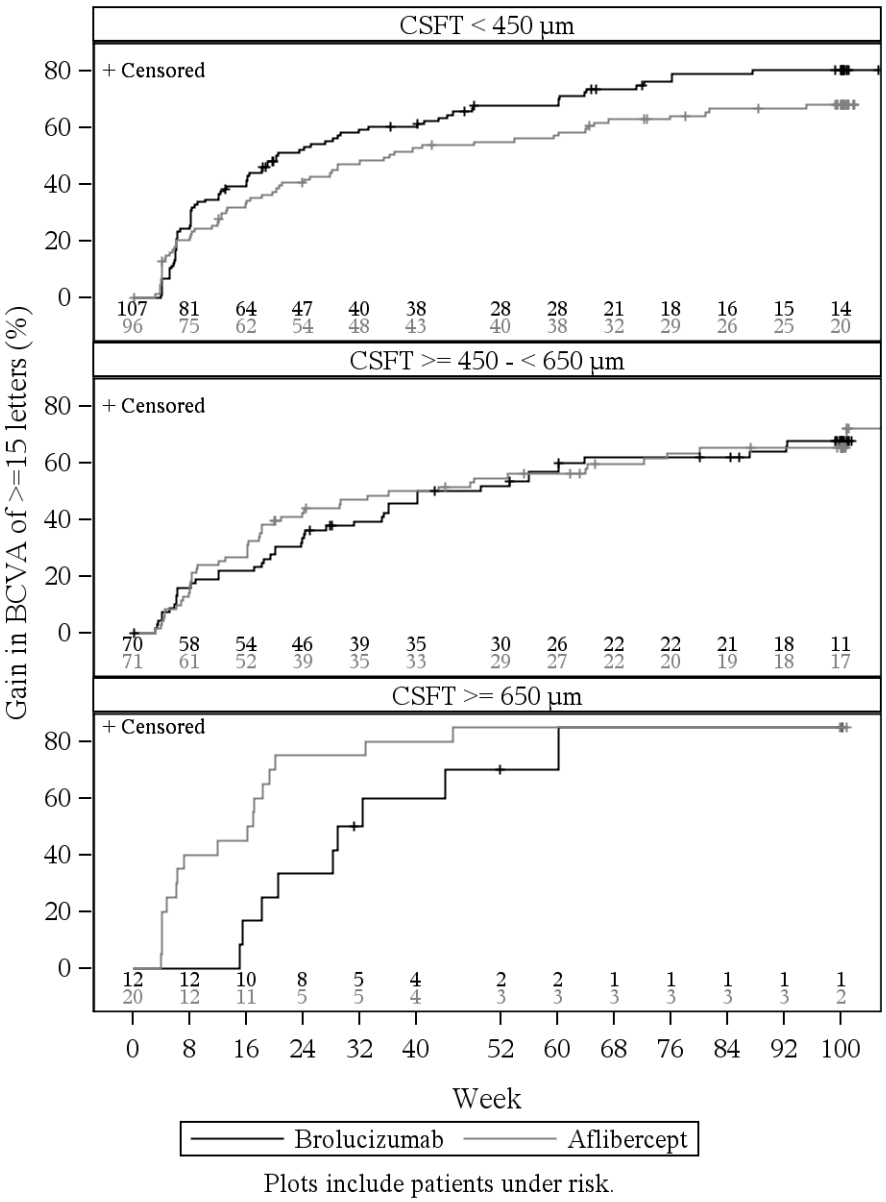
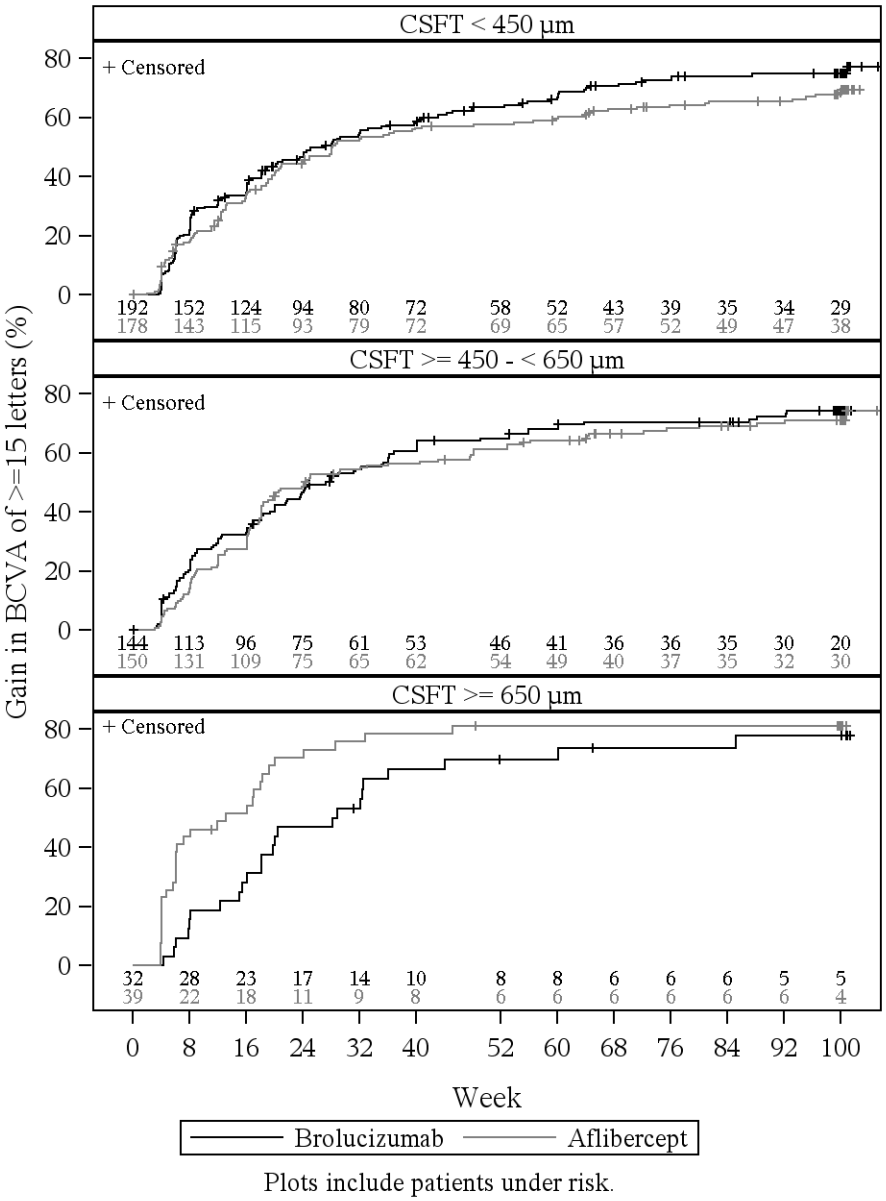


Figure 6.3.10.2.3 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), Kaplan-Meier plot, week 100, gain of >=15 letters for Pooled Analysis

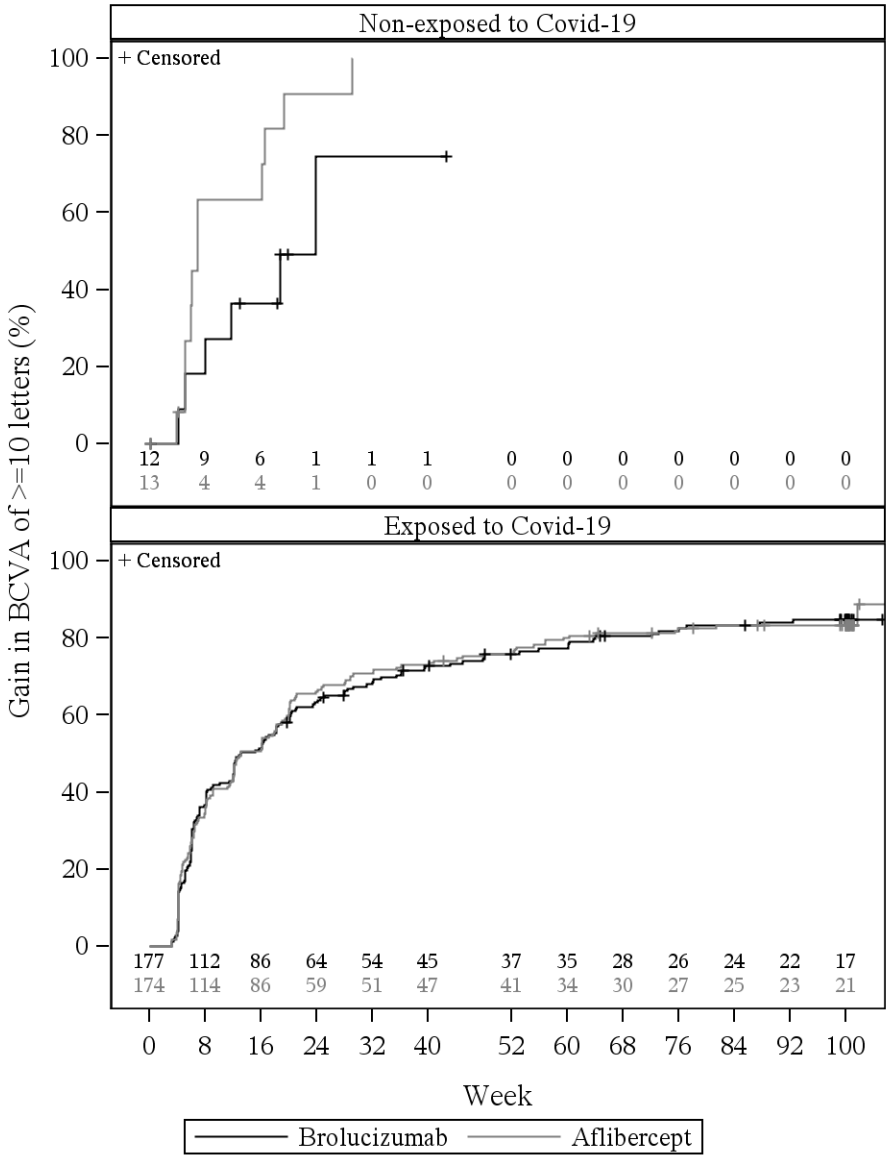


Plots include patients under risk.

Figure 6.3.13 BCVA - Gain of 10 respectively 15 letters by exposure (week 100) (FAS), Kaplan-Meier plot, week 100

Figure 6.3.13.1 BCVA - Gain of 10 respectively 15 letters by exposure (week 100) (FAS), Kaplan-Meier plot, week 100, gain of >=10 letters

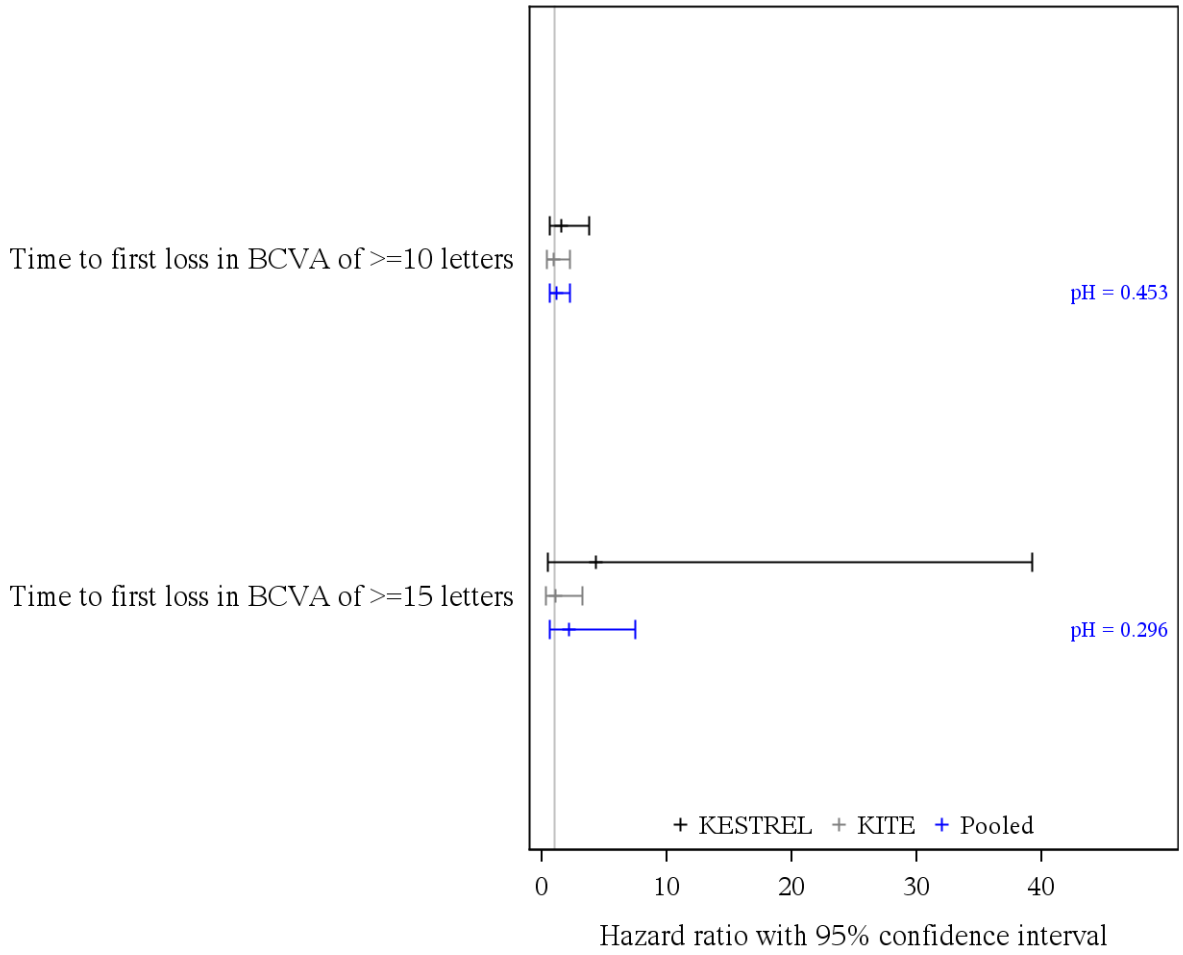
Figure 6.3.13.1.1 BCVA - Gain of 10 respectively 15 letters by exposure (week 100) (FAS), Kaplan-Meier plot, week 100, gain of >=10 letters for Kestrel



Plots include patients under risk.

7 BCVA: Time-to-event analysis (Loss)

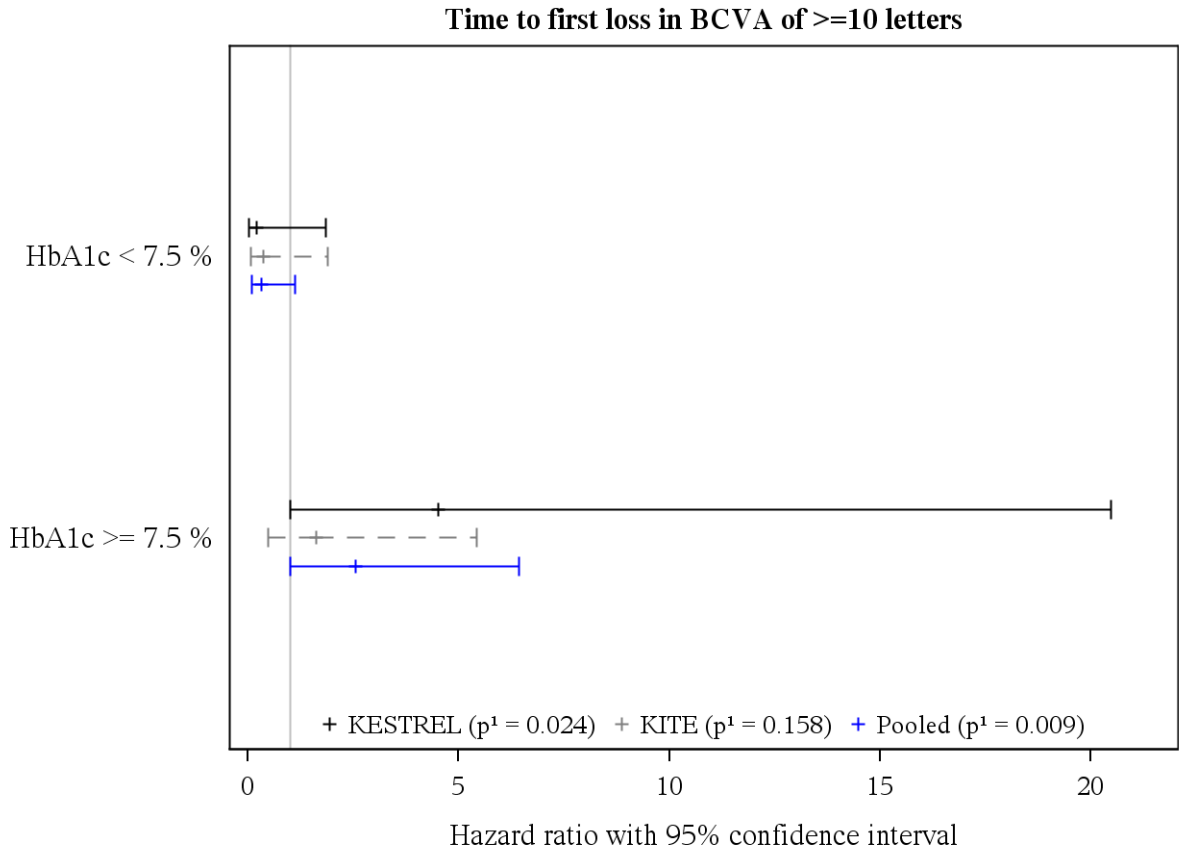
Figure 7.1.1 BCVA - Loss of 10 respectively 15 letters (FAS), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

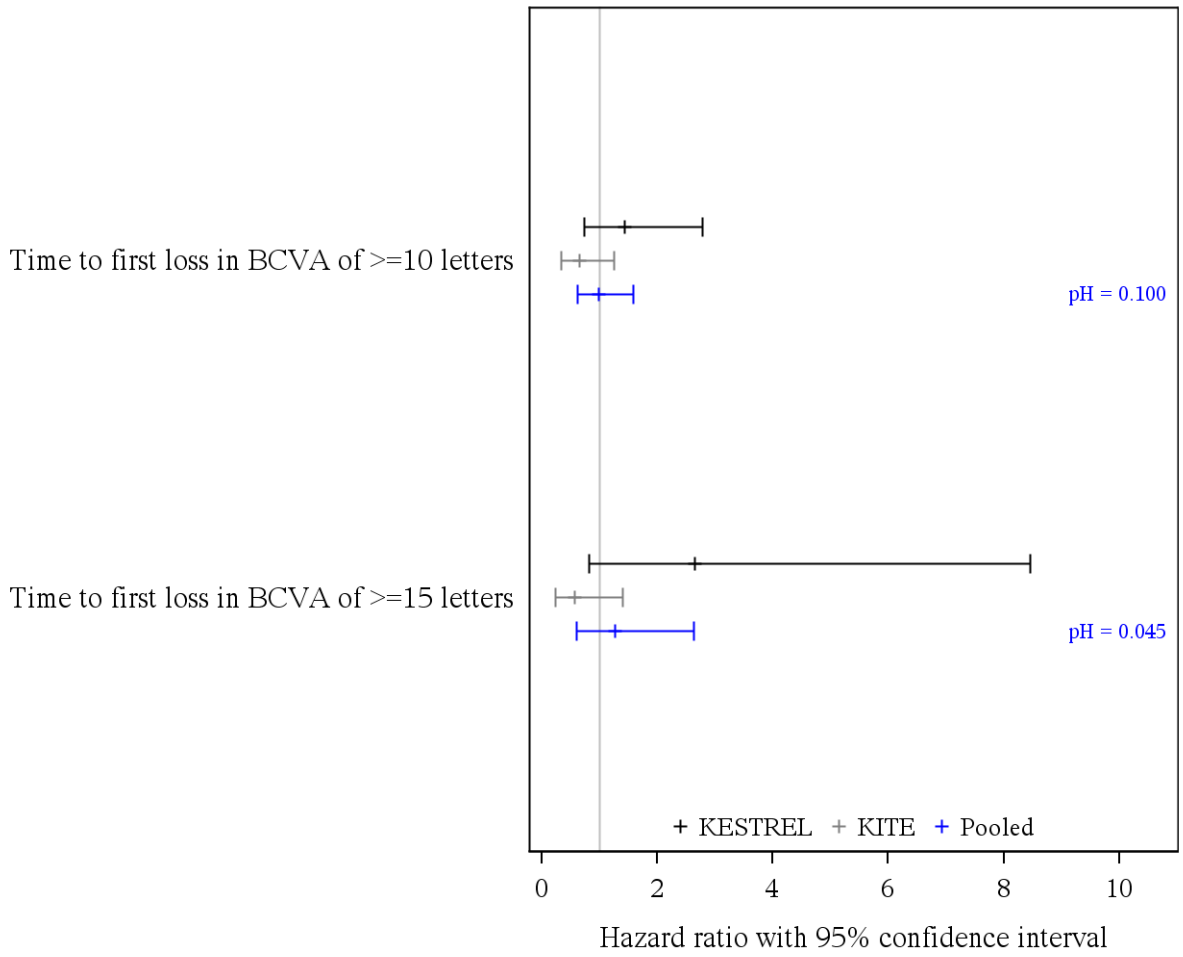
Figure 7.1.7 BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS), forest plot, week 52

Figure 7.1.7.1 BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS), forest plot, week 52, loss of >=10 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.453$

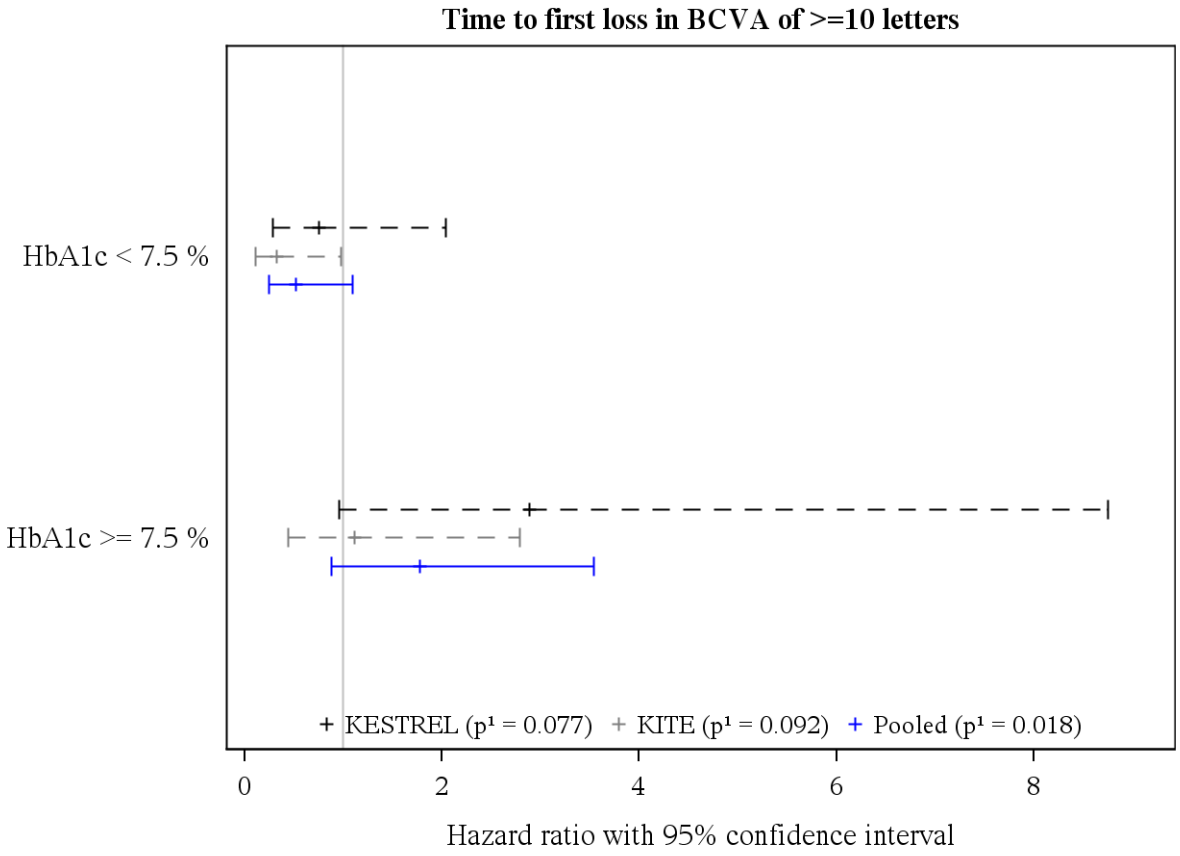
Figure 7.2.1 BCVA - Loss of 10 respectively 15 letters (FAS), forest plot, week 100



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 7.2.7 BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS), forest plot, week 100

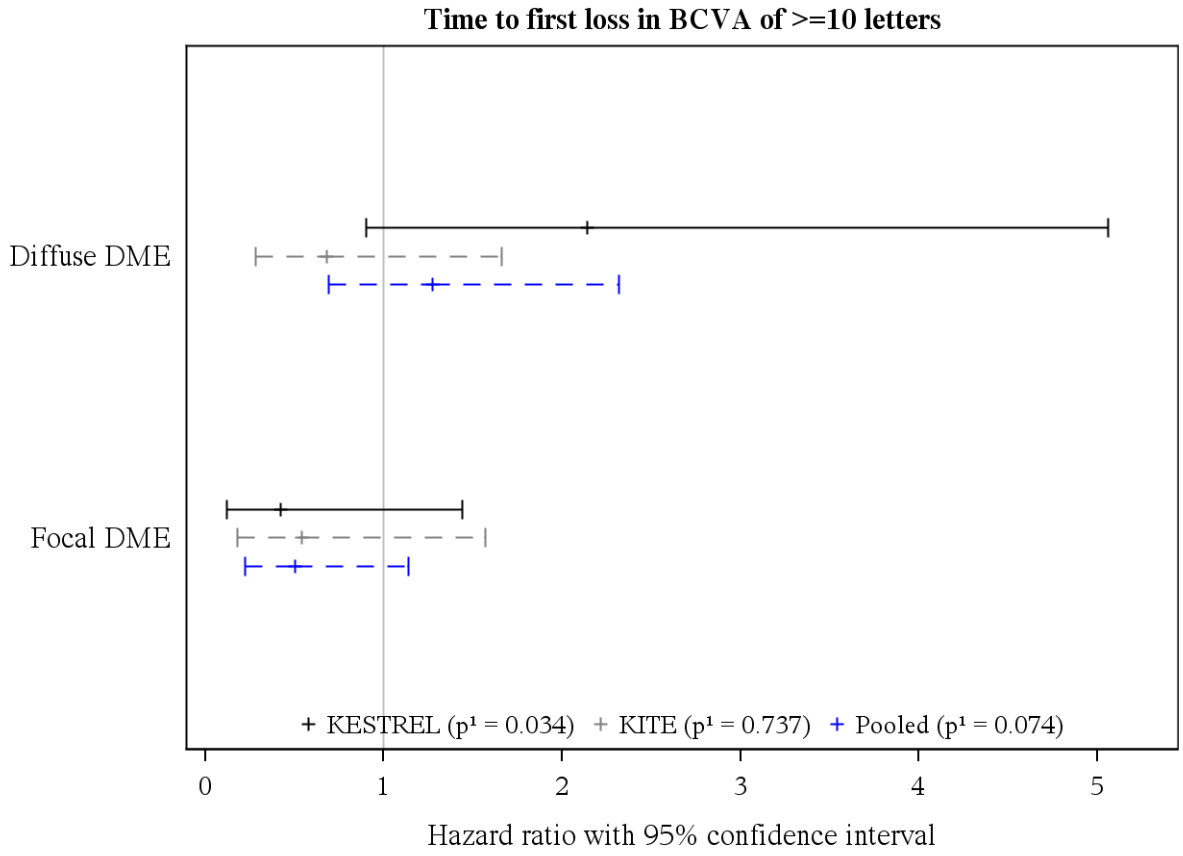
Figure 7.2.7.1 BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS), forest plot, week 100, loss of >=10 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.100$

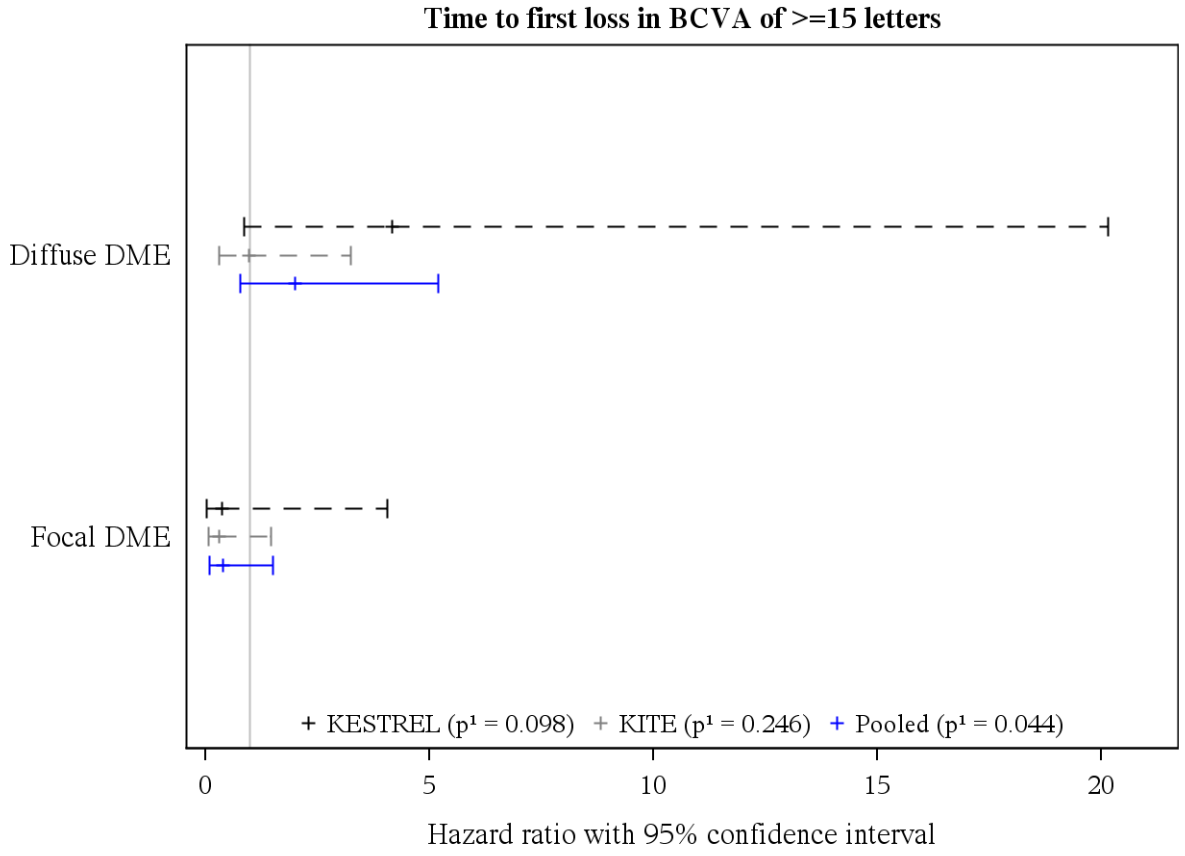
Figure 7.2.9 BCVA - Loss of 10 respectively 15 letters by DME type (FAS), forest plot, week 100

Figure 7.2.9.1 BCVA - Loss of 10 respectively 15 letters by DME type (FAS), forest plot, week 100, loss of >=10 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.100$

Figure 7.2.9.2 BCVA - Loss of 10 respectively 15 letters by DME type (FAS), forest plot, week 100, Time to first loss in BCVA of >=15 letters



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.045$

Figure 7.3.1 BCVA - Loss of 10 respectively 15 letters (FAS), Kaplan-Meier plot, week 100

Figure 7.3.1.1 BCVA - Loss of 10 respectively 15 letters (FAS), Kaplan-Meier plot, week 100, loss of >=10 letters

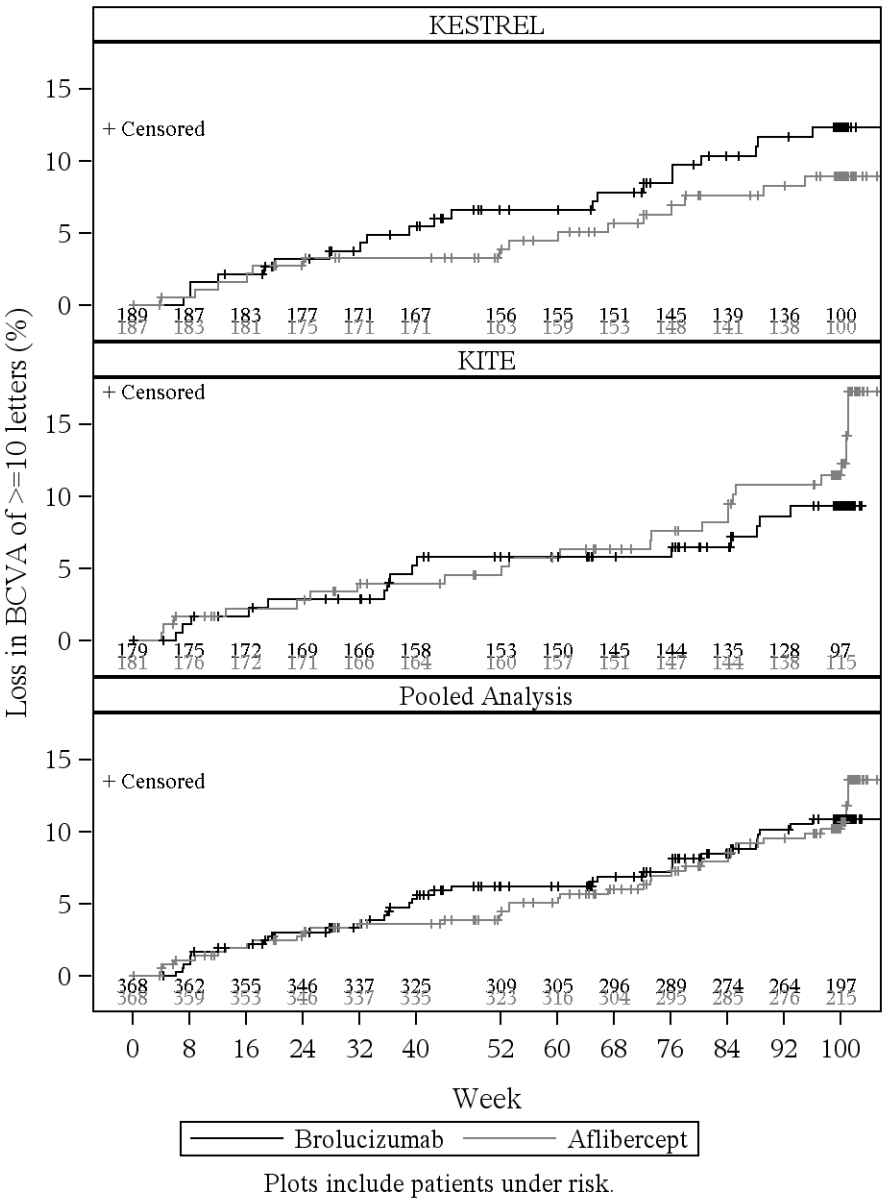
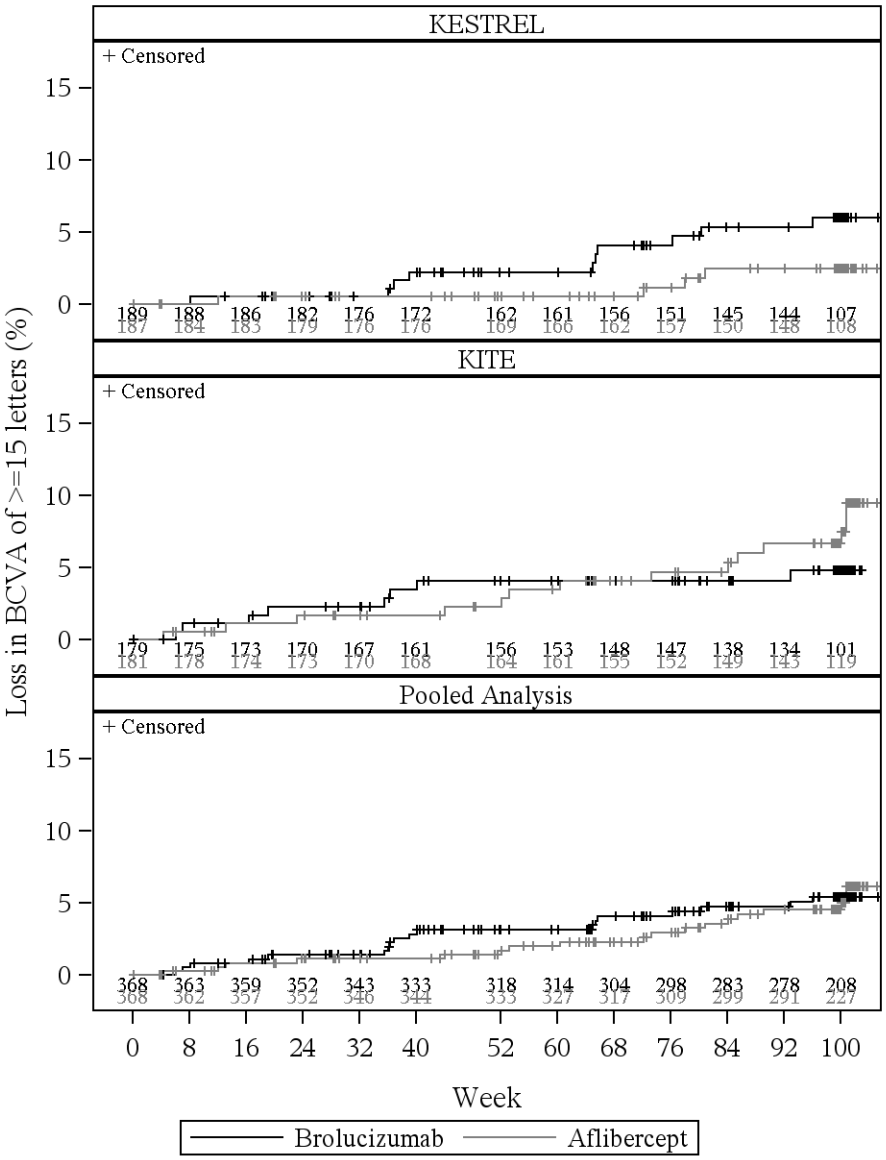


Figure 7.3.1.2 BCVA - Loss of 10 respectively 15 letters (FAS), Kaplan-Meier plot, week 100, loss of >=15 letters

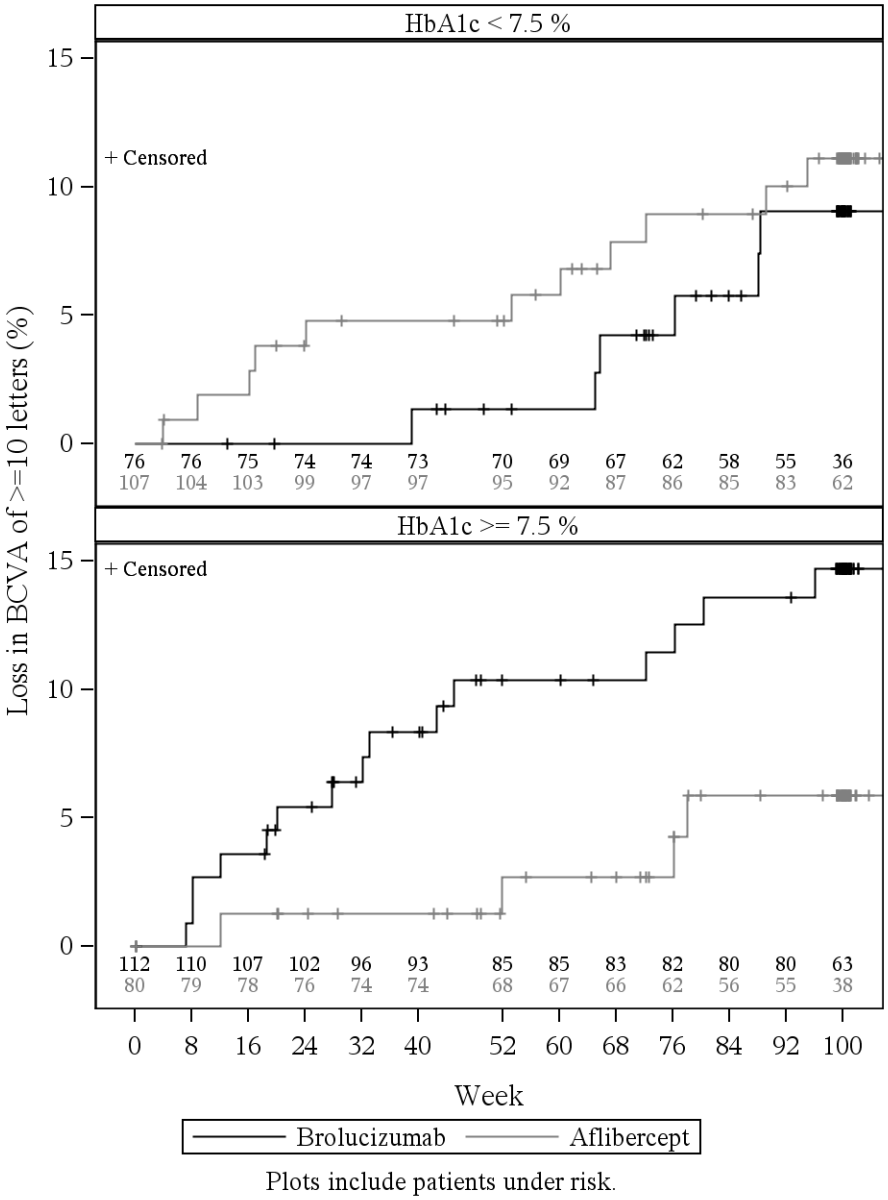


Plots include patients under risk.

Figure 7.3.7 BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS), Kaplan-Meier plot, week 100

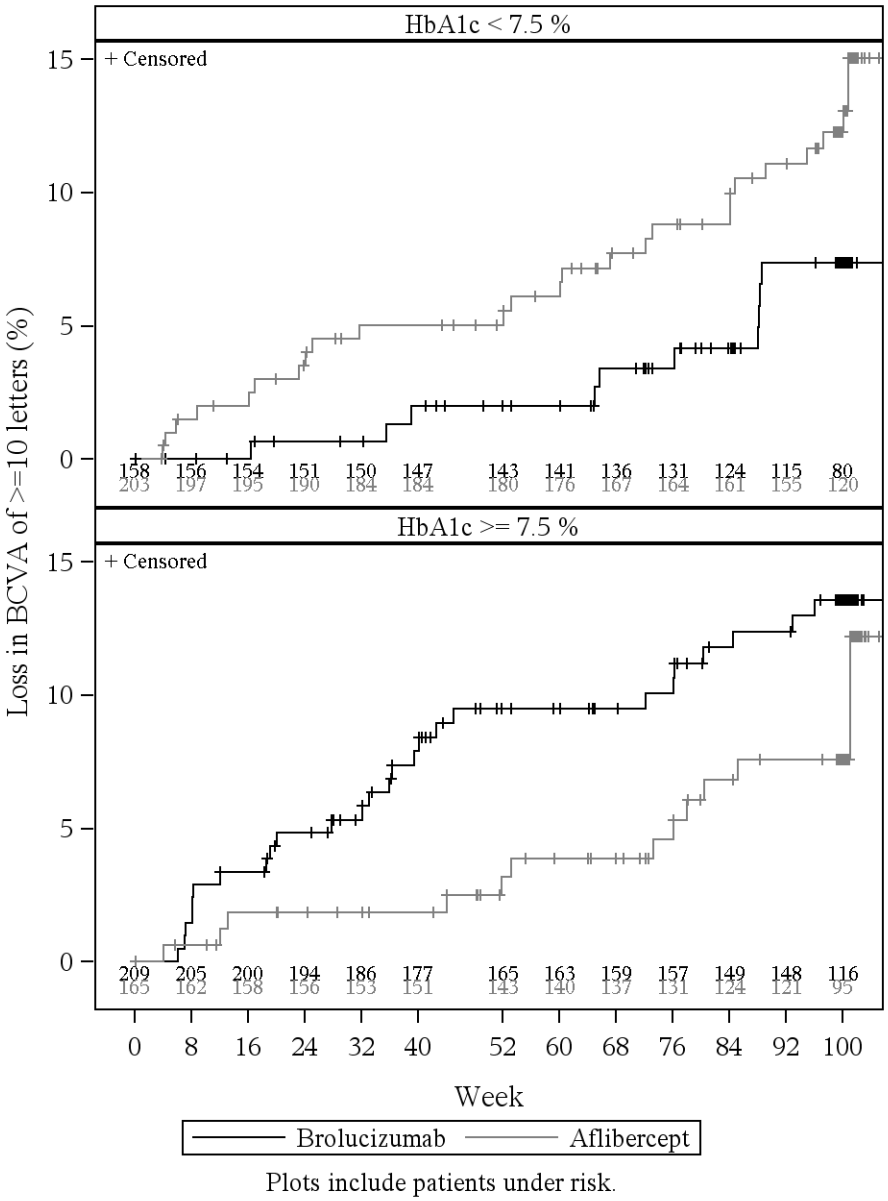
Figure 7.3.7.1 BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS), Kaplan-Meier plot, week 100, loss of >=10 letters

Figure 7.3.7.1.1 BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS), Kaplan-Meier plot, week 100, loss of >=10 letters for Kestrel



Plots include patients under risk.

Figure 7.3.7.1.3 BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS), Kaplan-Meier plot, week 100, loss of >=10 letters for Pooled Analysis

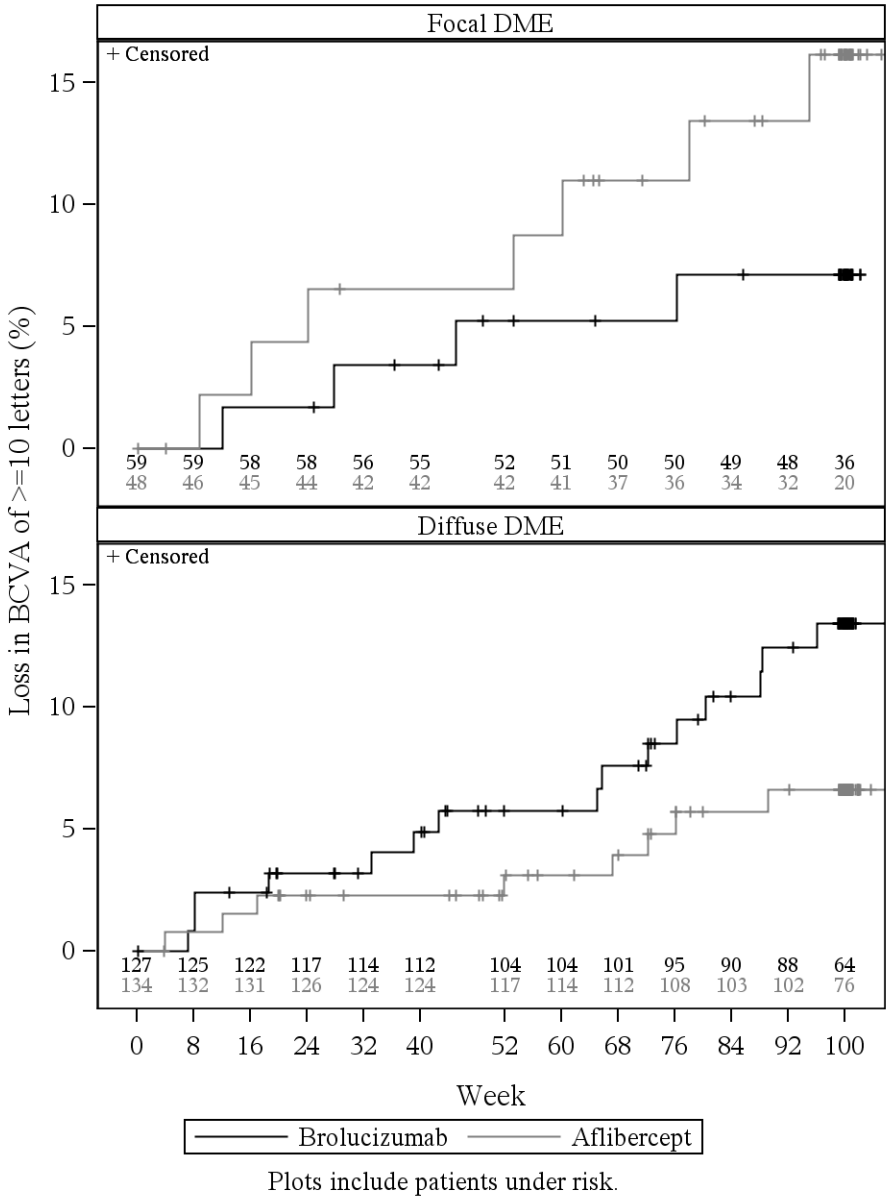


Plots include patients under risk.

Figure 7.3.9 BCVA - Loss of 10 respectively 15 letters by DME type (FAS), Kaplan-Meier plot, week 100

Figure 7.3.9.1 BCVA - Loss of 10 respectively 15 letters by DME type (FAS), Kaplan-Meier plot, week 100, loss of >=10 letters

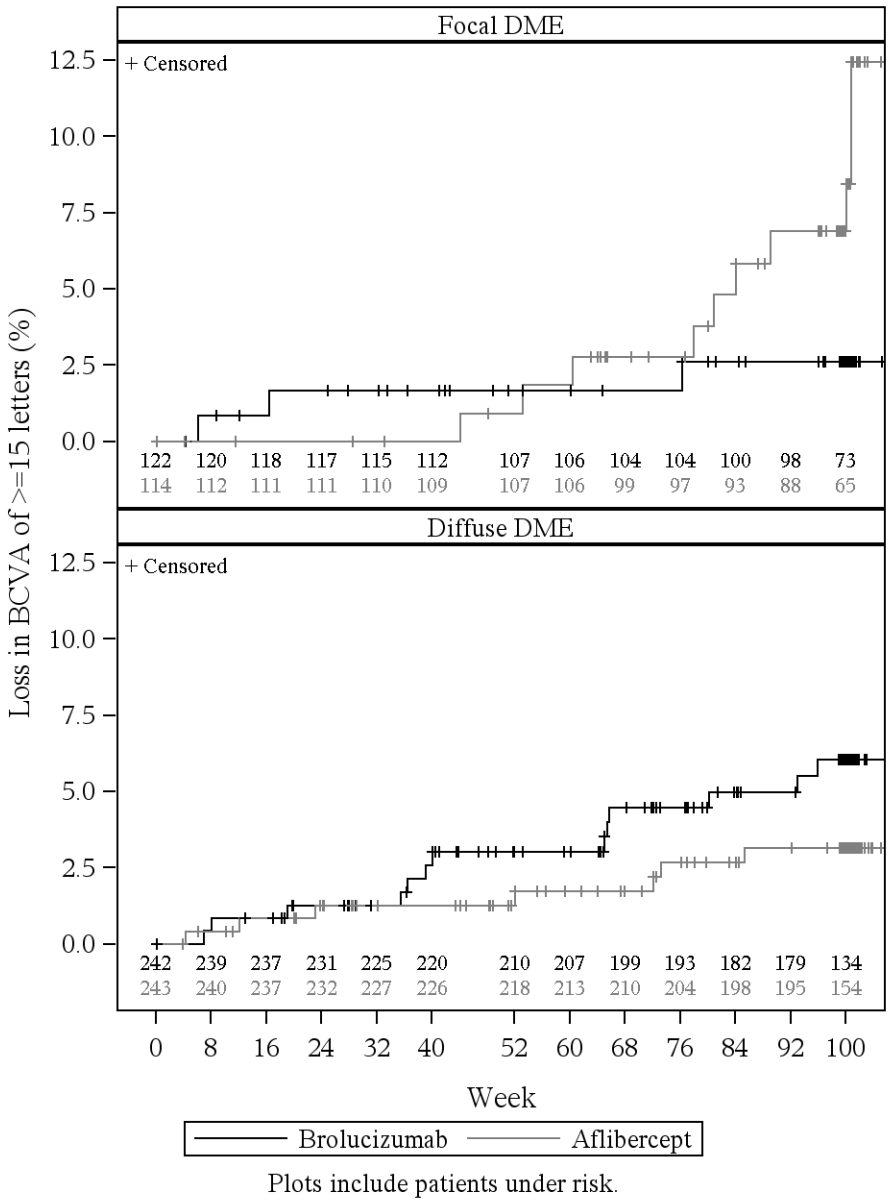
Figure 7.3.9.1.1 BCVA - Loss of 10 respectively 15 letters by DME type (FAS), Kaplan-Meier plot, week 100, loss of >=10 letters for Kestrel



Plots include patients under risk.

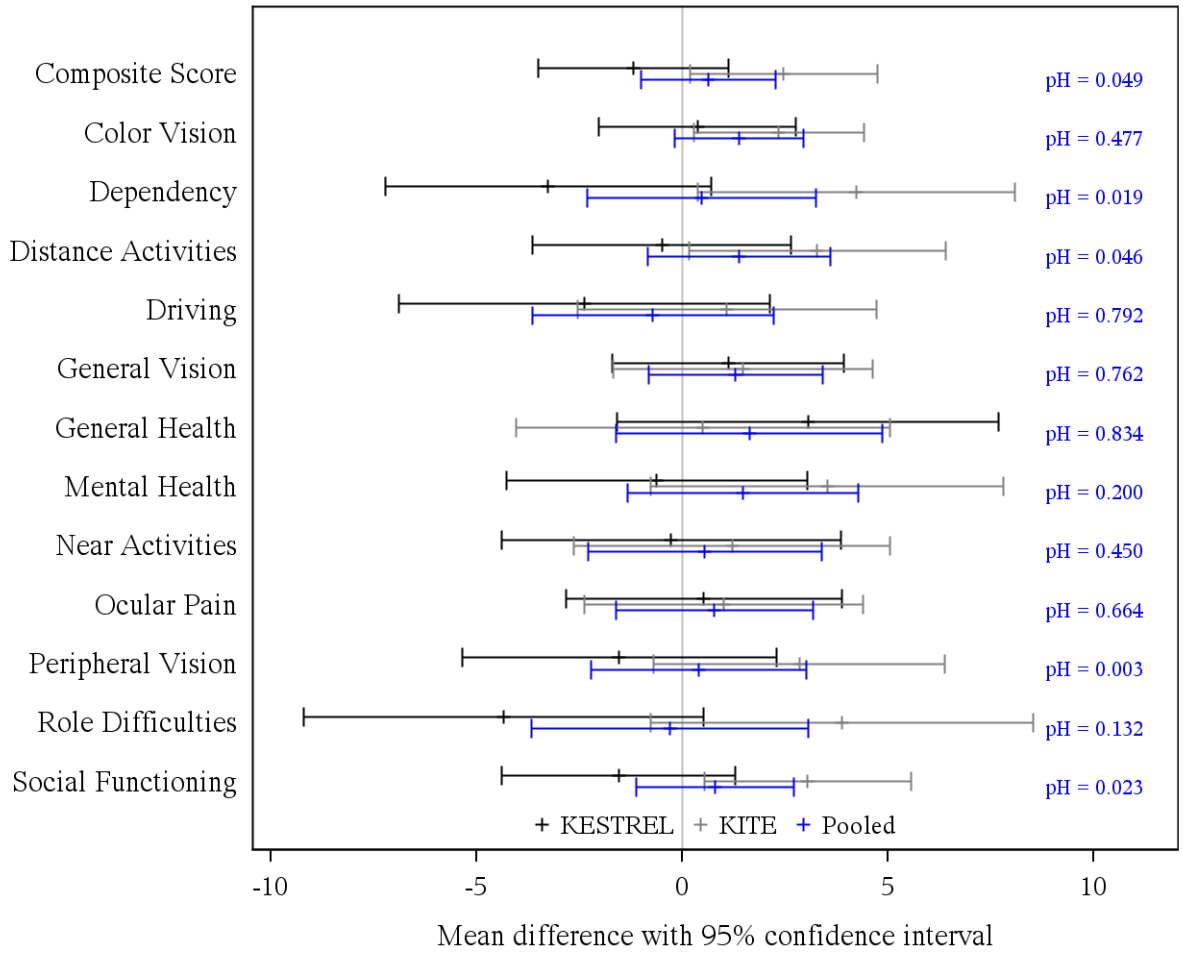
Figure 7.3.9.2 BCVA - Loss of 10 respectively 15 letters by DME type (FAS), Kaplan-Meier plot, week 100, loss of >=15 letters

Figure 7.3.9.2.3 BCVA - Loss of 10 respectively 15 letters by DME type (FAS), Kaplan-Meier plot, week 100, loss of >=15 letters for Pooled Analysis



8 VFQ: Continuous analysis

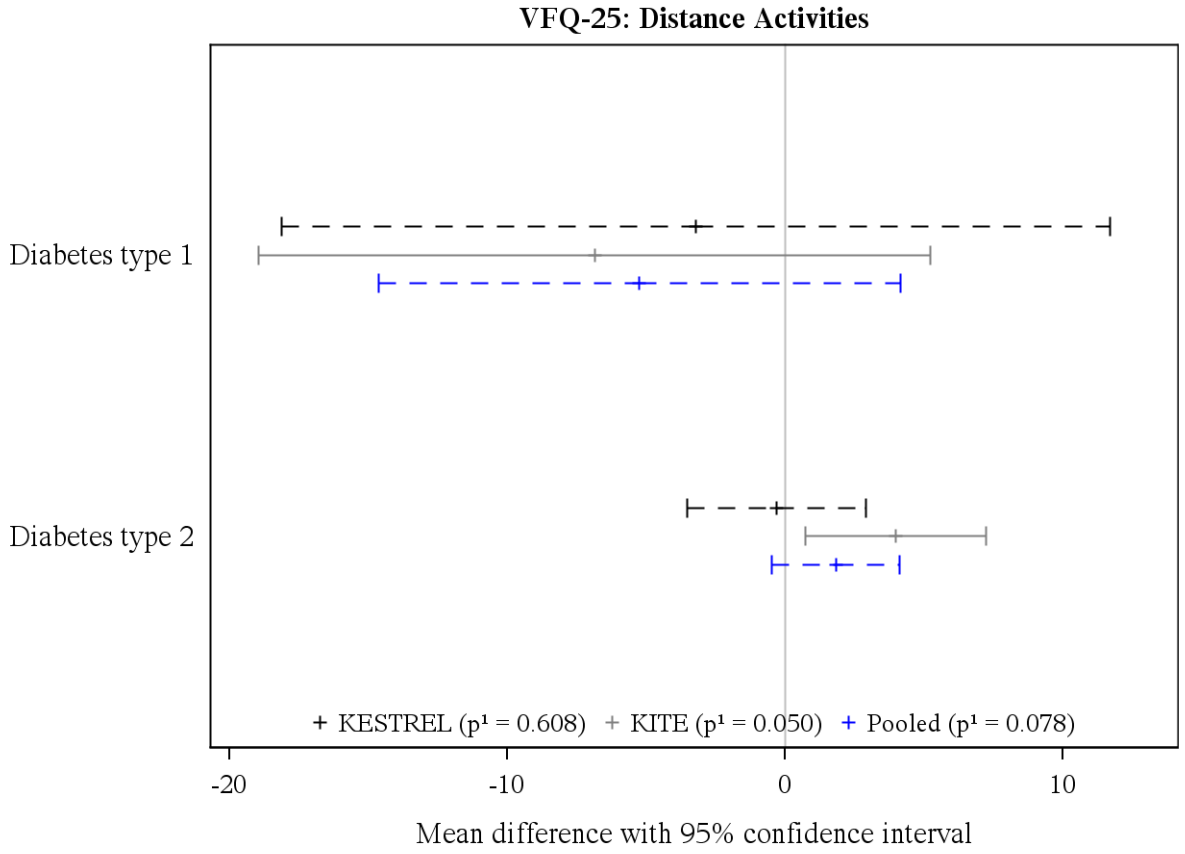
Figure 8.1.1 VFQ (FAS), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

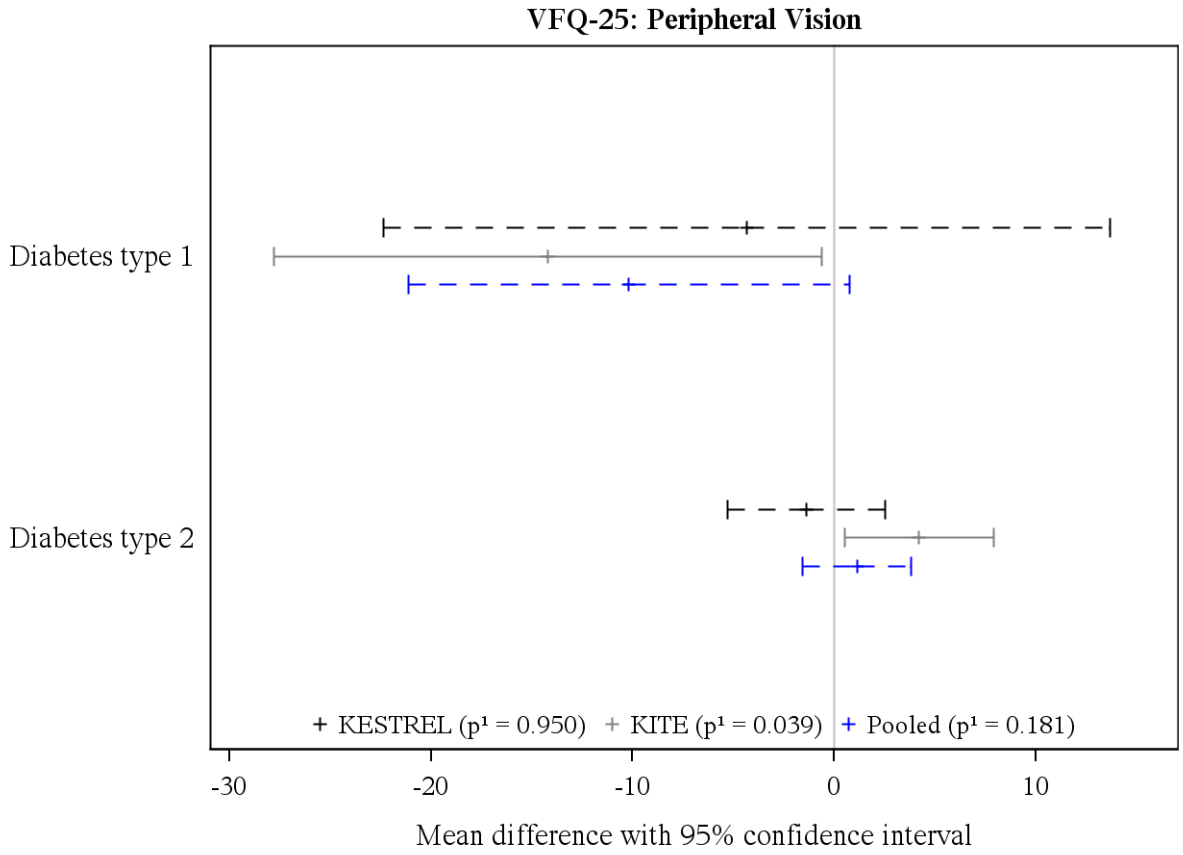
Figure 8.1.6 VFQ by diabetes type (FAS), forest plot, week 52

Figure 8.1.6.1 VFQ by diabetes type (FAS), forest plot, week 52, Distance Activities



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.046$

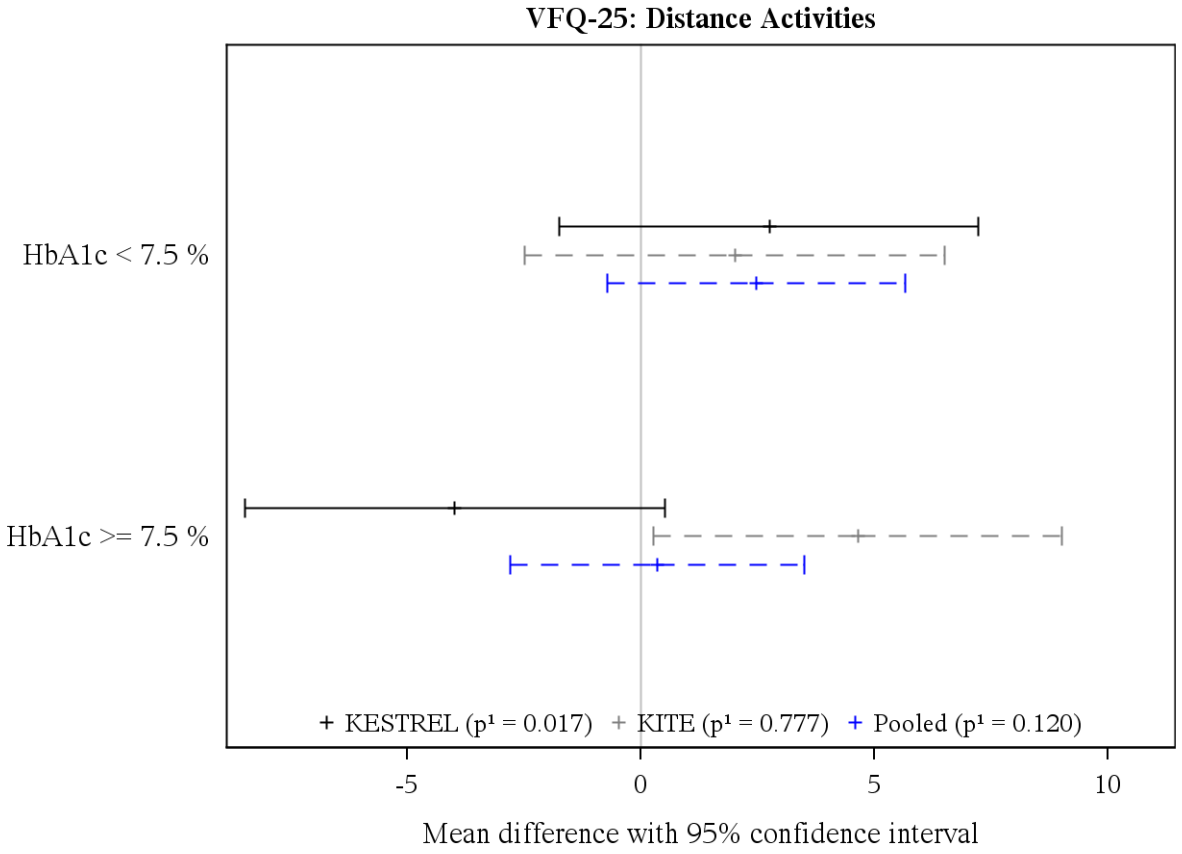
Figure 8.1.6.2 VFQ by diabetes type (FAS), forest plot, week 52, Peripheral Vision



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.003$

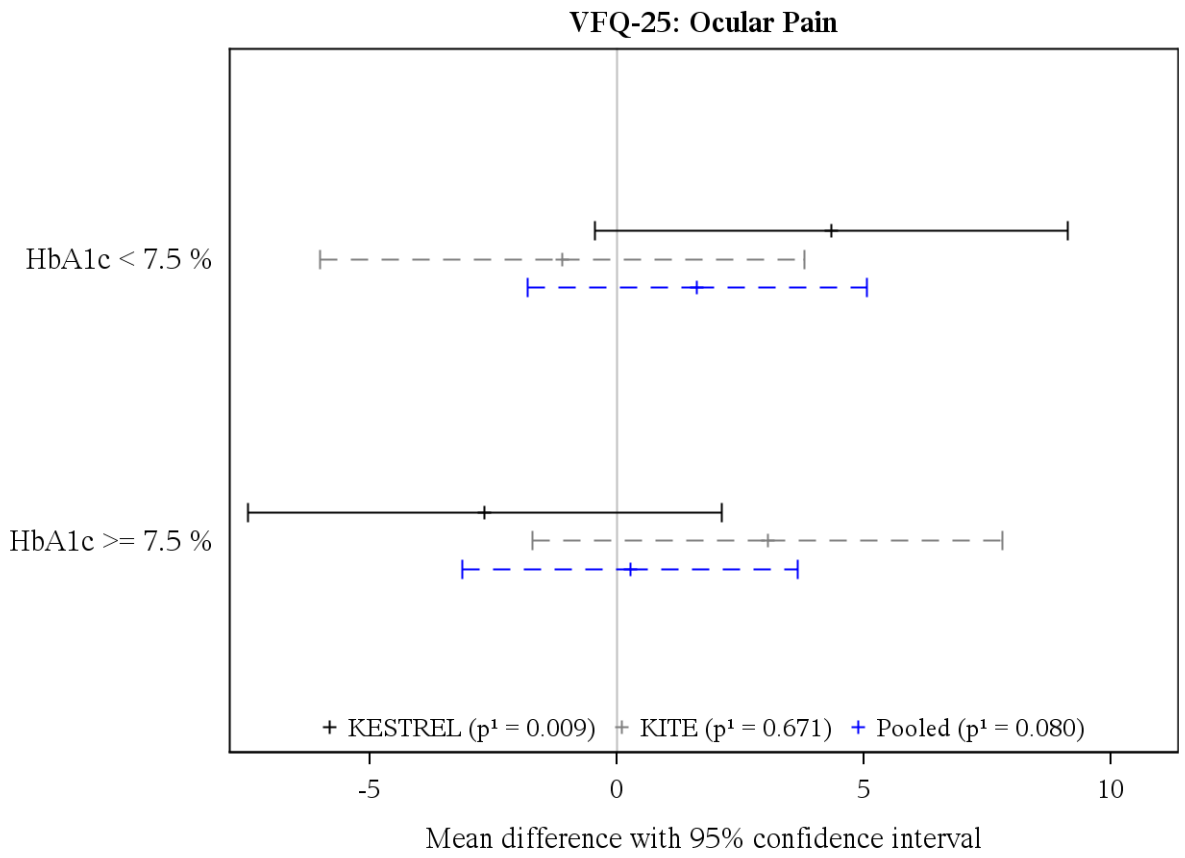
Figure 8.1.7 VFQ by HbA1c (FAS), forest plot, week 52

Figure 8.1.7.1 VFQ by HbA1c (FAS), forest plot, week 52, Distance Activities



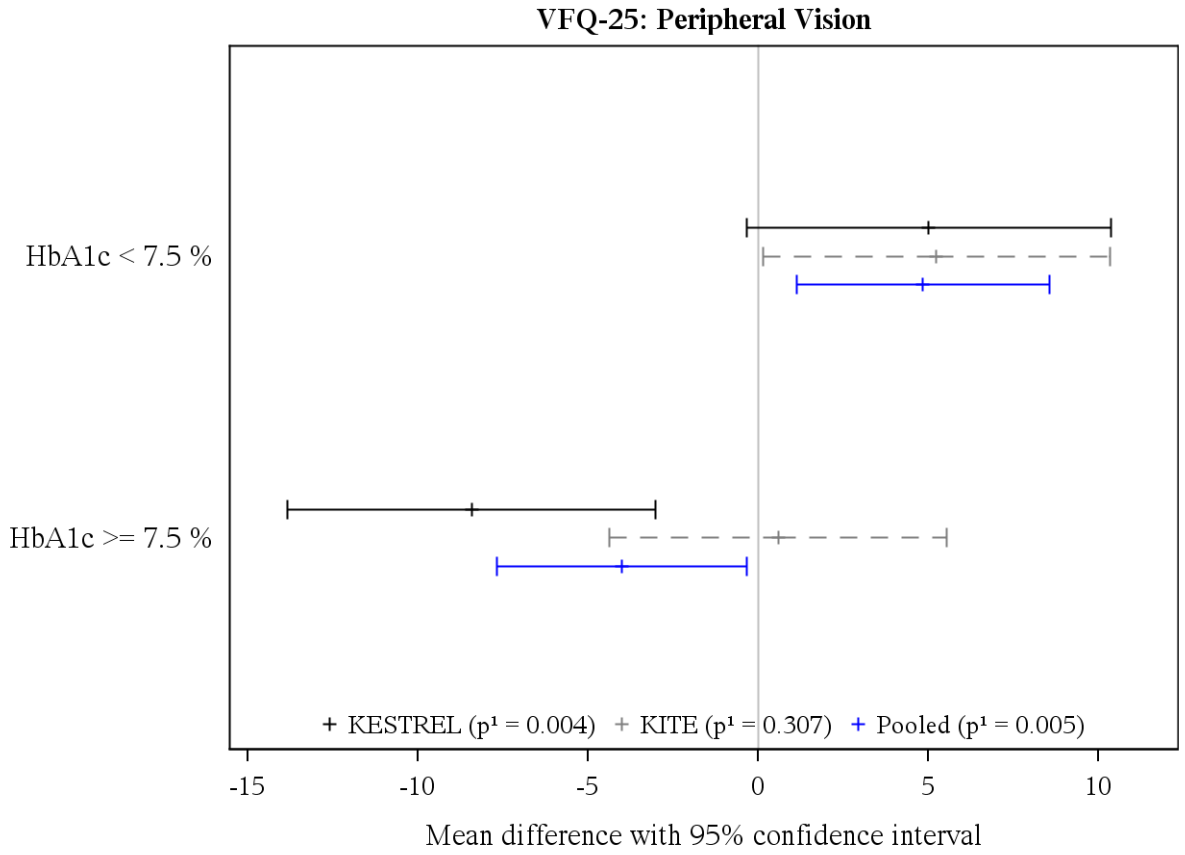
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.046$

Figure 8.1.7.2 VFQ by HbA1c (FAS), forest plot, week 52, Ocular Pain



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.664$

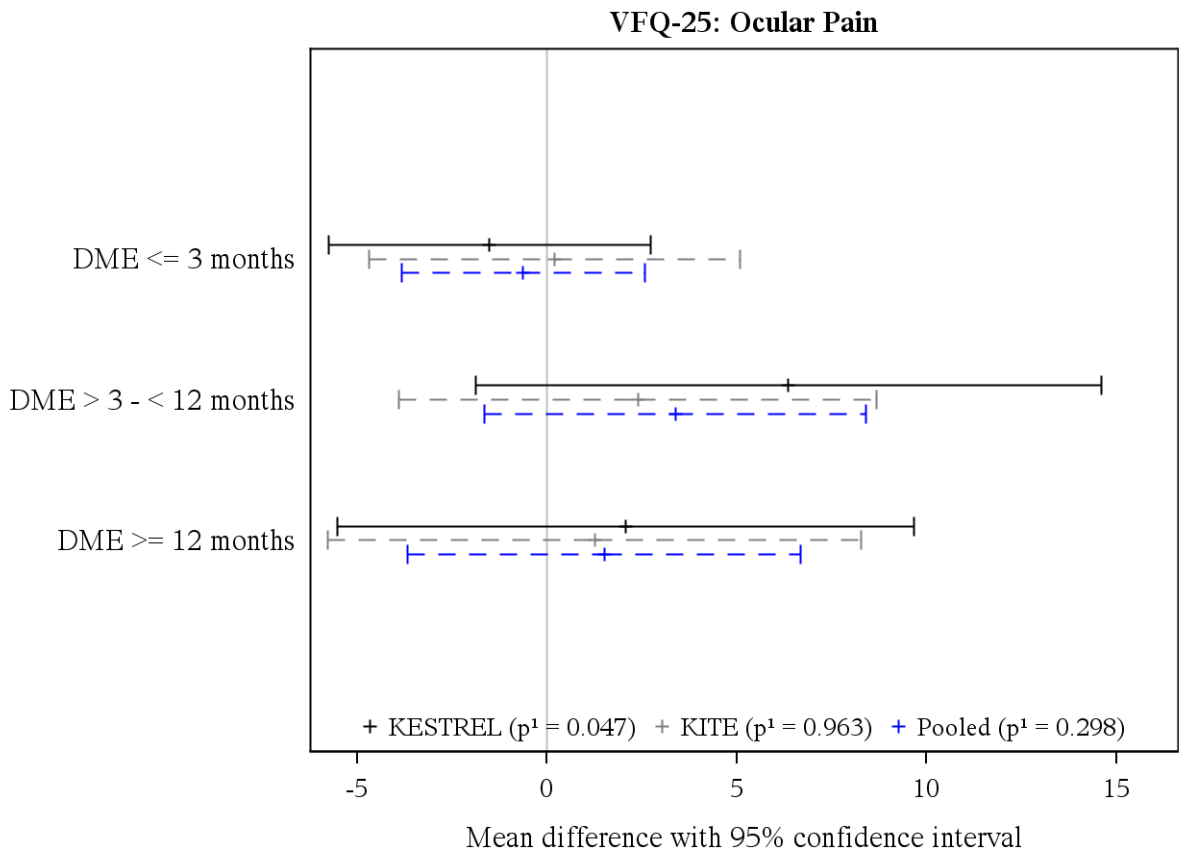
Figure 8.1.7.3 VFQ by HbA1c (FAS), forest plot, week 52, Peripheral Vision



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.003$

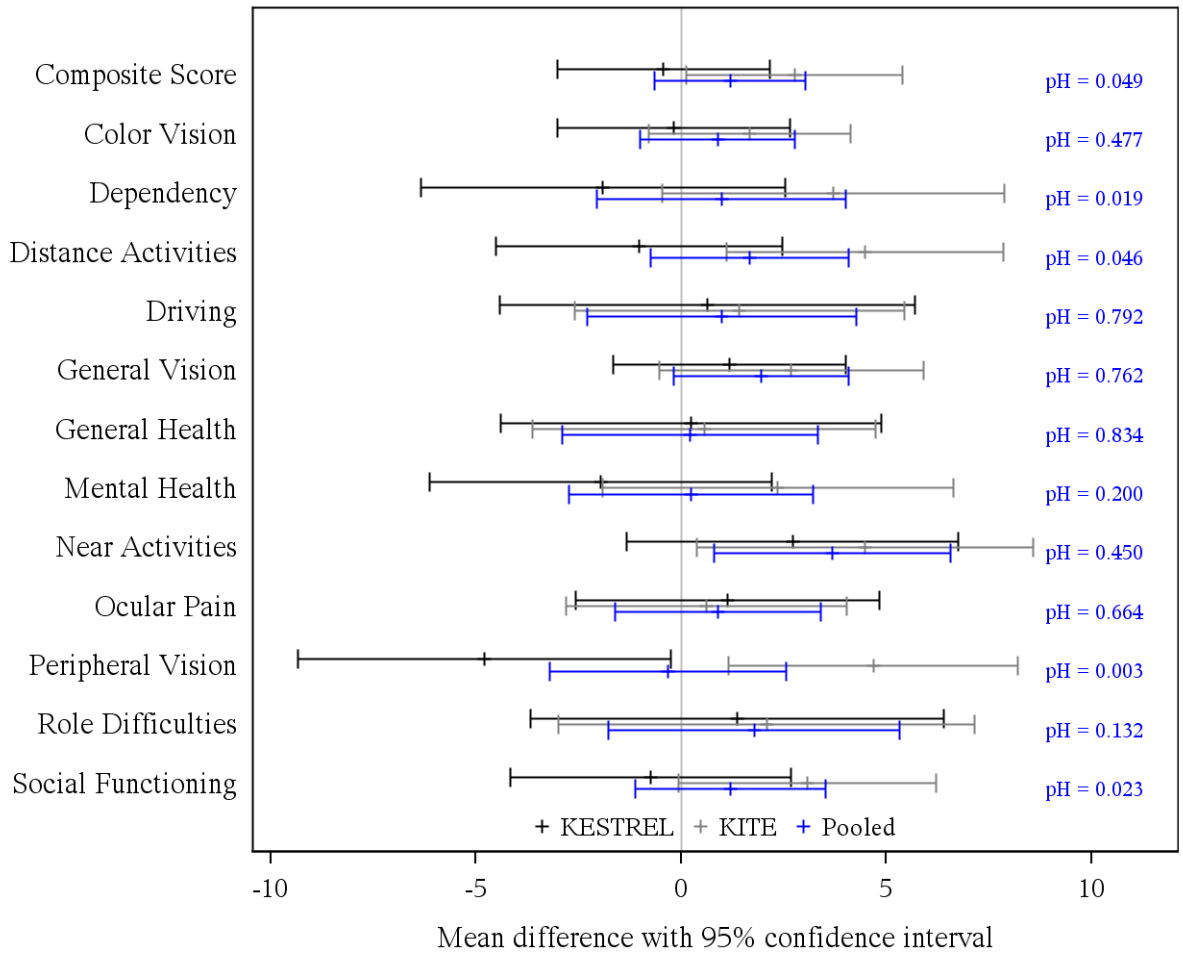
Figure 8.1.8 VFQ by duration of DME (FAS), forest plot, week 52

Figure 8.1.8.1 VFQ by duration of DME (FAS), forest plot, week 52, Ocular Pain



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.664$

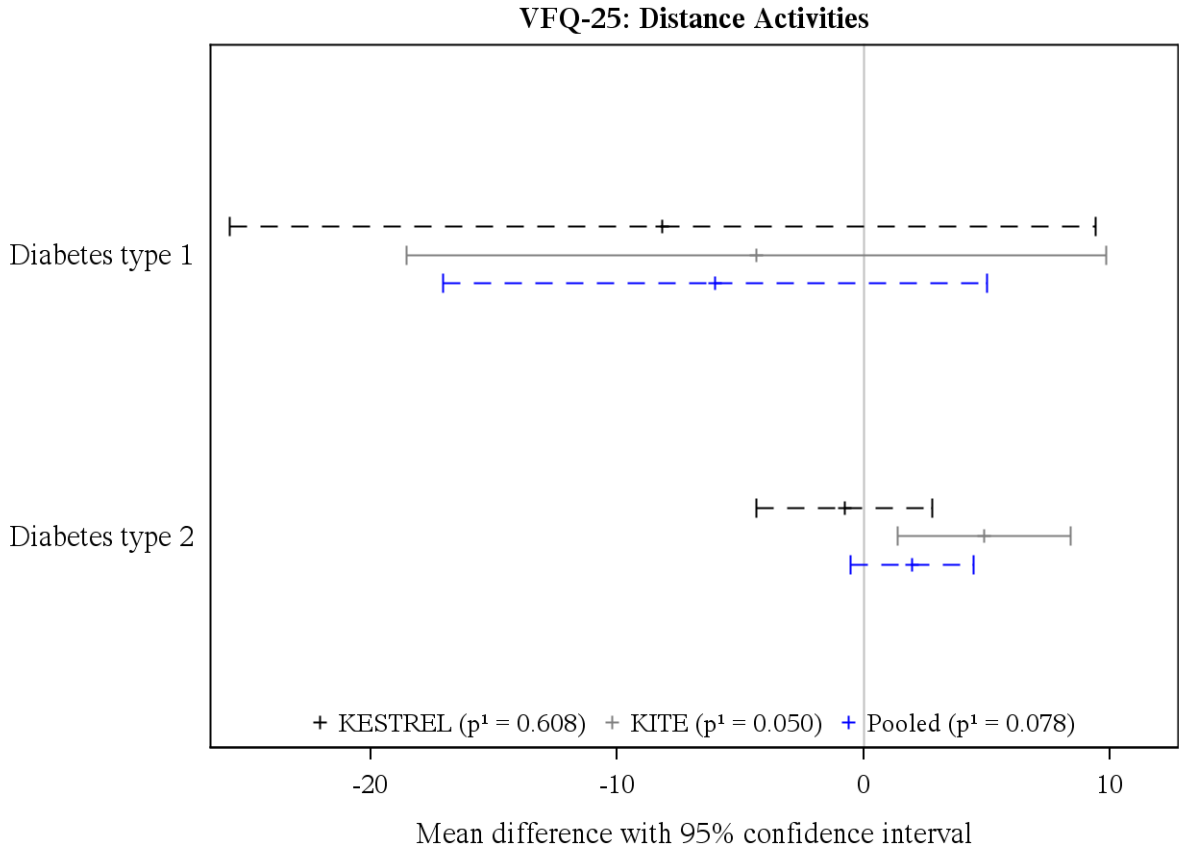
Figure 8.2.1 VFQ (FAS), forest plot, week 100



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

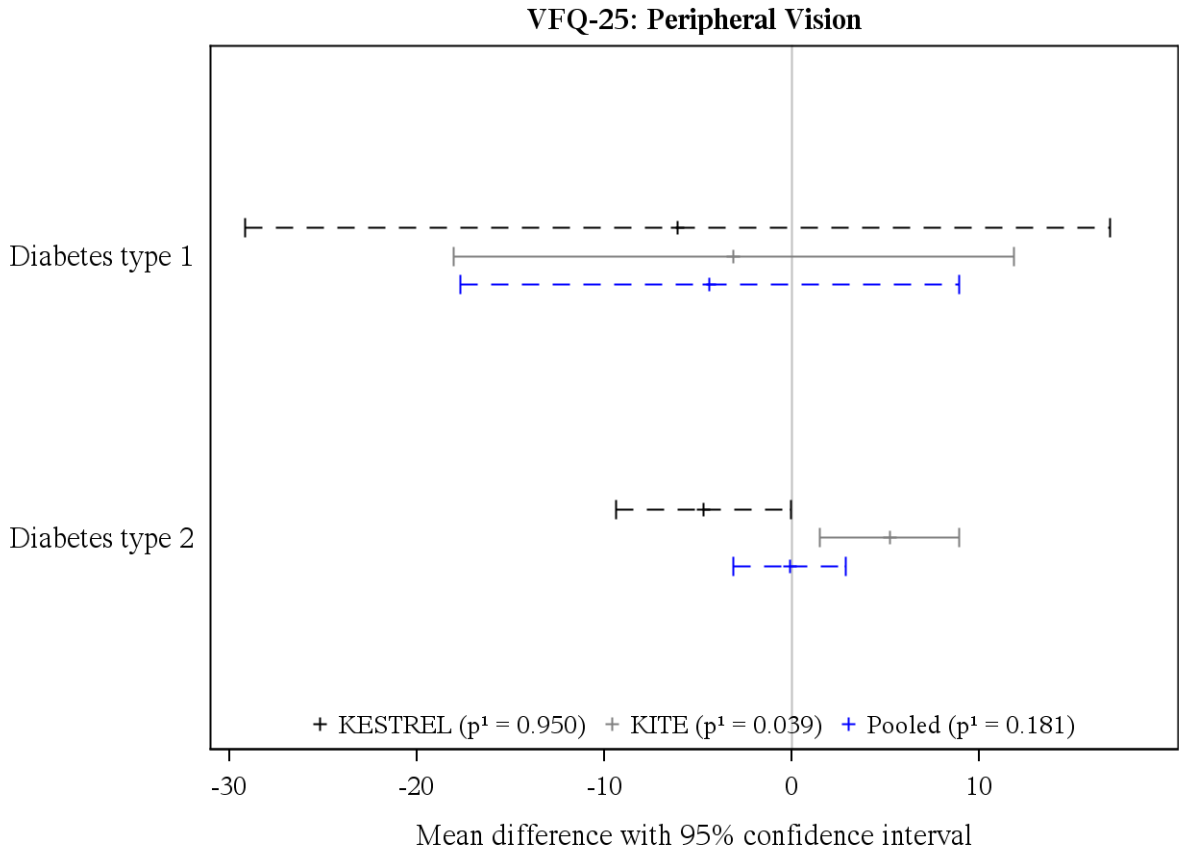
Figure 8.2.6 VFQ by diabetes type (FAS), forest plot, week 100

Figure 8.2.6.1 VFQ by diabetes type (FAS), forest plot, week 100, Distance Activities



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.046$

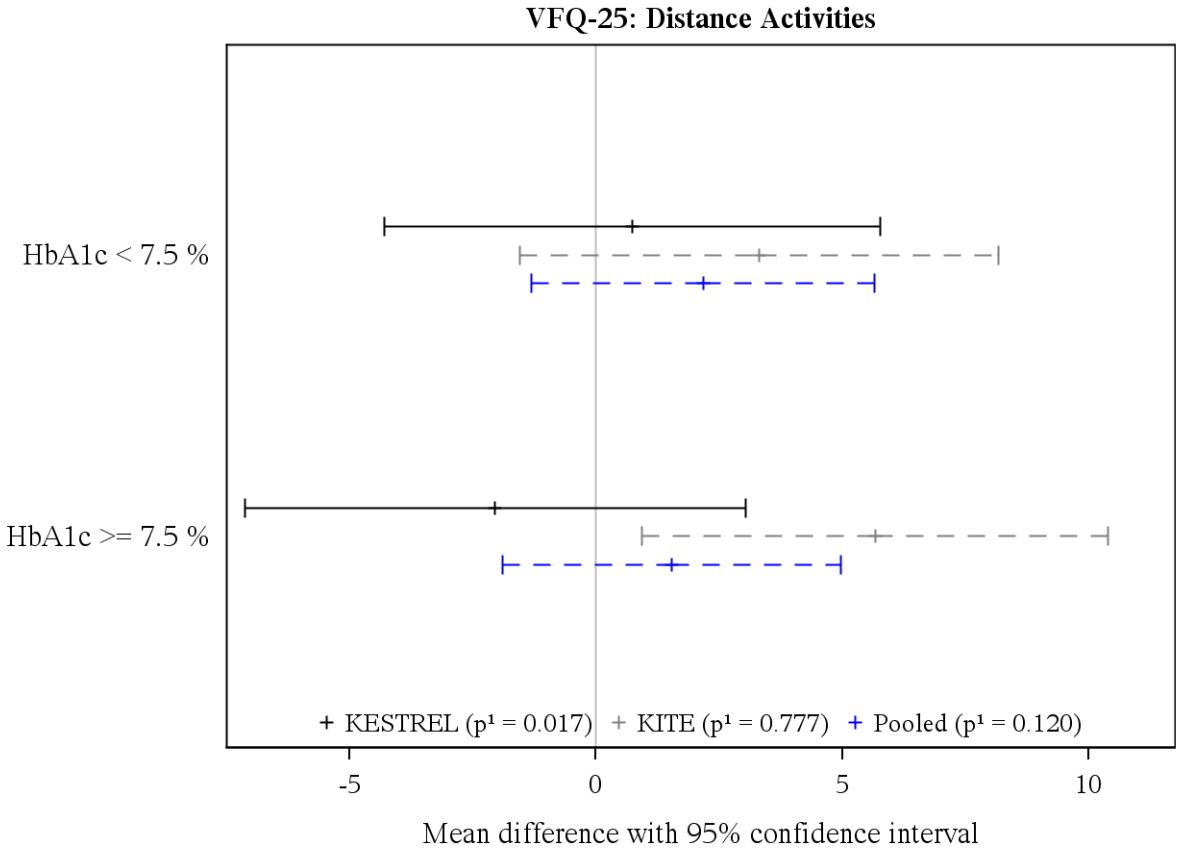
Figure 8.2.6.2 VFQ by diabetes type (FAS), forest plot, week 100, Peripheral Vision



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.003$

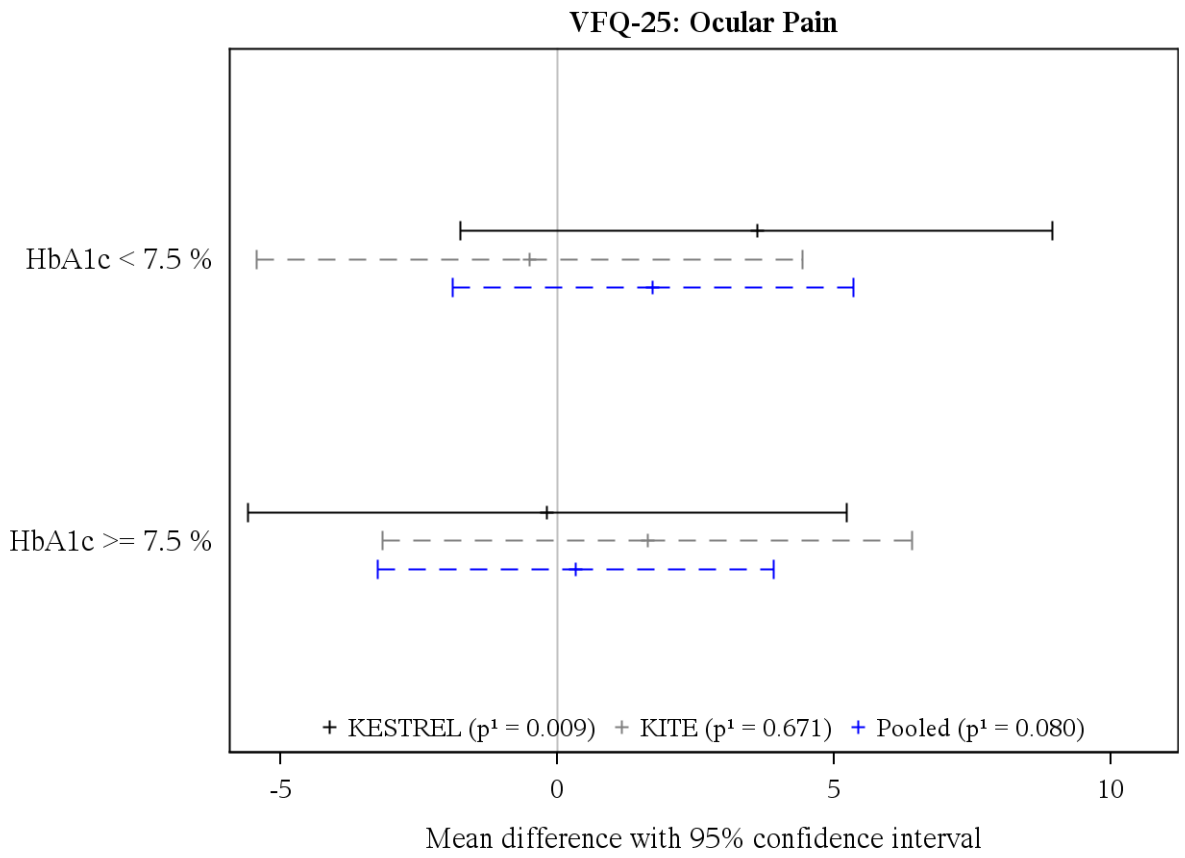
Figure 8.2.7 VFQ by HbA1c (FAS), forest plot, week 100

Figure 8.2.7.1 VFQ by HbA1c (FAS), forest plot, week 100, Distance Activities



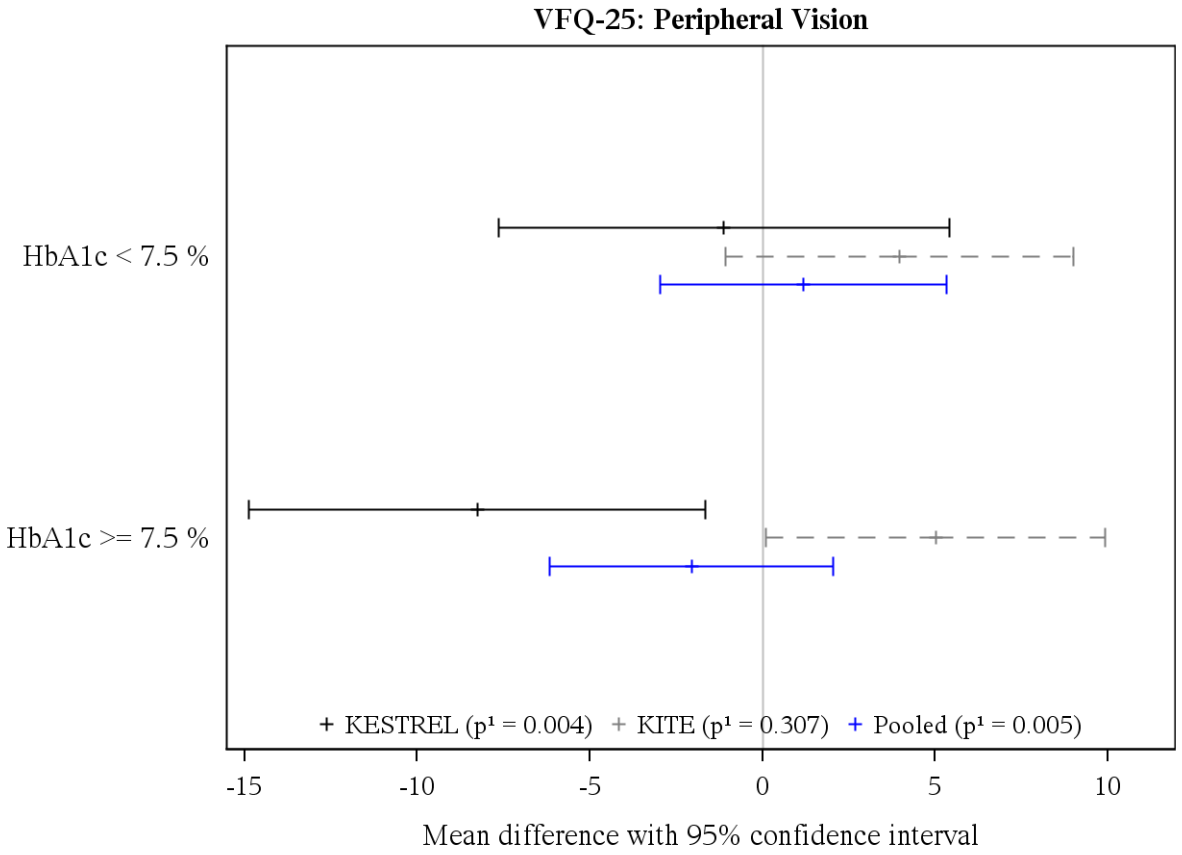
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.046$

Figure 8.2.7.2 VFQ by HbA1c (FAS), forest plot, week 100, Ocular Pain



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.664$

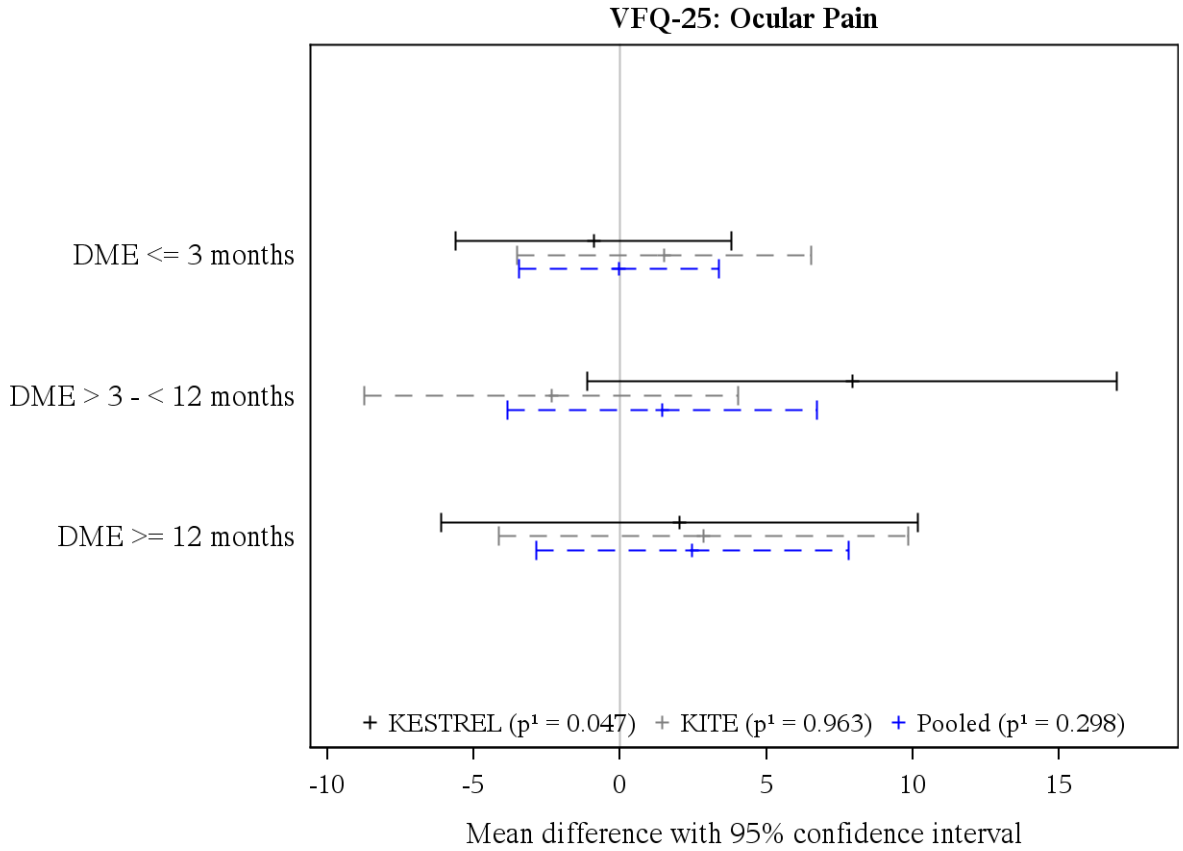
Figure 8.2.7.3 VFQ by HbA1c (FAS), forest plot, week 100, Peripheral Vision



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.003$

Figure 8.2.8 VFQ by duration of DME (FAS), forest plot, week 100

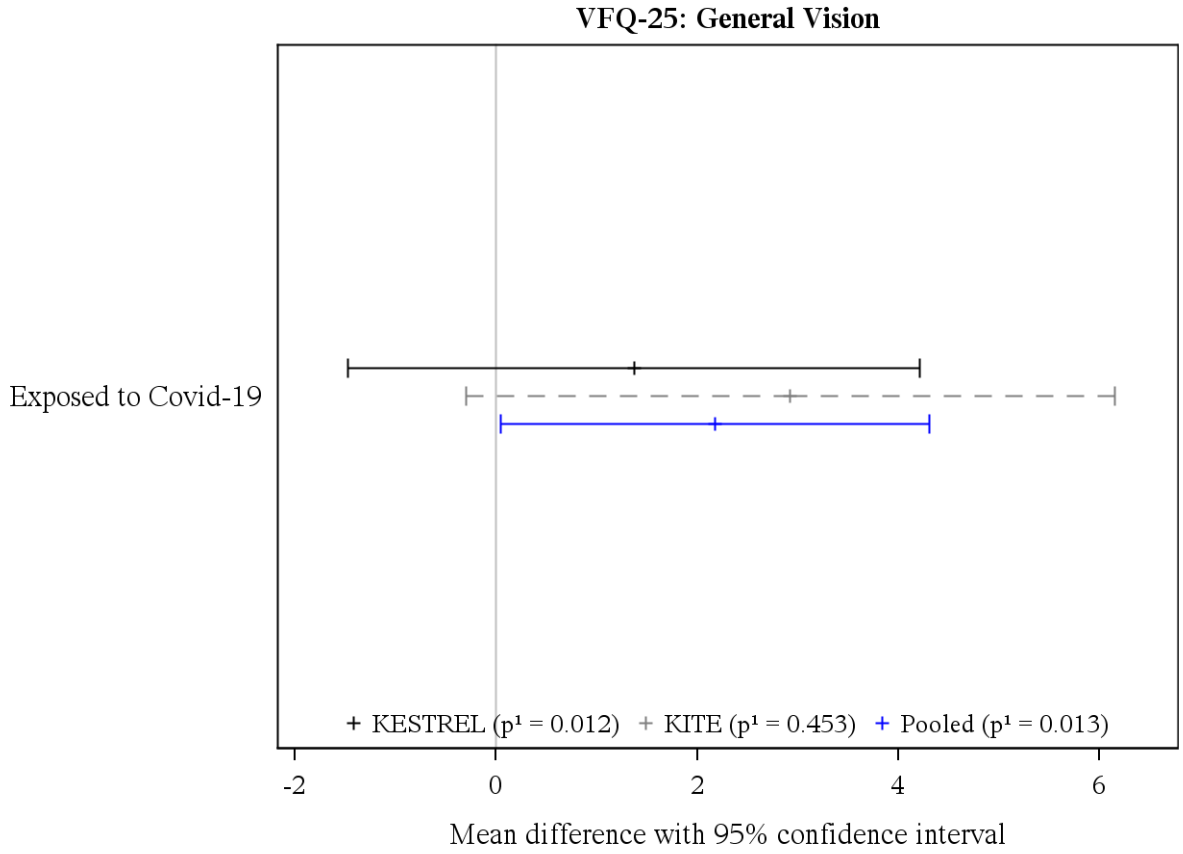
Figure 8.2.8.1 VFQ by duration of DME (FAS), forest plot, week 100, Ocular Pain



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.664$

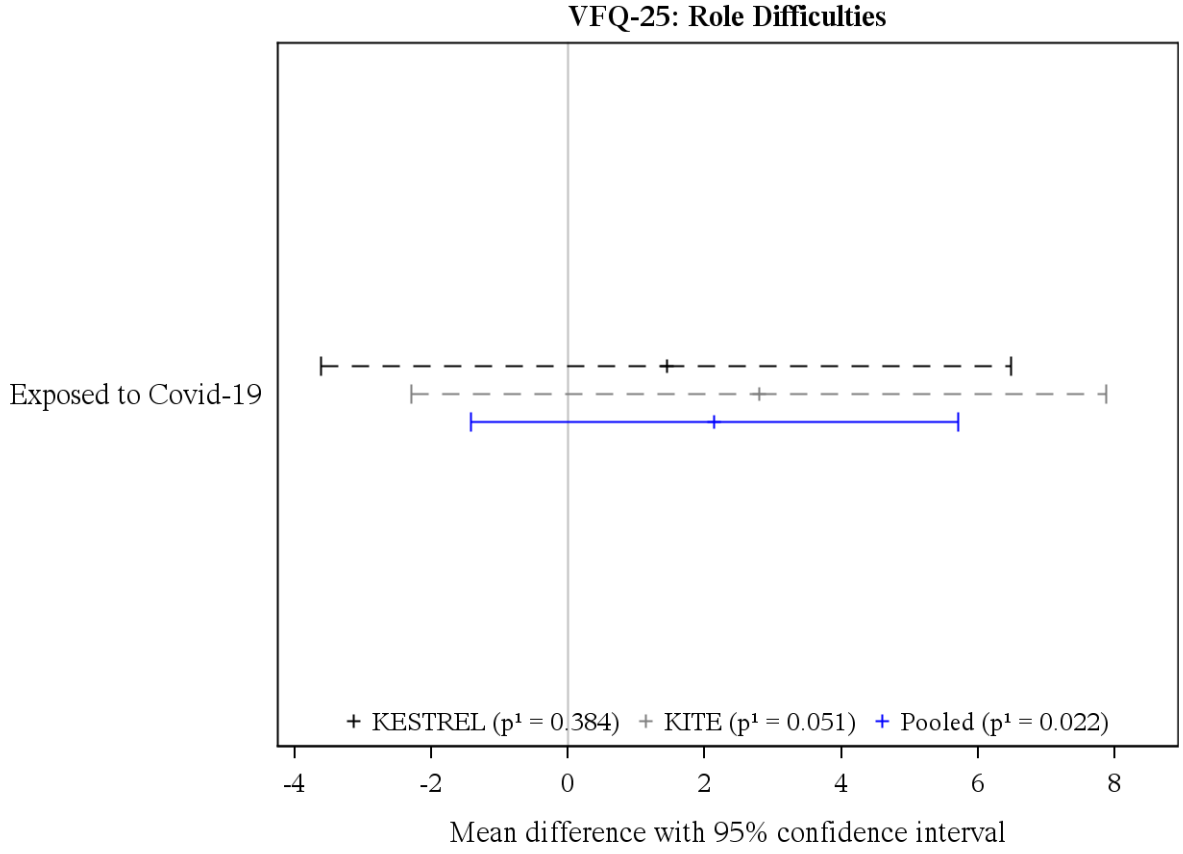
Figure 8.2.13 VFQ by exposure (week 100) (FAS), forest plot, week 100

Figure 8.2.13.1 VFQ by exposure (week 100) (FAS), forest plot, week 100, General Vision



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.762$

Figure 8.2.13.2 VFQ by exposure (week 100) (FAS), forest plot, week 100, Role Difficulties



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.132$

Figure 8.3.1 VFQ (FAS), boxplot, week 100

Figure 8.3.1.1 VFQ (FAS), boxplot, week 100, Composite Score

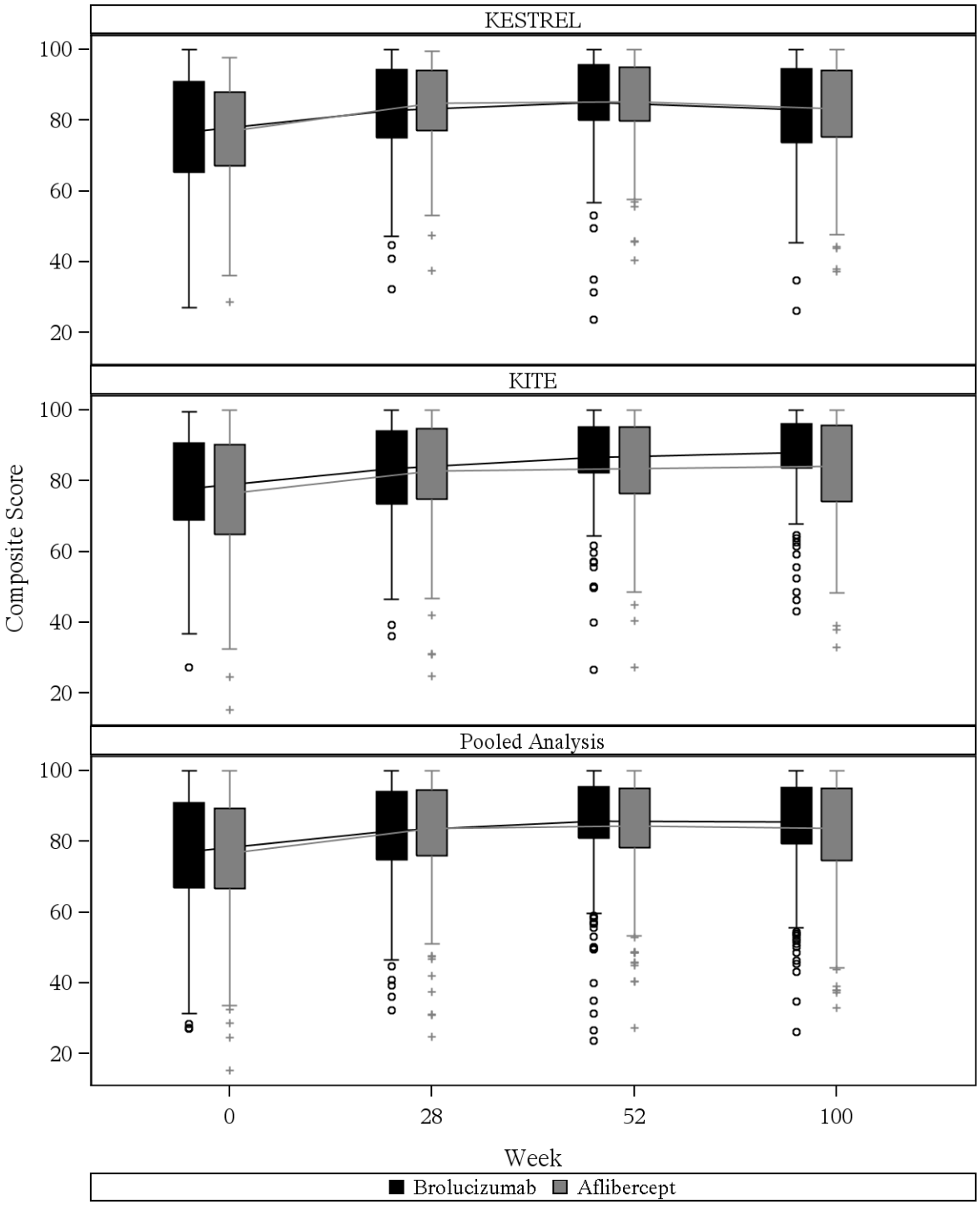


Figure 8.3.1.2 VFQ (FAS), boxplot, week 100, Color Vision

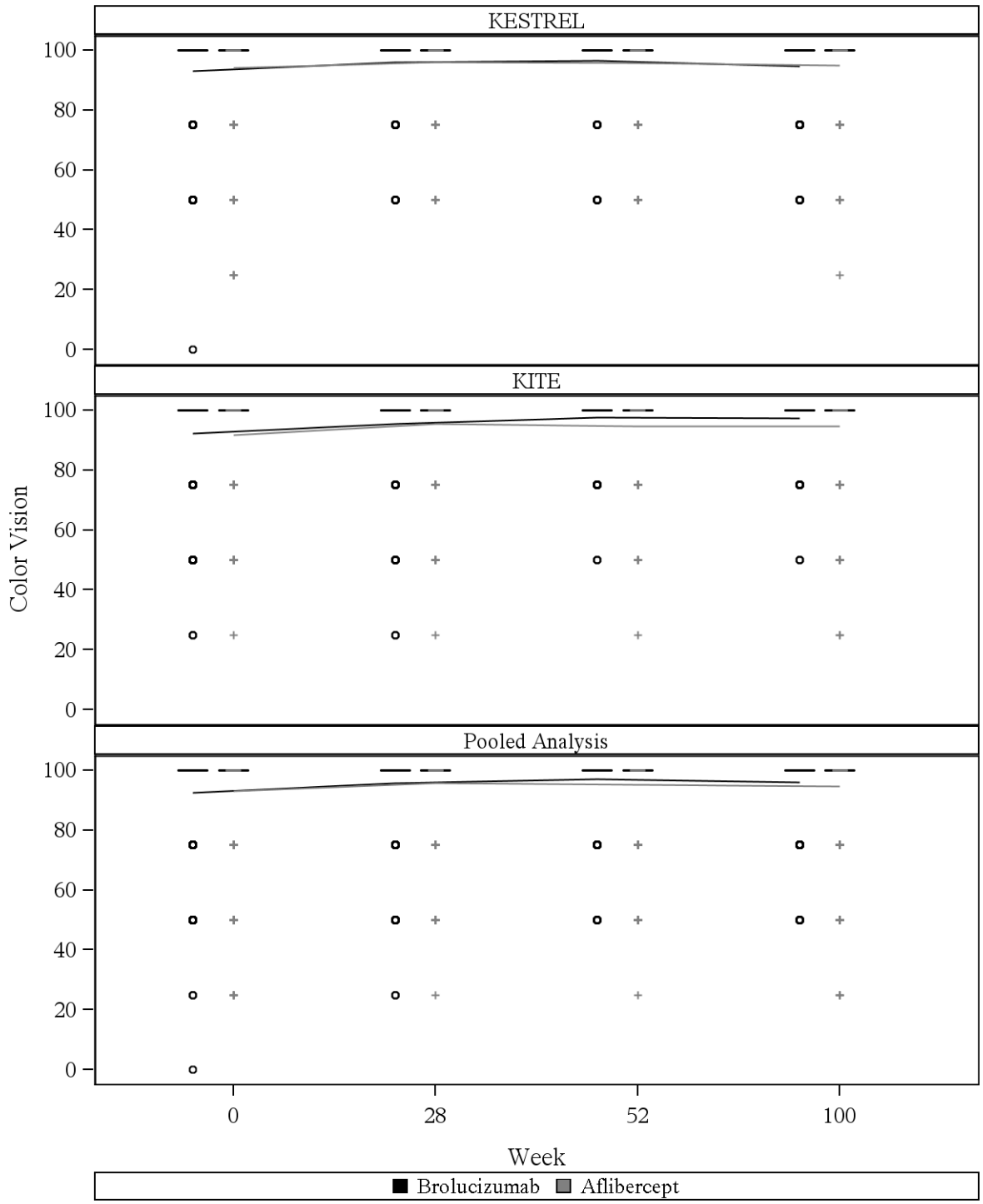


Figure 8.3.1.3 VFQ (FAS), boxplot, week 100, Dependency

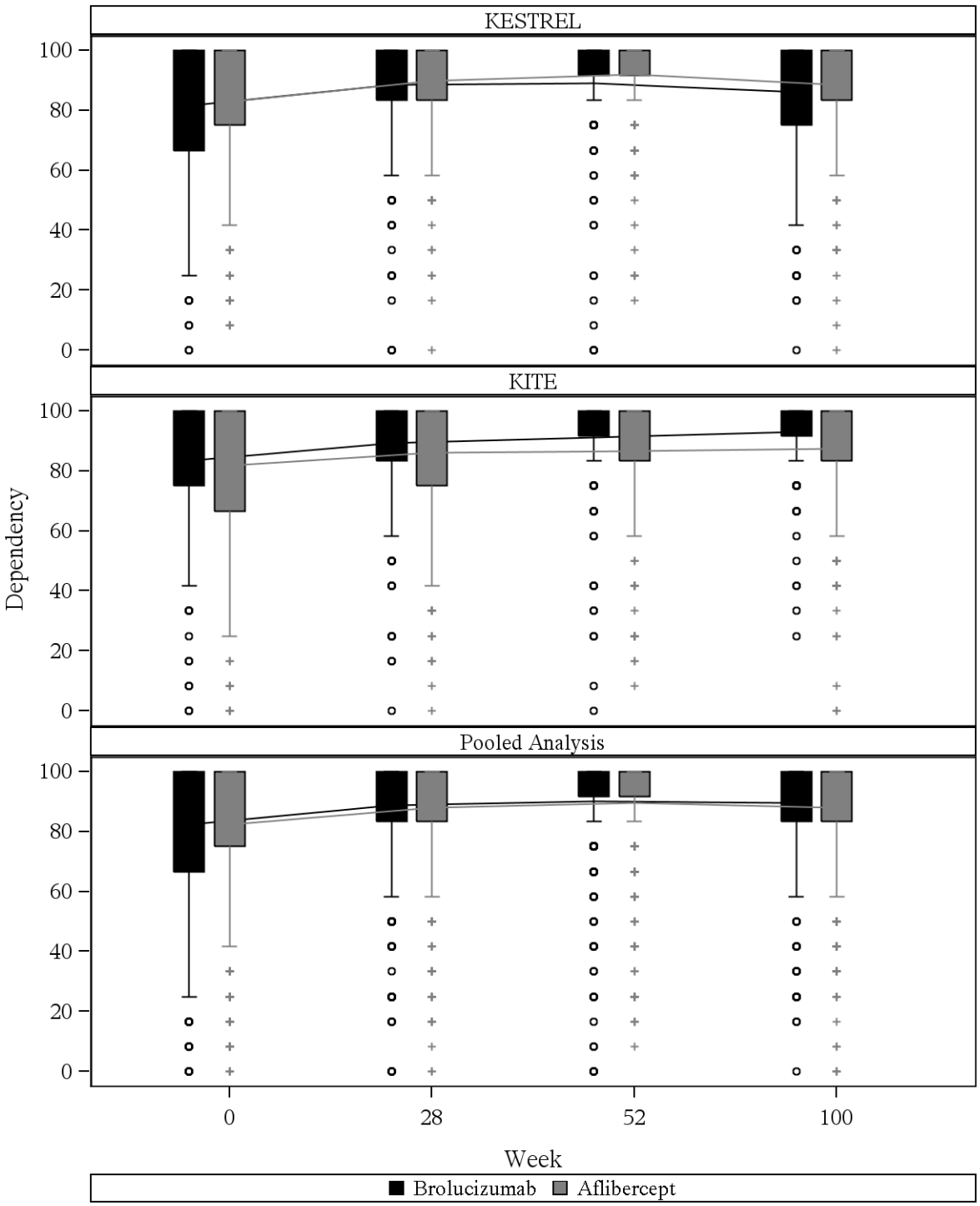


Figure 8.3.1.4 VFQ (FAS), boxplot, week 100, Distance Activities

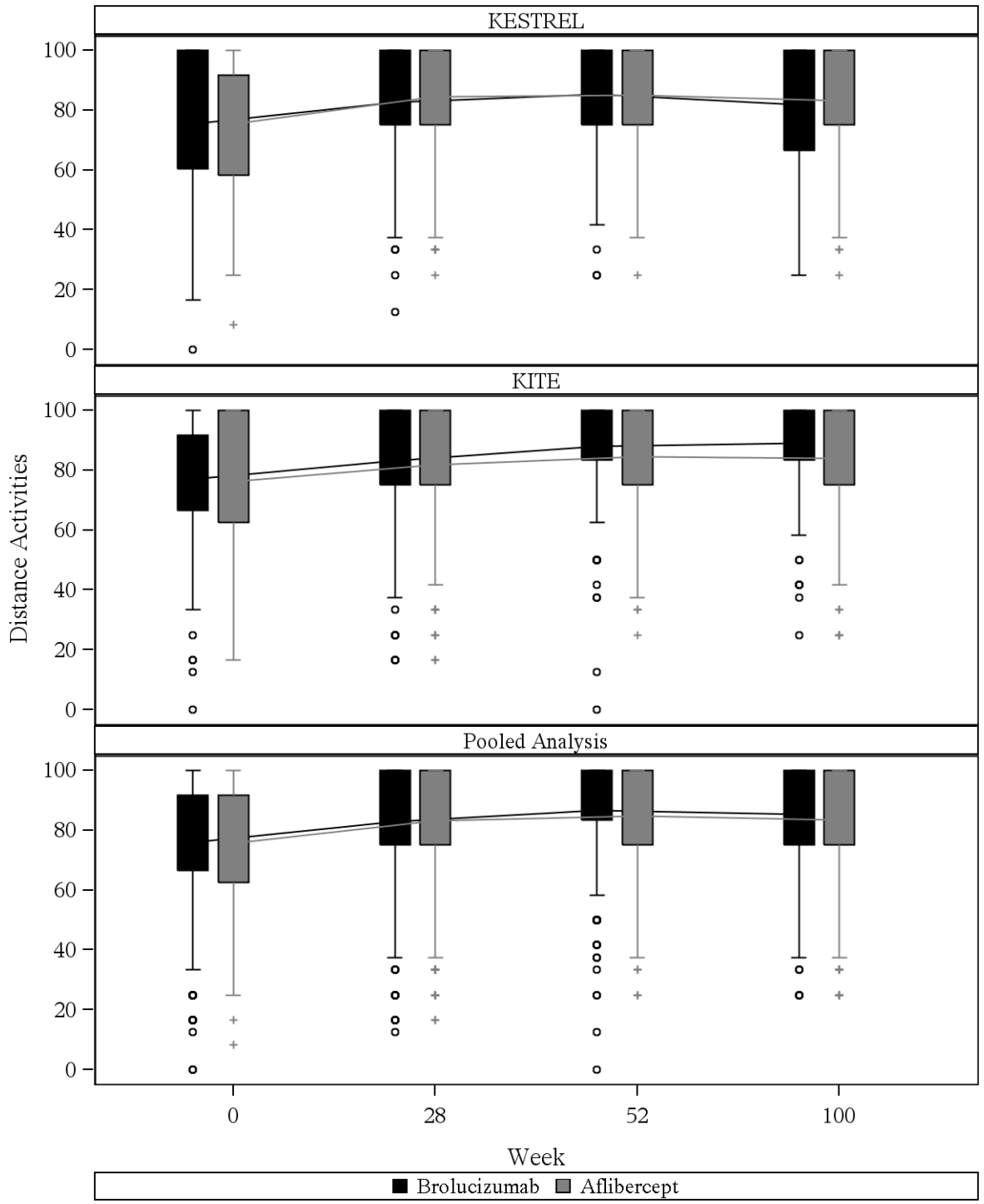


Figure 8.3.1.5 VFQ (FAS), boxplot, week 100, Driving

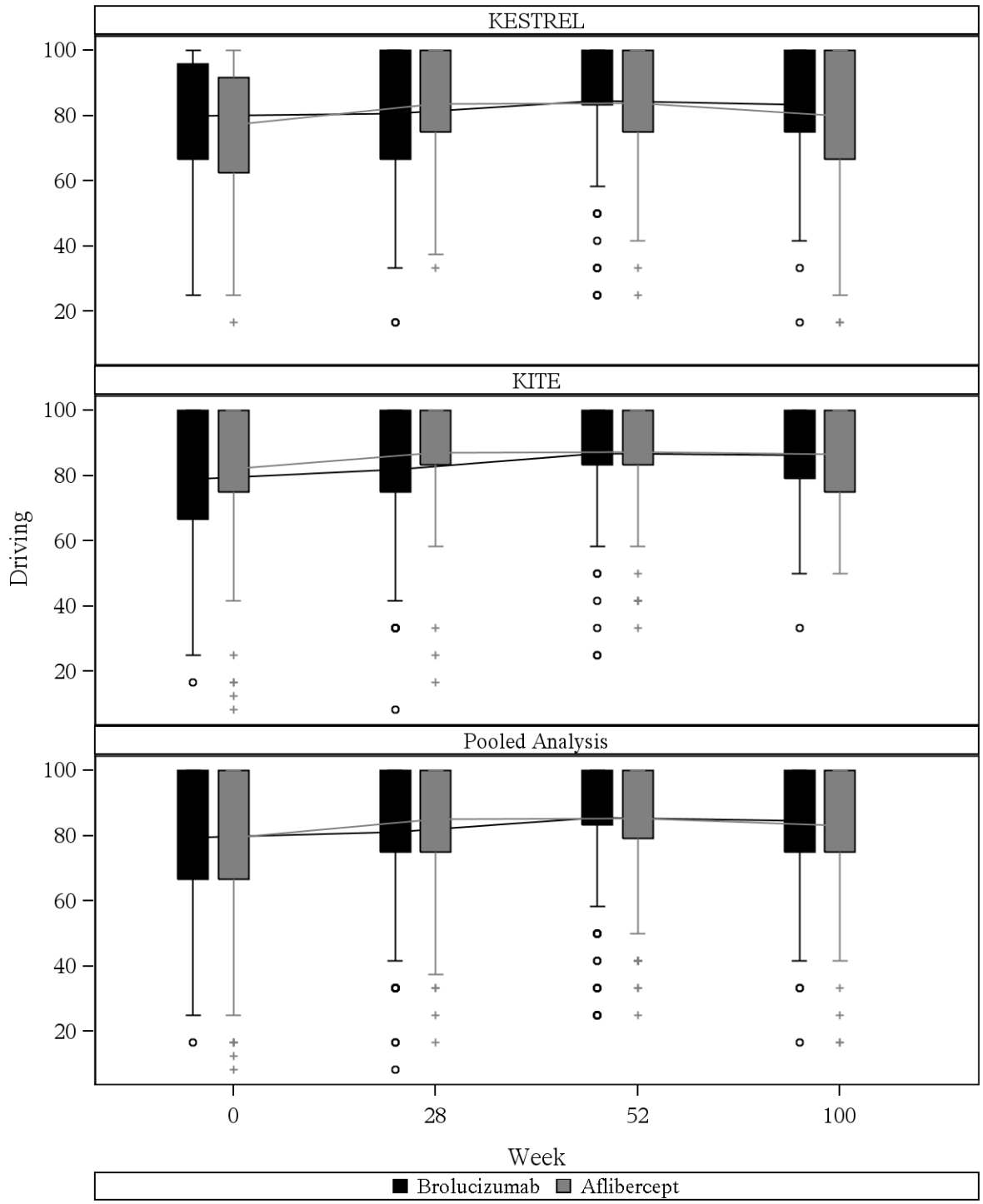


Figure 8.3.1.6 VFQ (FAS), boxplot, week 100, General Vision

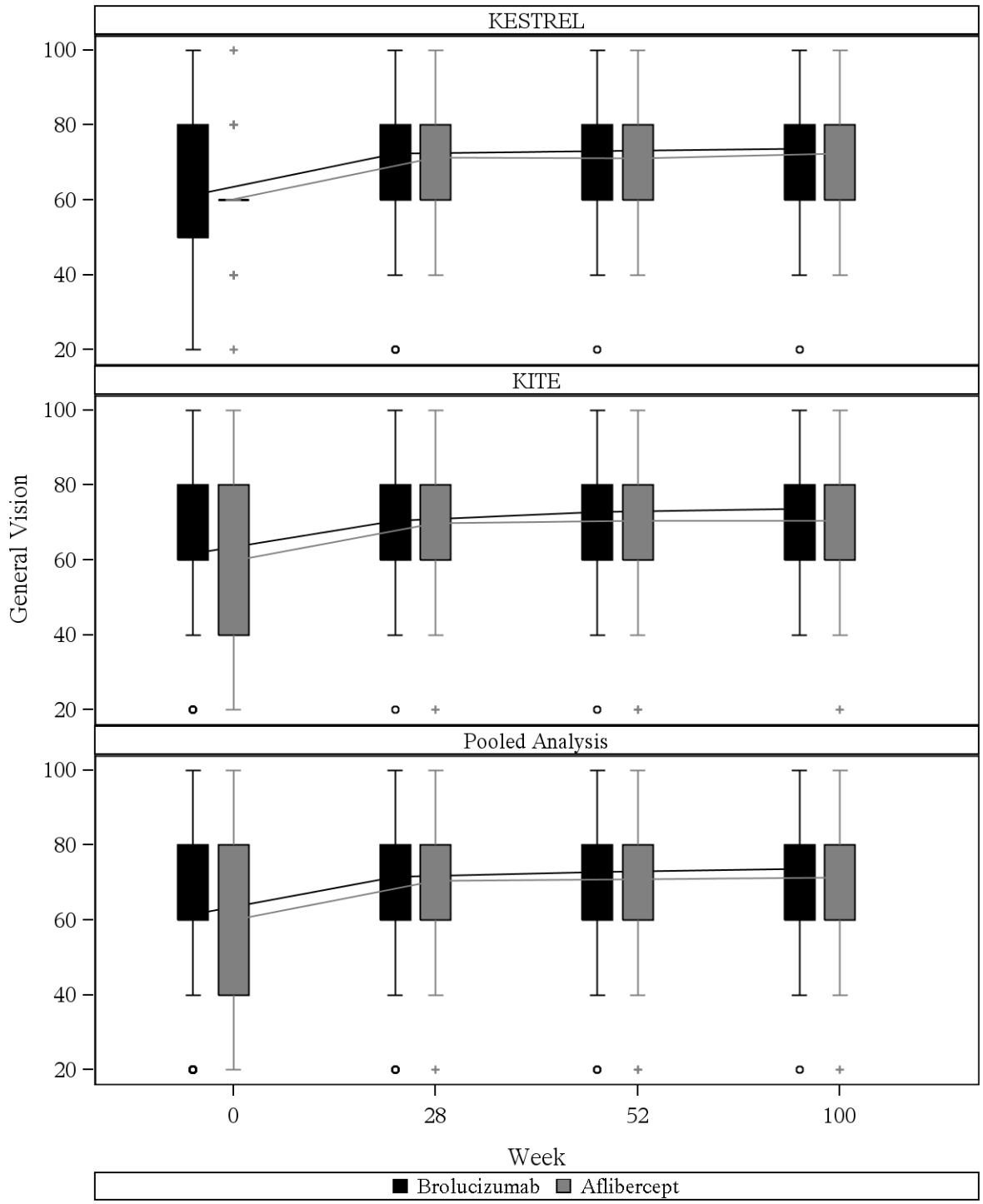


Figure 8.3.1.7 VFQ (FAS), boxplot, week 100, General Health

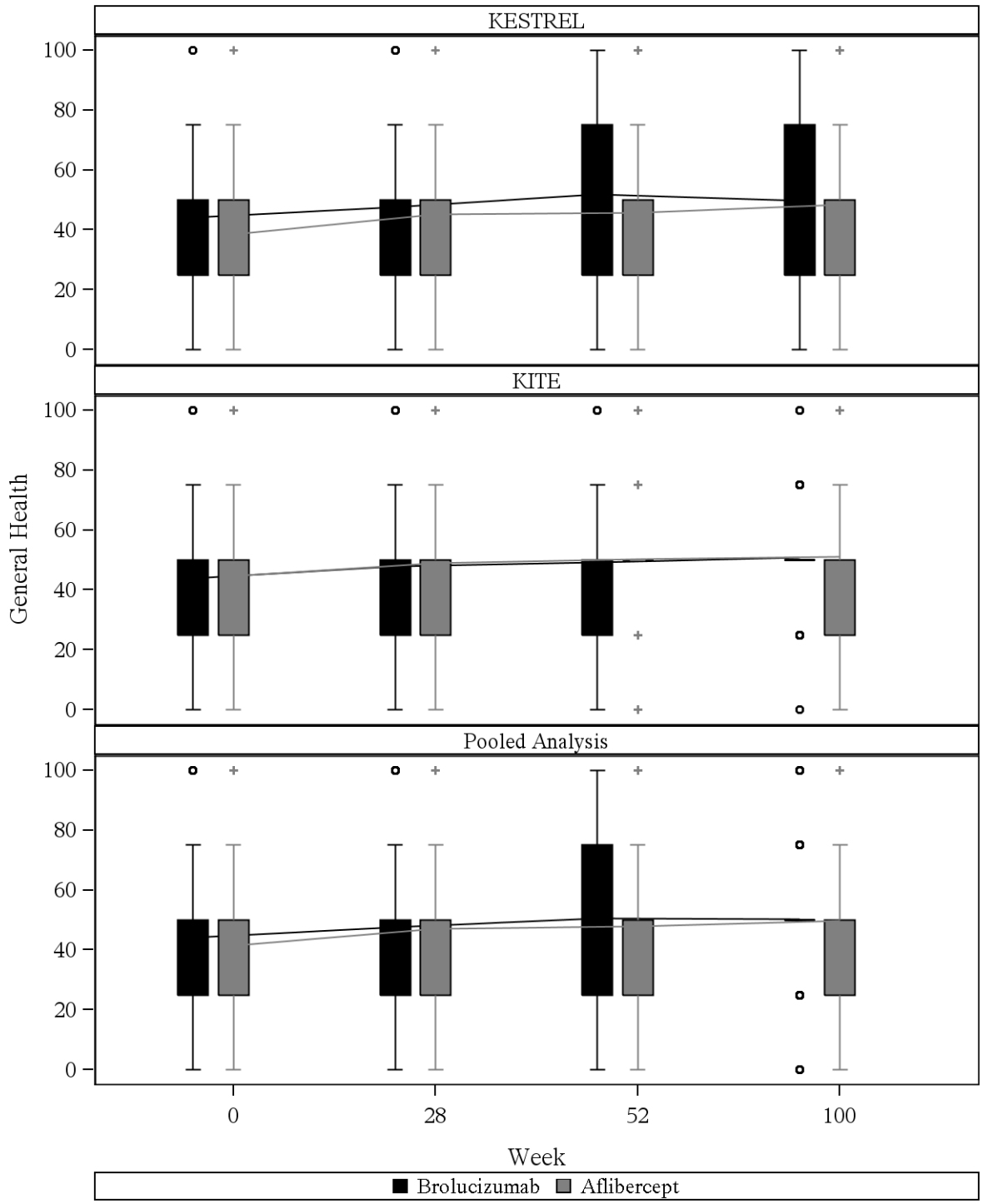


Figure 8.3.1.8 VFQ (FAS), boxplot, week 100, Mental Health

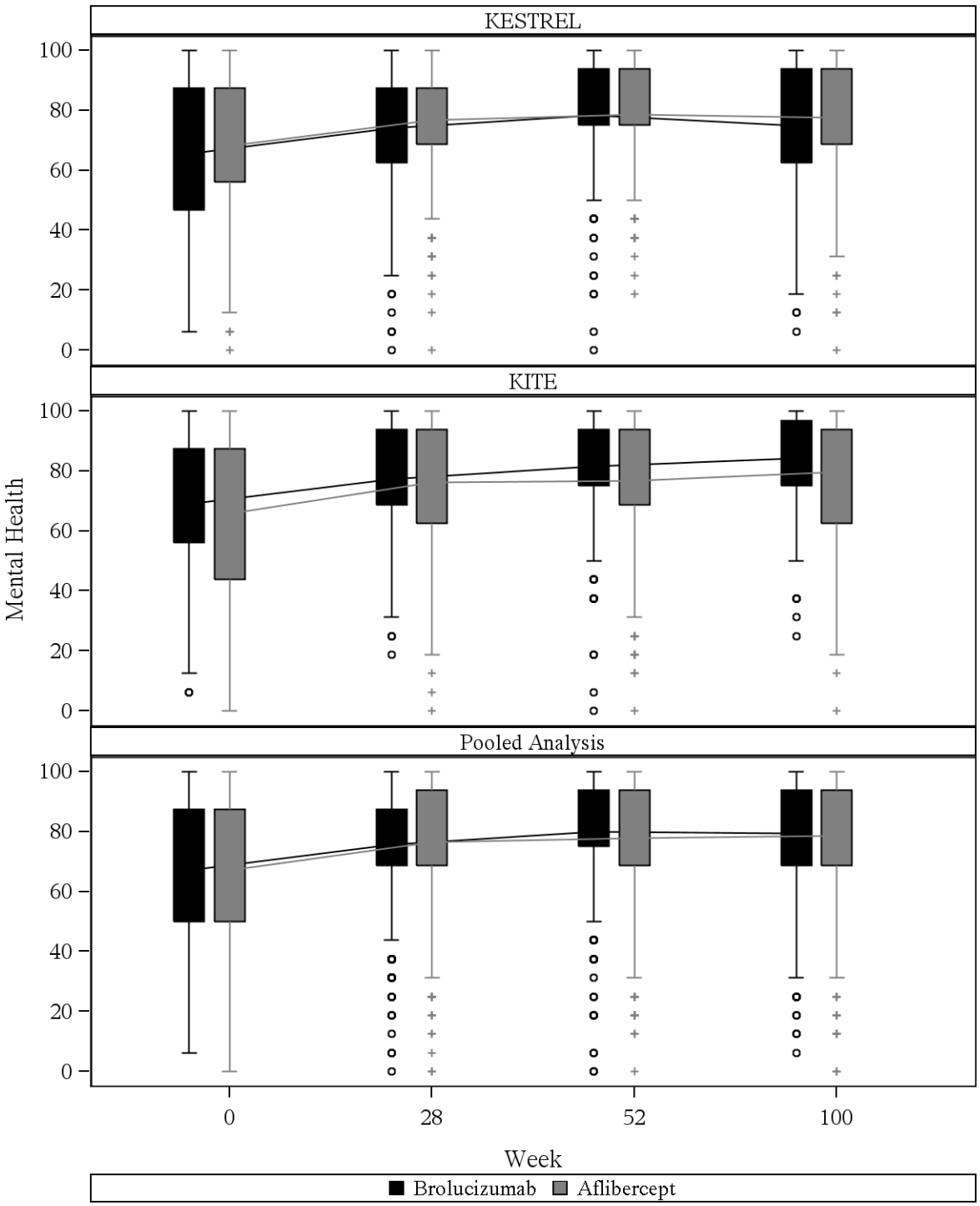


Figure 8.3.1.9 VFQ (FAS), boxplot, week 100, Near Activities

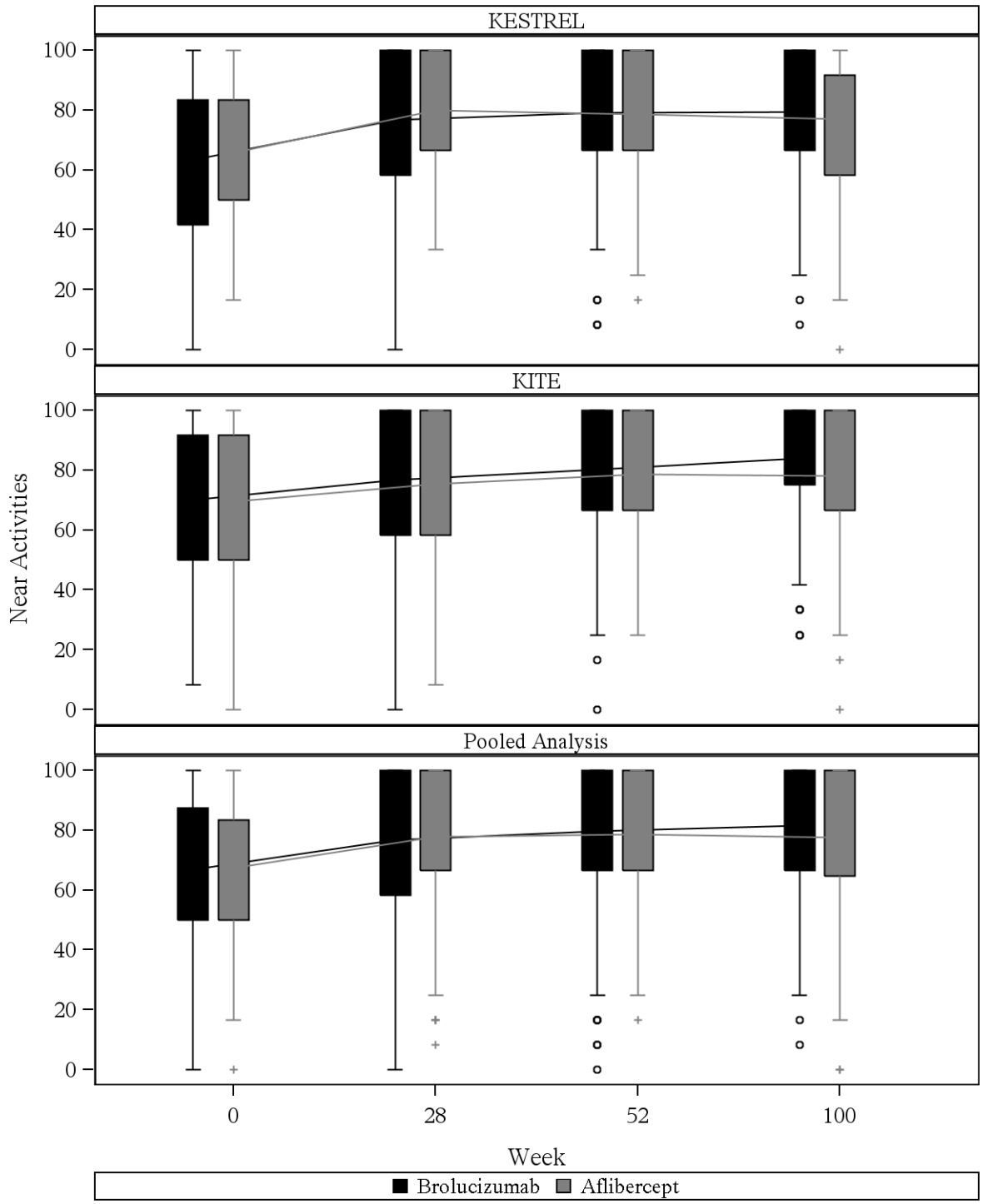


Figure 8.3.1.10 VFQ (FAS), boxplot, week 100, Ocular Pain

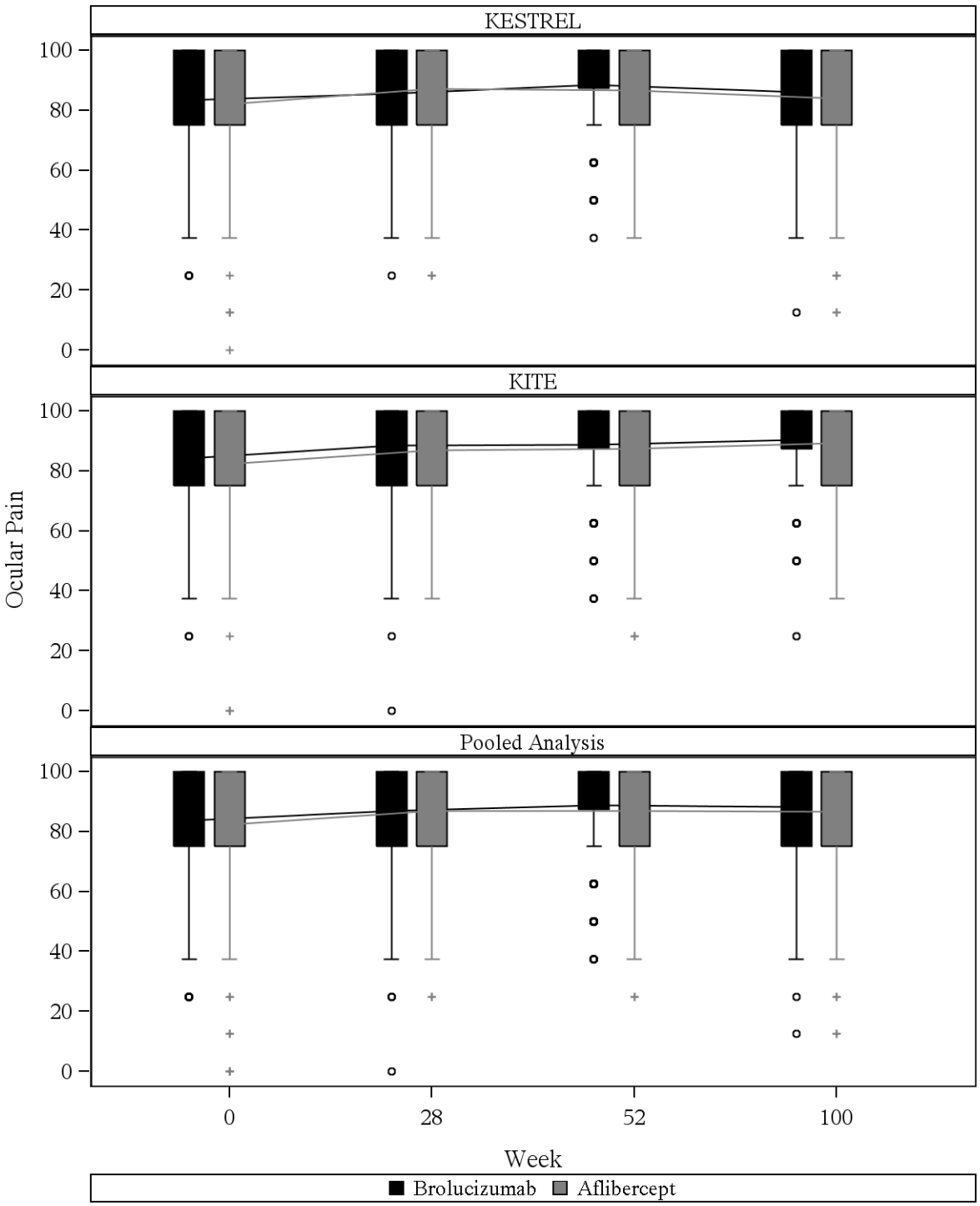


Figure 8.3.1.11 VFQ (FAS), boxplot, week 100, Peripheral Vision

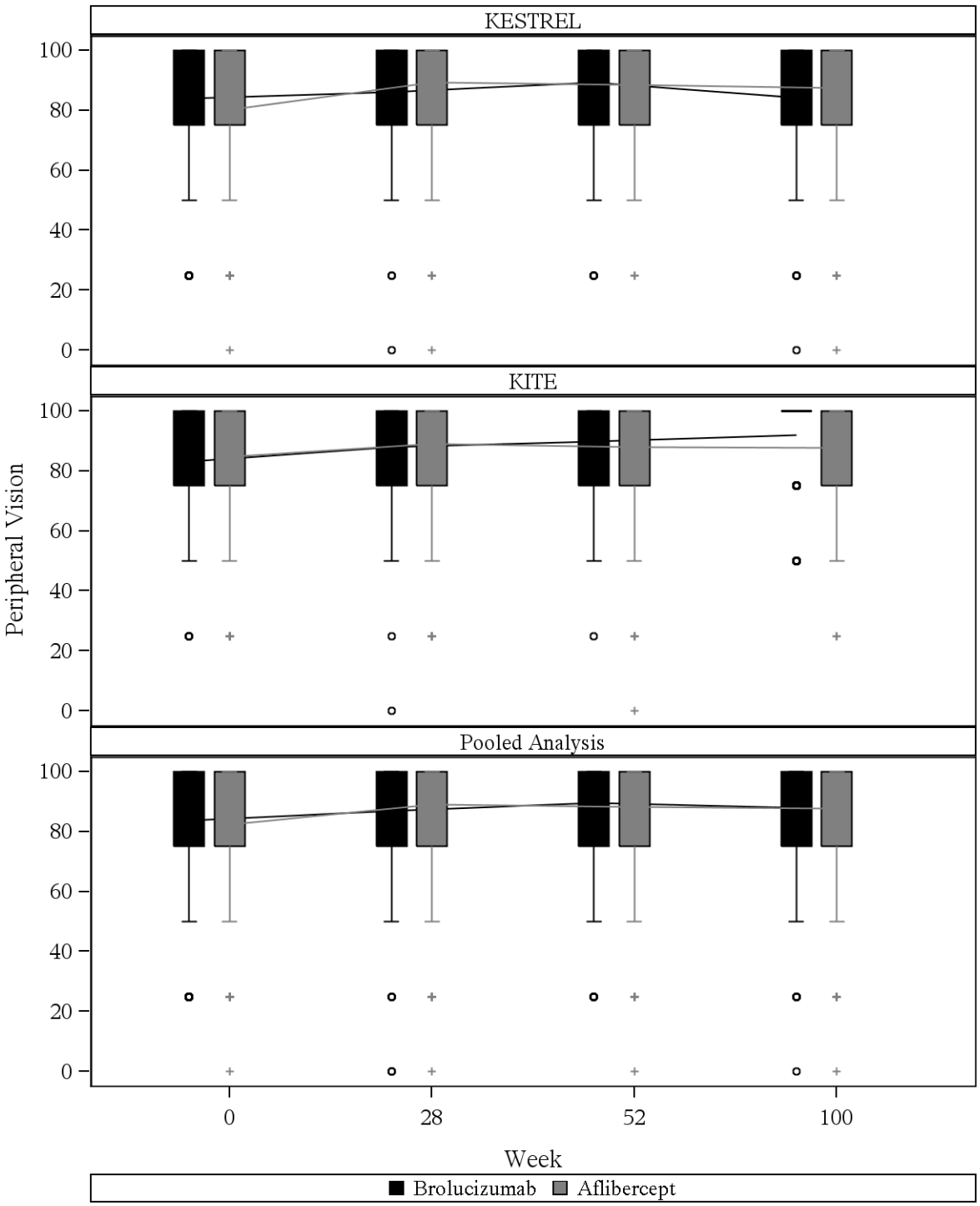


Figure 8.3.1.12 VFQ (FAS), boxplot, week 100, Role Difficulties

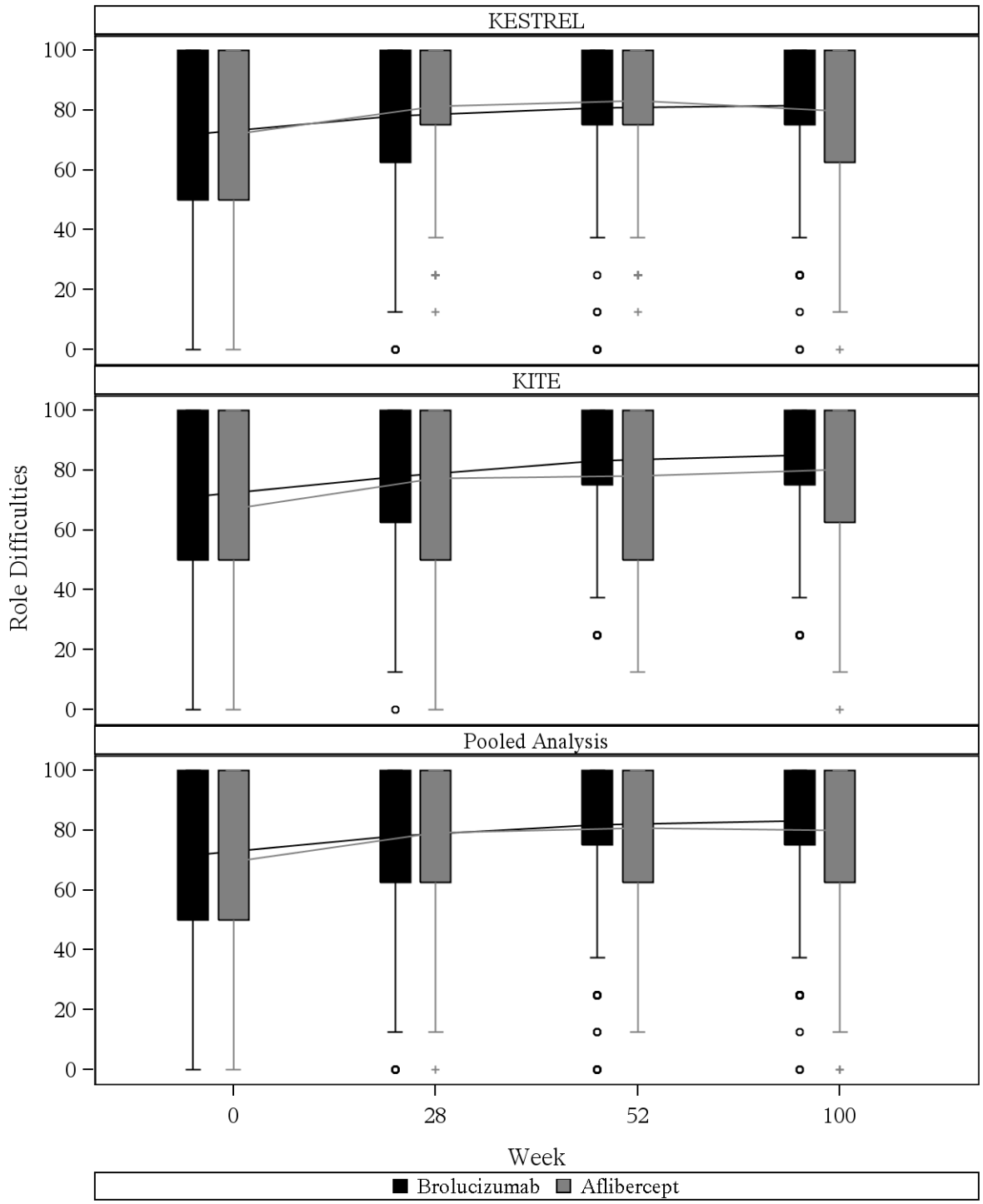


Figure 8.3.1.13 VFQ (FAS), boxplot, week 100, Social Functioning

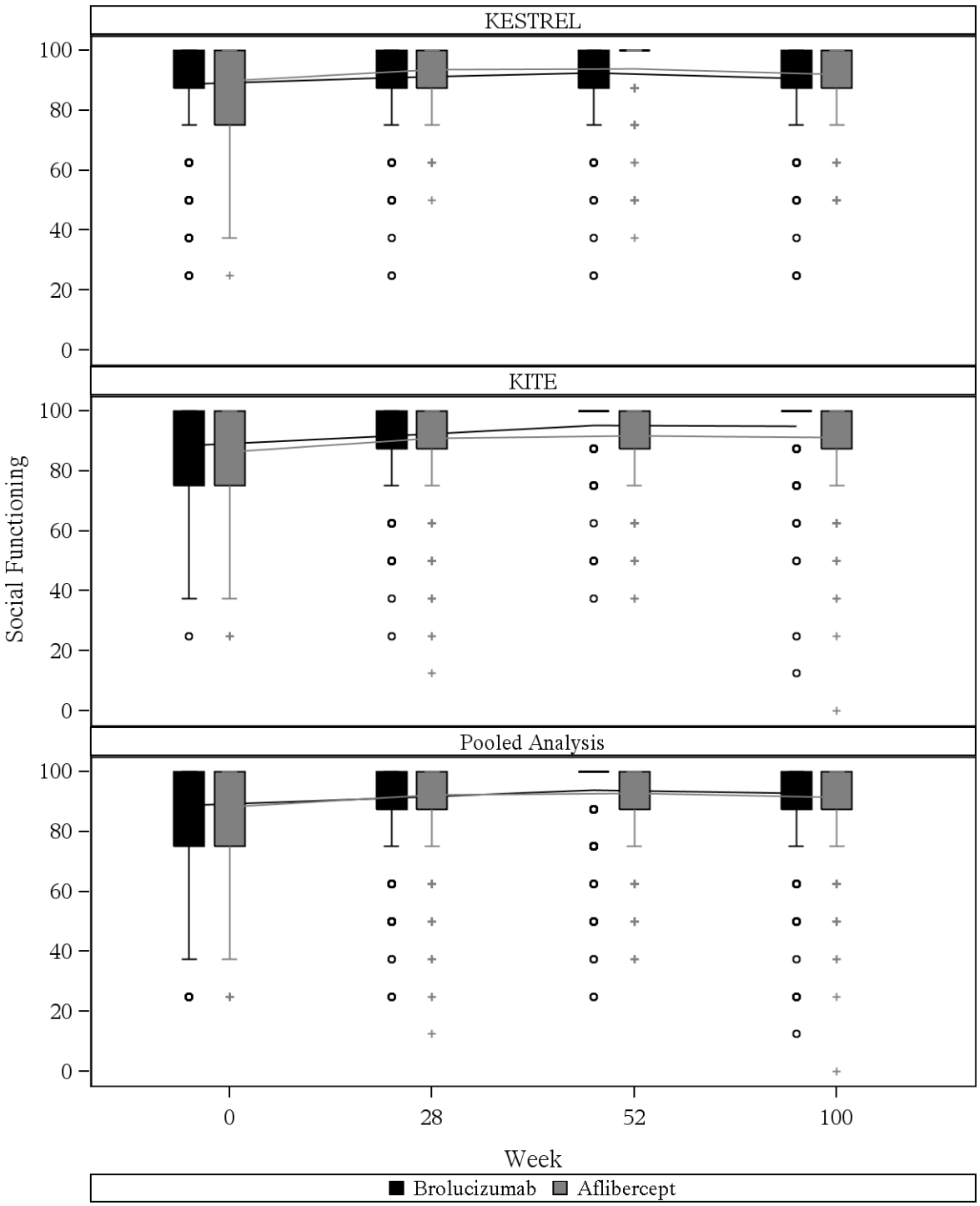


Figure 8.3.6 VFQ by diabetes type (FAS), boxplot, week 100

Figure 8.3.6.1 VFQ by diabetes type (FAS), boxplot, week 100, Distance Activities

Figure 8.3.6.1.2 VFQ by diabetes type (FAS), boxplot, week 100, Distance Activities for Kite

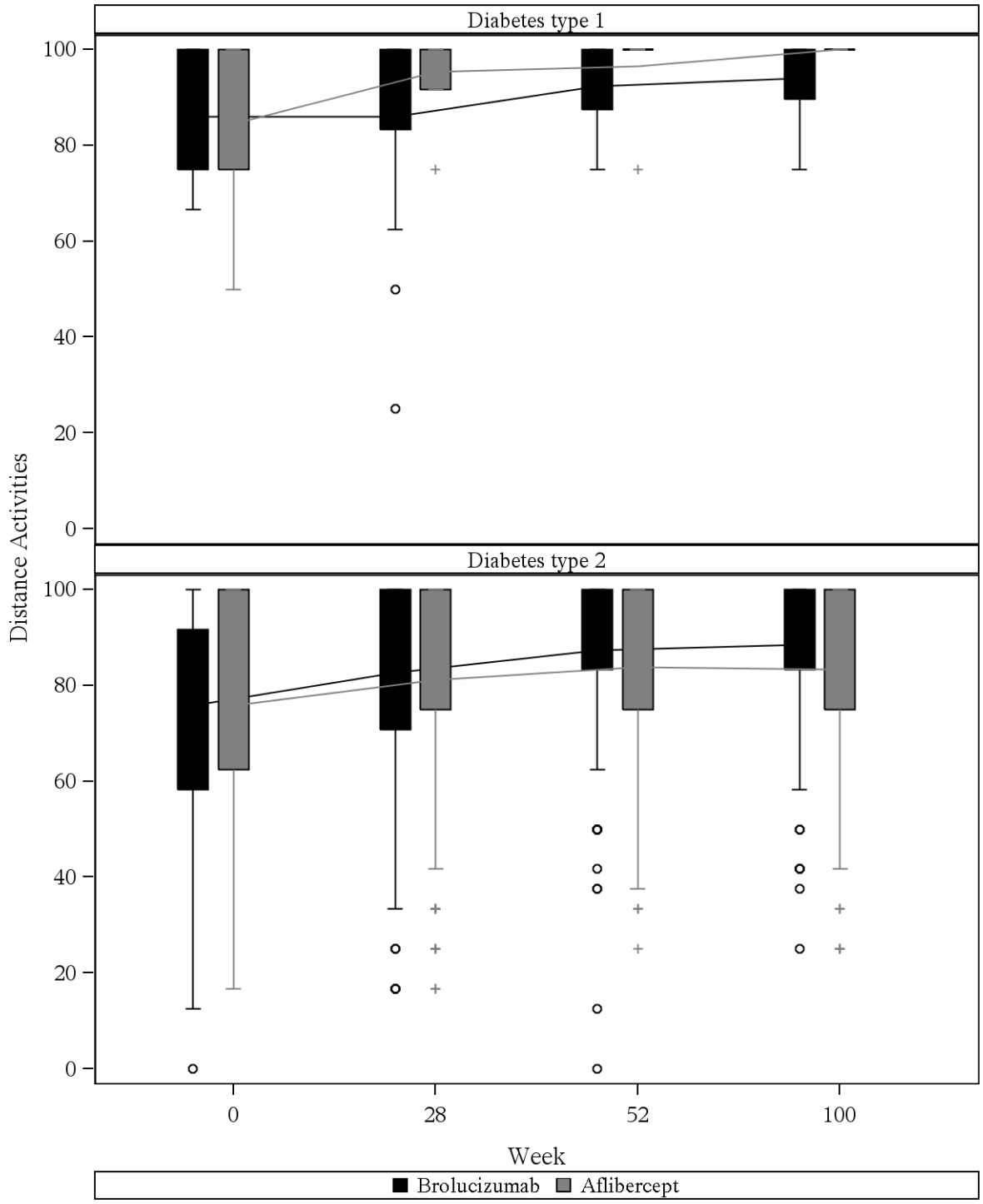


Figure 8.3.6.2 VFQ by diabetes type (FAS), boxplot, week 100, Peripheral Vision

Figure 8.3.6.2.2 VFQ by diabetes type (FAS), boxplot, week 100, Peripheral Vision for Kite

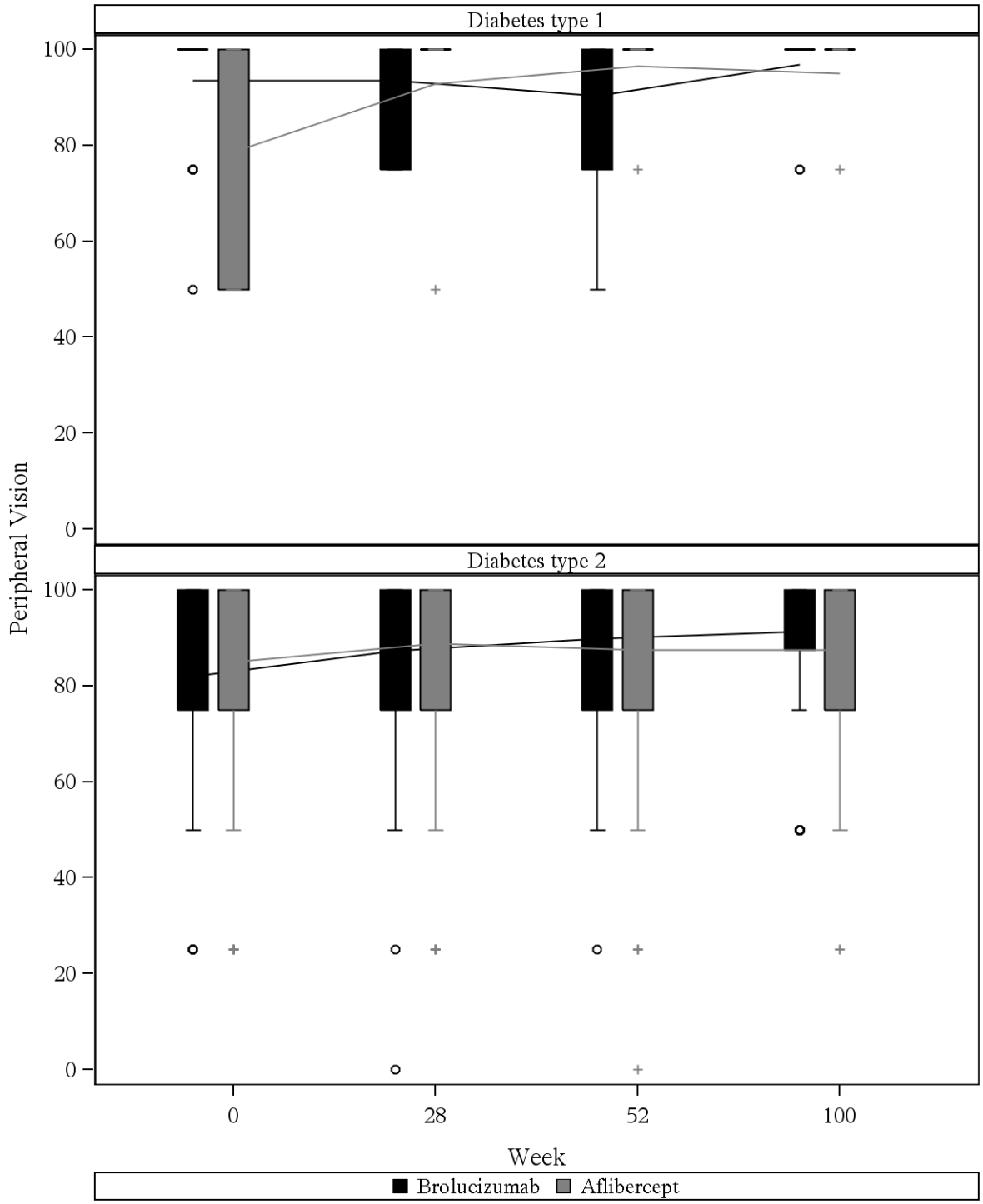


Figure 8.3.7 VFQ by HbA1c (FAS), boxplot, week 100

Figure 8.3.7.1 VFQ by HbA1c (FAS), boxplot, week 100, Distance Activities

Figure 8.3.7.1.1 VFQ by HbA1c (FAS), boxplot, week 100, Distance Activities for Kestrel

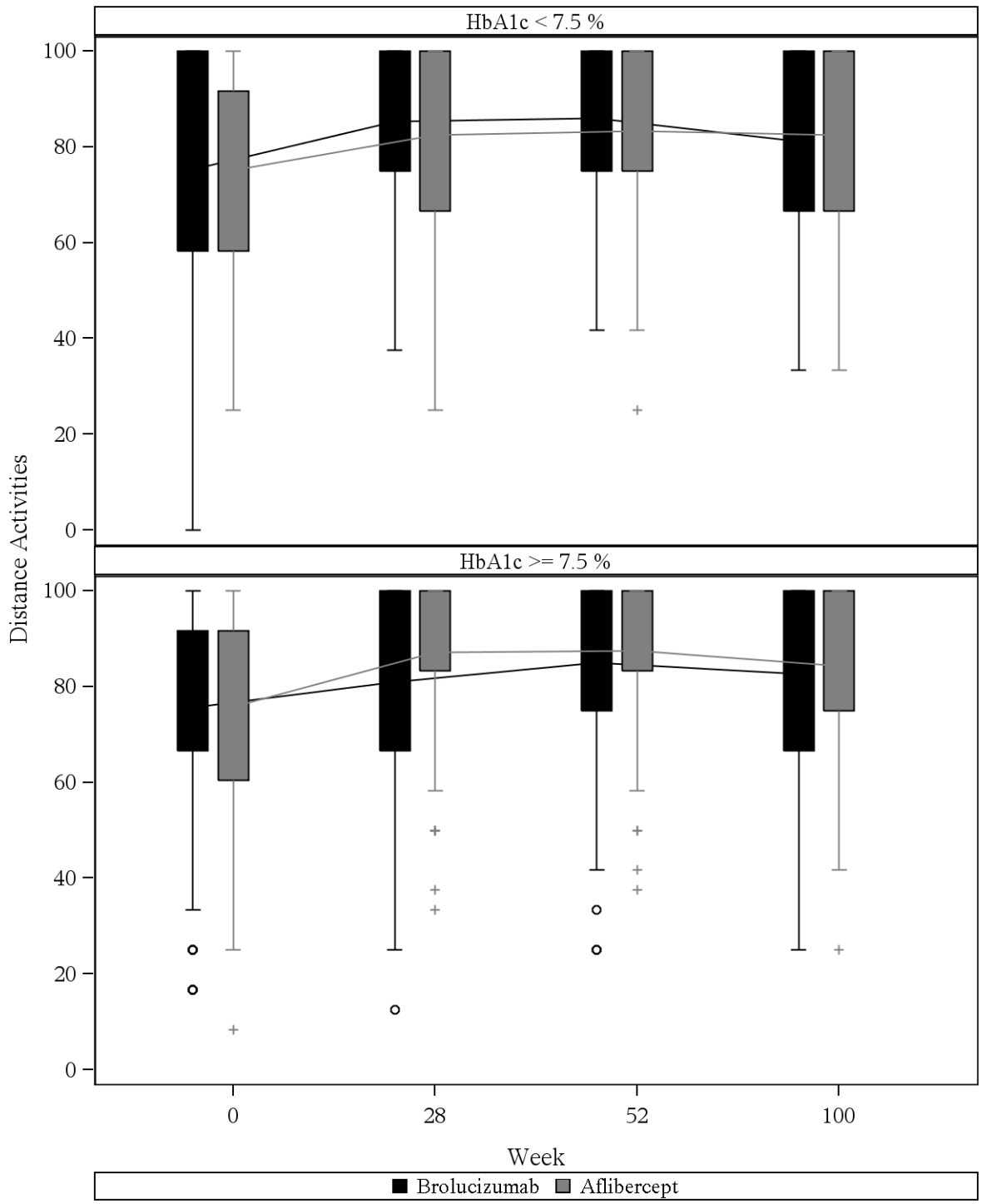


Figure 8.3.7.2 VFQ by HbA1c (FAS), boxplot, week 100, Ocular Pain

Figure 8.3.7.2.1 VFQ by HbA1c (FAS), boxplot, week 100, Ocular Pain for Kestrel

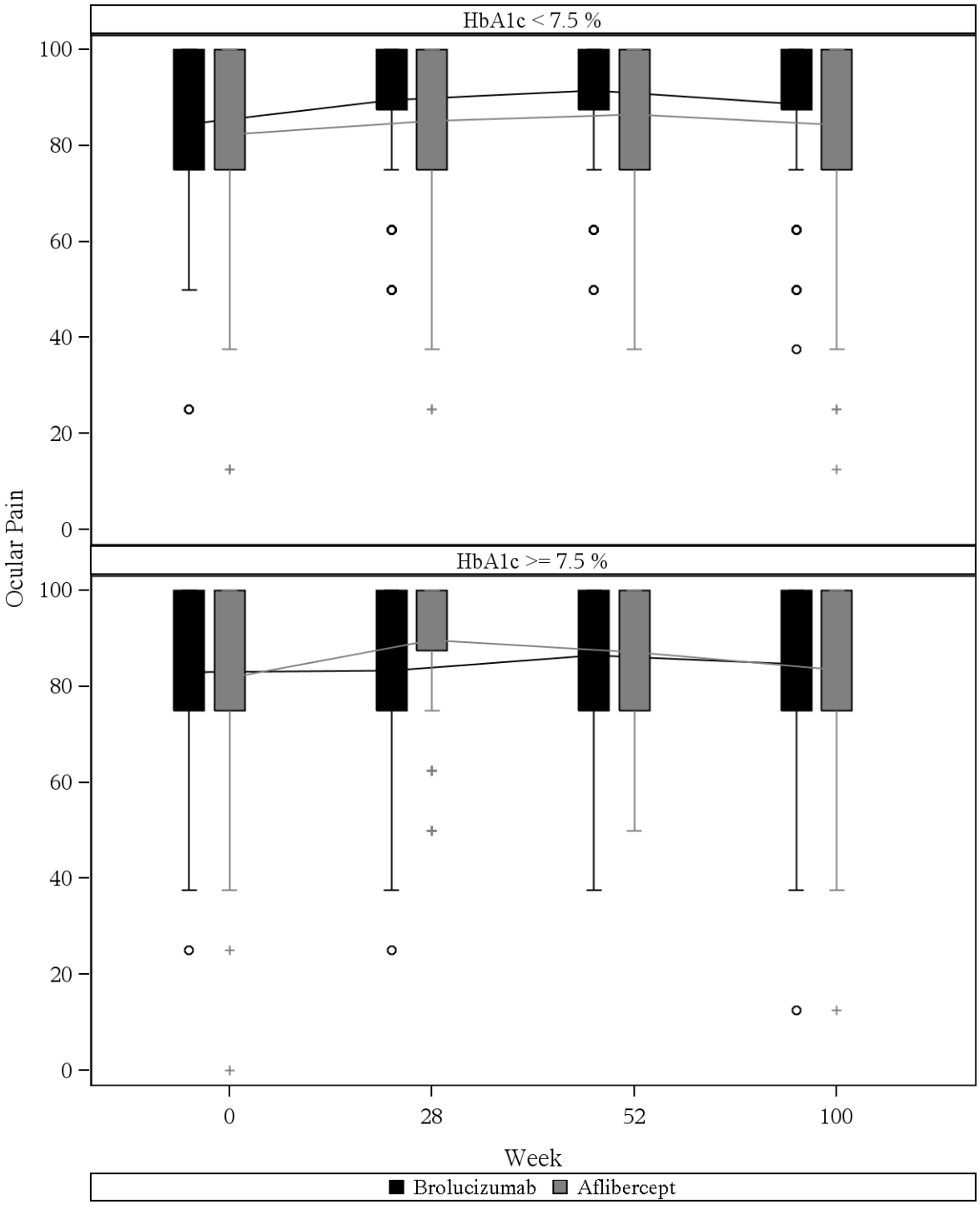


Figure 8.3.7.3 VFQ by HbA1c (FAS), boxplot, week 100, Peripheral Vision

Figure 8.3.7.3.1 VFQ by HbA1c (FAS), boxplot, week 100, Peripheral Vision for Kestrel

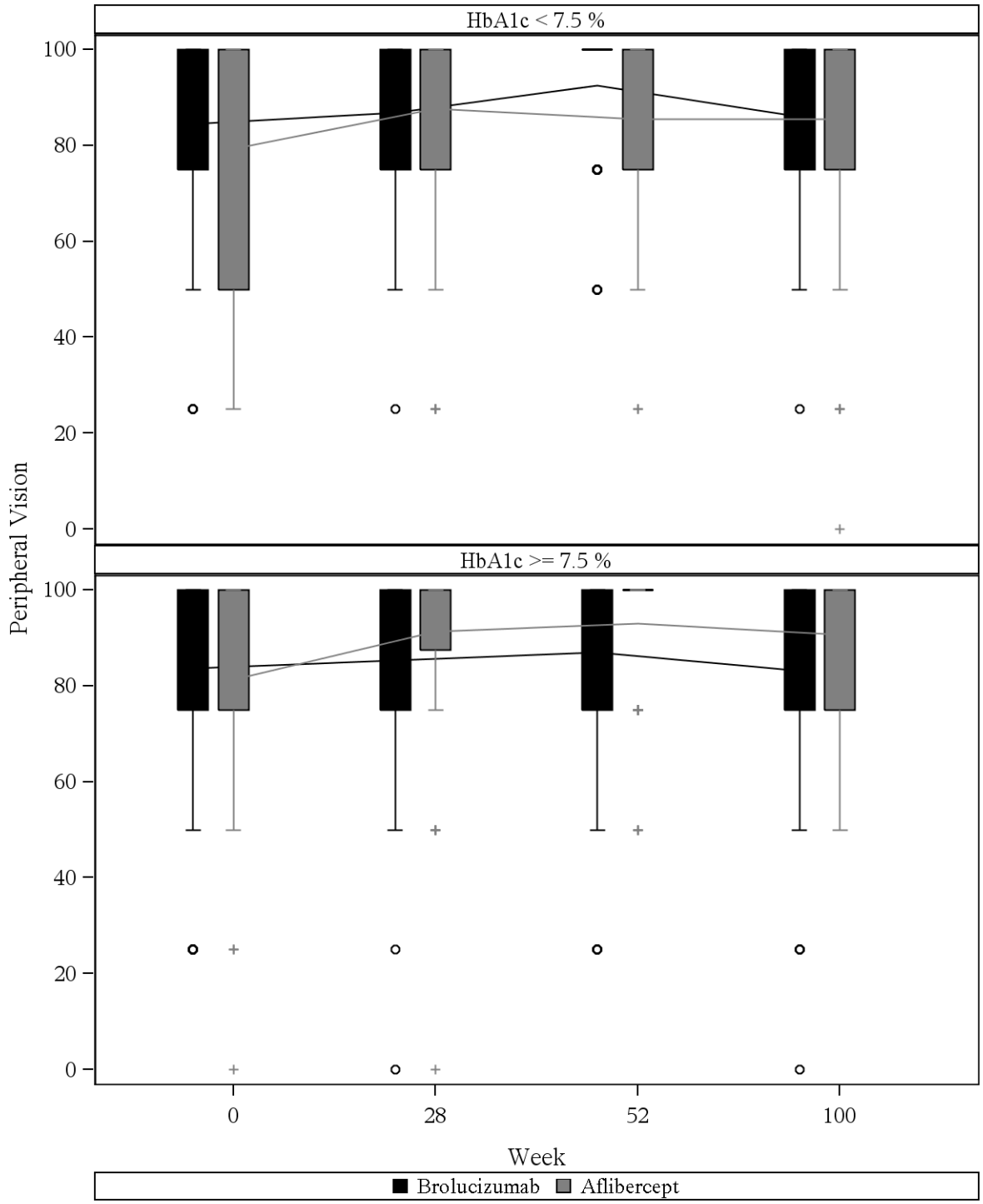


Figure 8.3.7.3.3 VFQ by HbA1c (FAS), boxplot, week 100, Peripheral Vision for Pooled Analysis

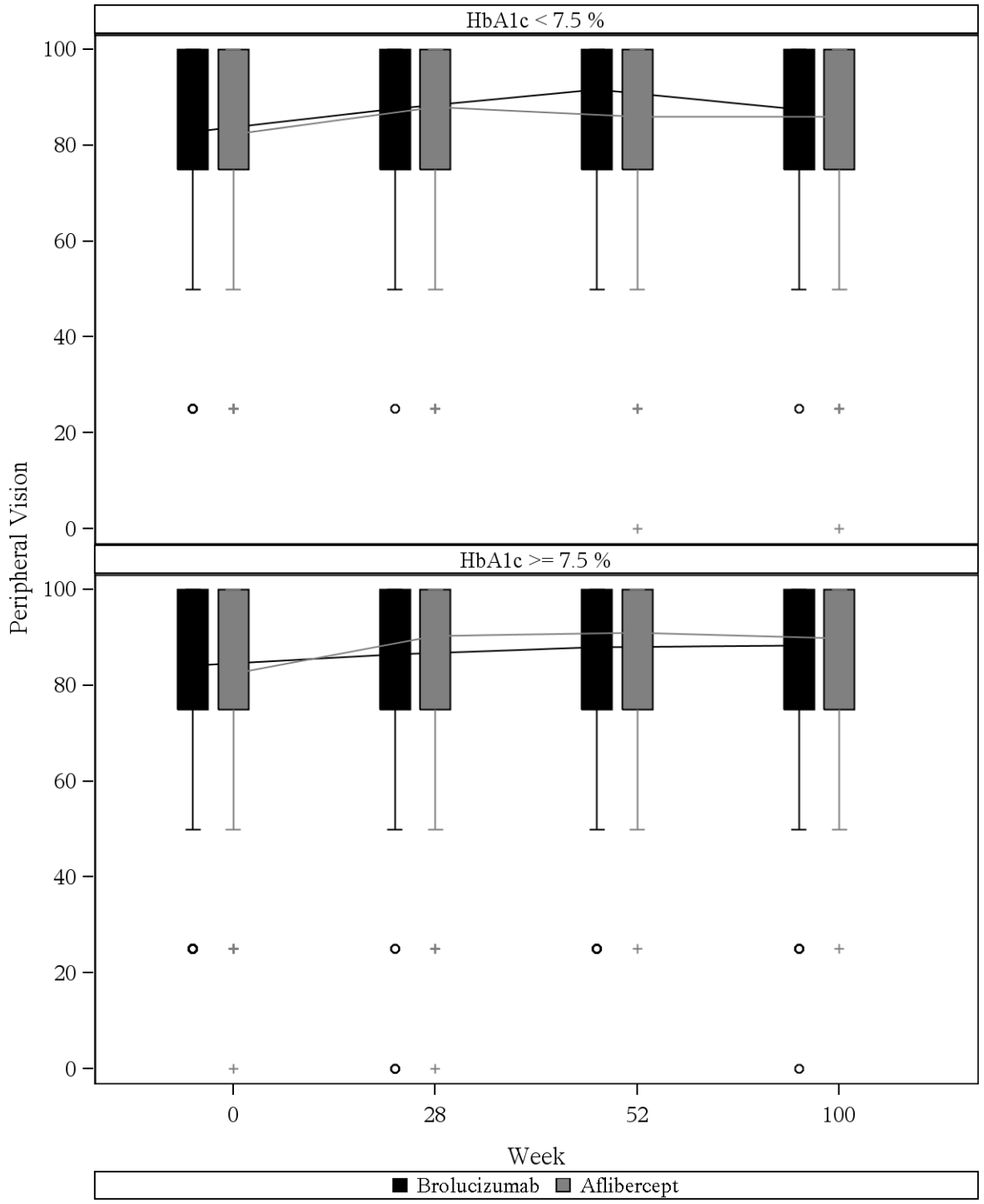


Figure 8.3.8 VFQ by duration of DME (FAS), boxplot, week 100

Figure 8.3.8.1 VFQ by duration of DME (FAS), boxplot, week 100, Ocular Pain

Figure 8.3.8.1.1 VFQ by duration of DME (FAS), boxplot, week 100, Ocular Pain for Kestrel

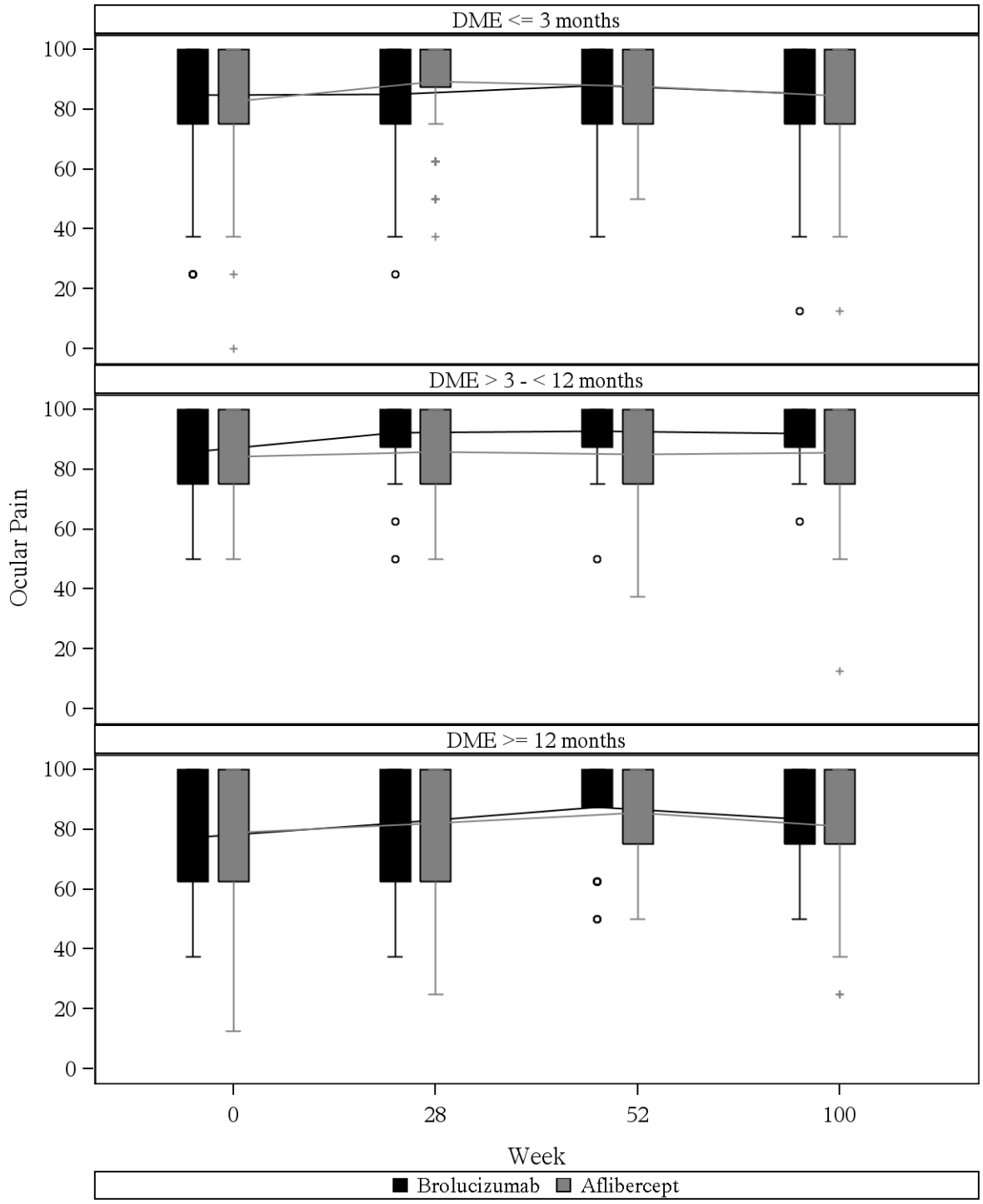


Figure 8.3.13 VFQ by exposure (week 100) (FAS), boxplot, week 100

Figure 8.3.13.1 VFQ by exposure (week 100) (FAS), boxplot, week 100, General Vision

Figure 8.3.13.1.1 VFQ by exposure (week 100) (FAS), boxplot, week 100, General Vision for Kestrel

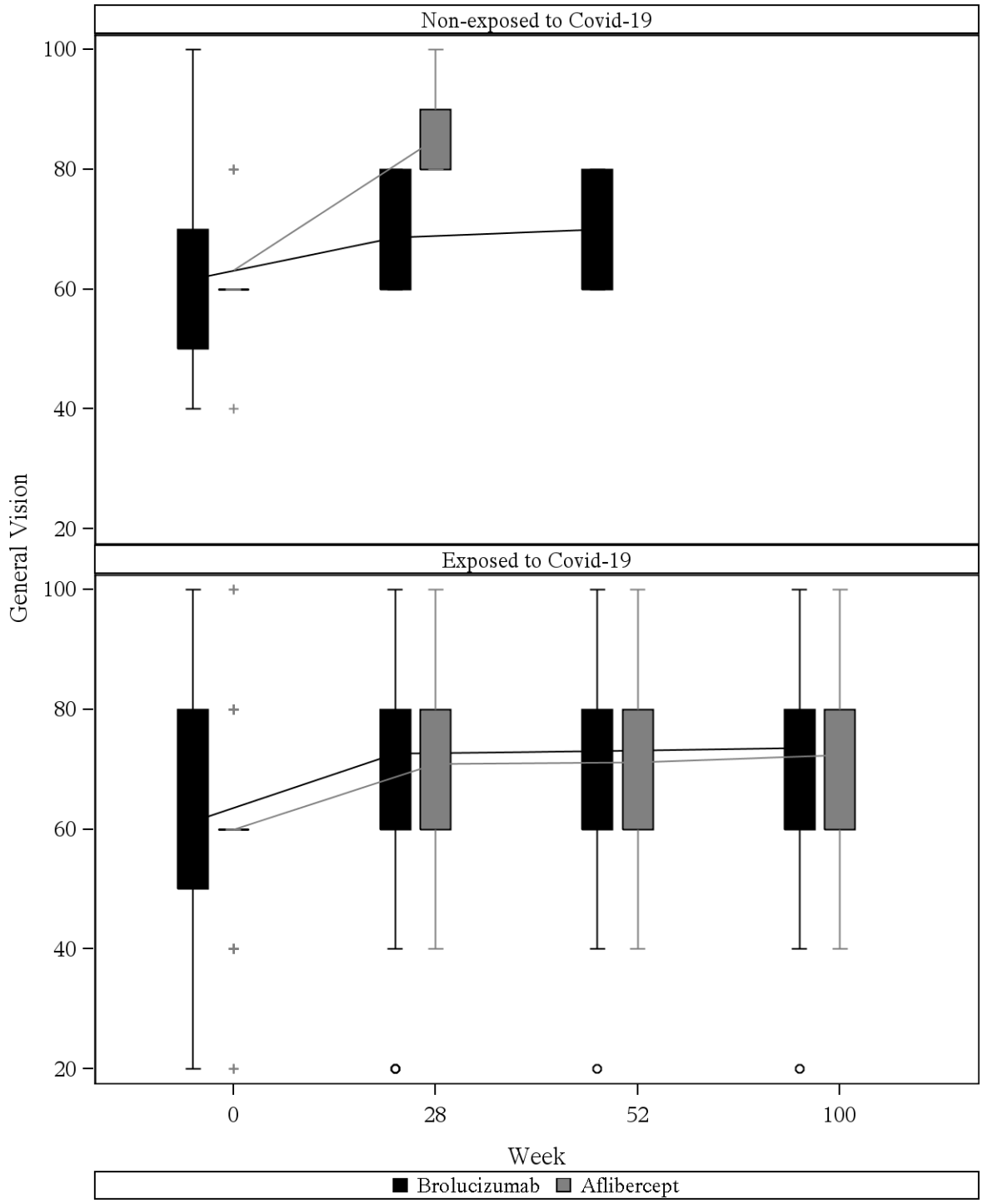


Figure 8.3.13.1.3 VFQ by exposure (week 100) (FAS), boxplot, week 100, General Vision for Pooled Analysis

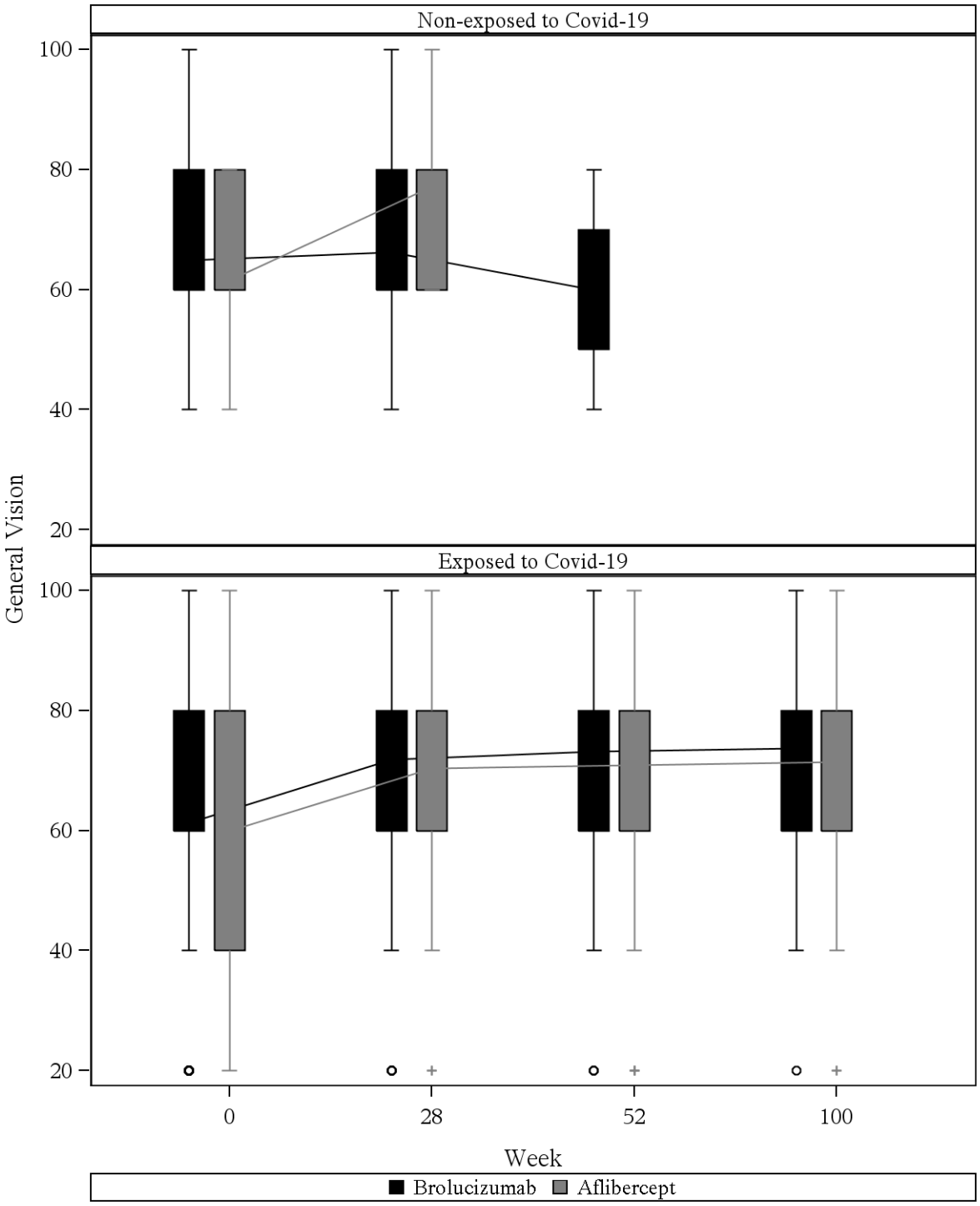
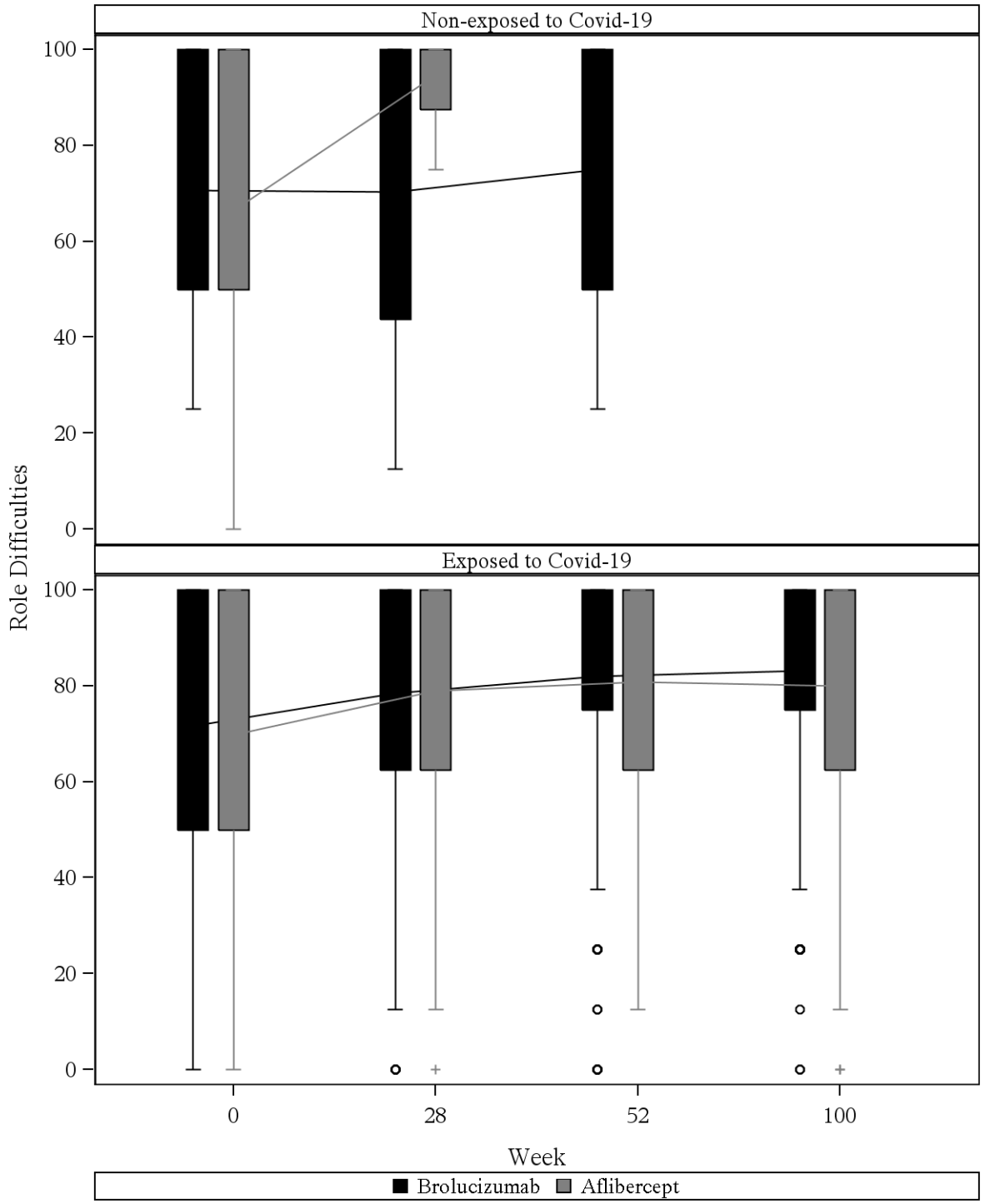


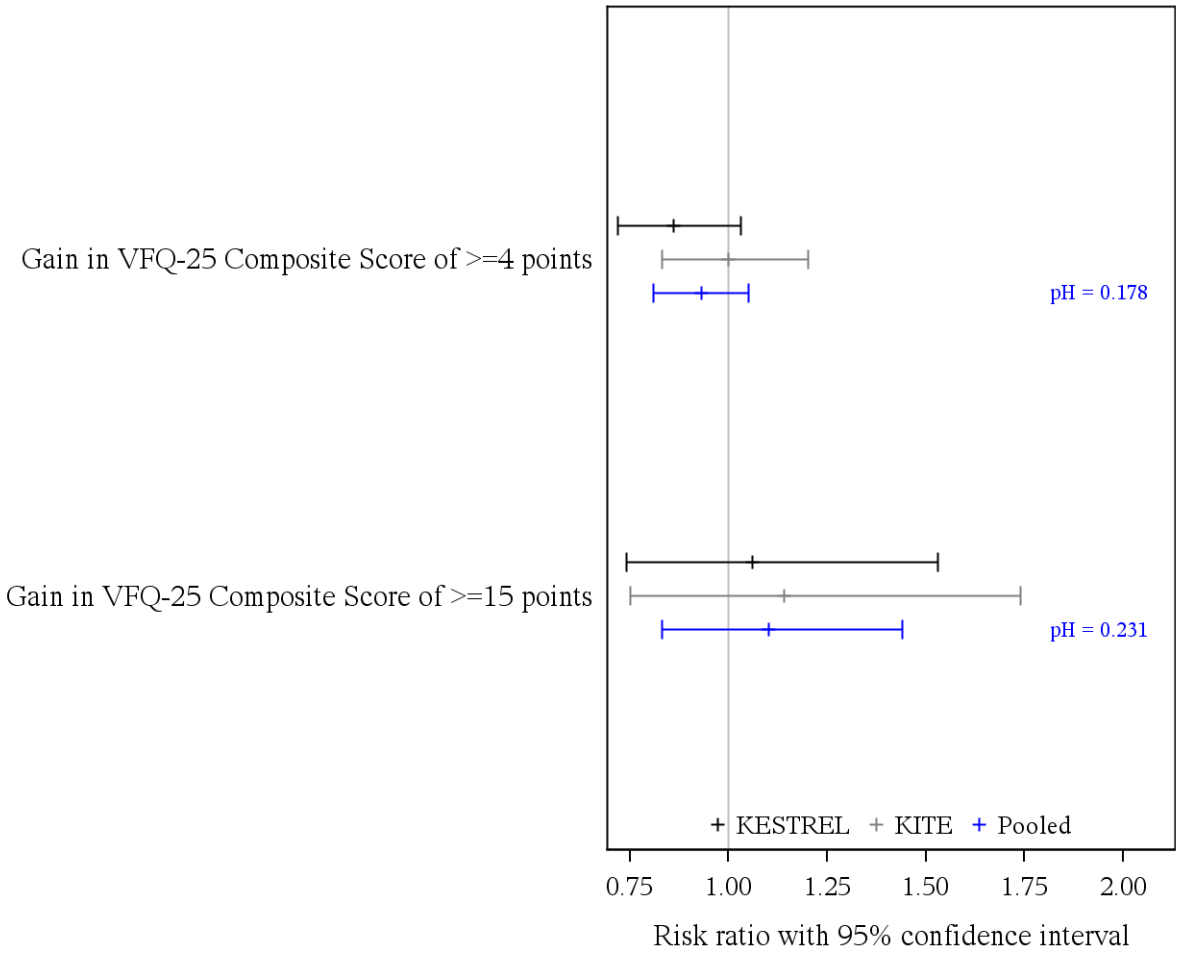
Figure 8.3.13.2 VFQ by exposure (week 100) (FAS), boxplot, week 100, Role Difficulties

Figure 8.3.13.2.3 VFQ by exposure (week 100) (FAS), boxplot, week 100, Role Difficulties for Pooled Analysis



9 VFQ: Binary analysis (Gain)

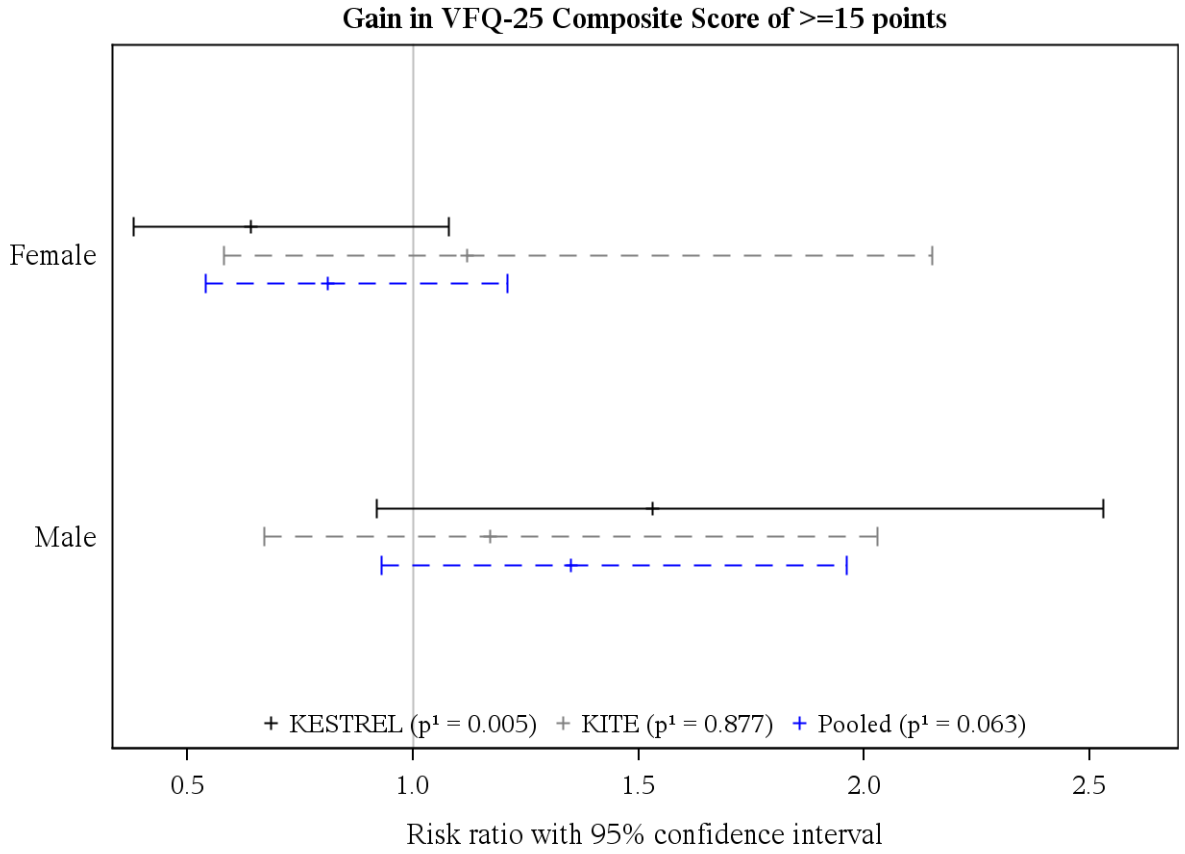
Figure 9.1.1 VFQ - Gain of 4 respectively 15 points (FAS), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 9.1.3 VFQ - Gain of 4 respectively 15 points by gender (FAS), forest plot, week 52

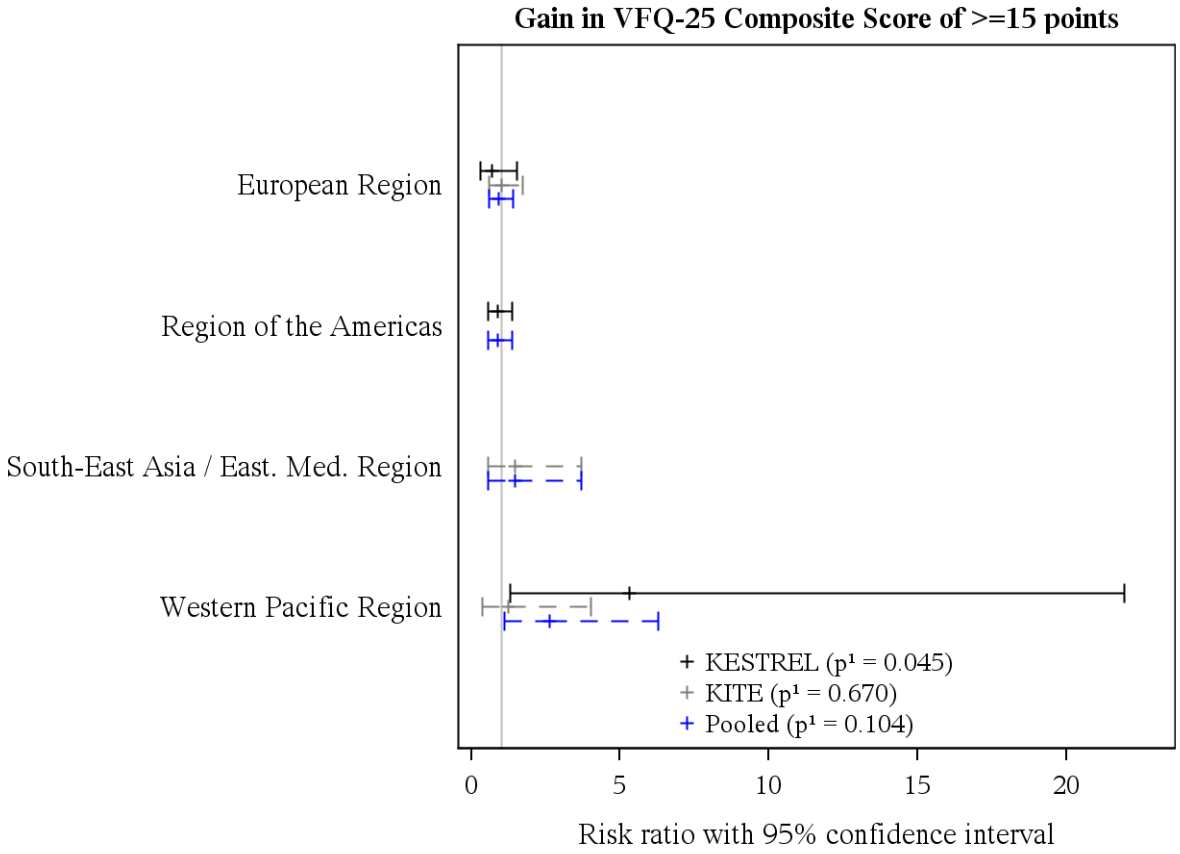
Figure 9.1.3.1 VFQ - Gain of 4 respectively 15 points by gender (FAS), forest plot, week 52, gain of >=15 points



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.231$

Figure 9.1.5 VFQ - Gain of 4 respectively 15 points by region (FAS), forest plot, week 52

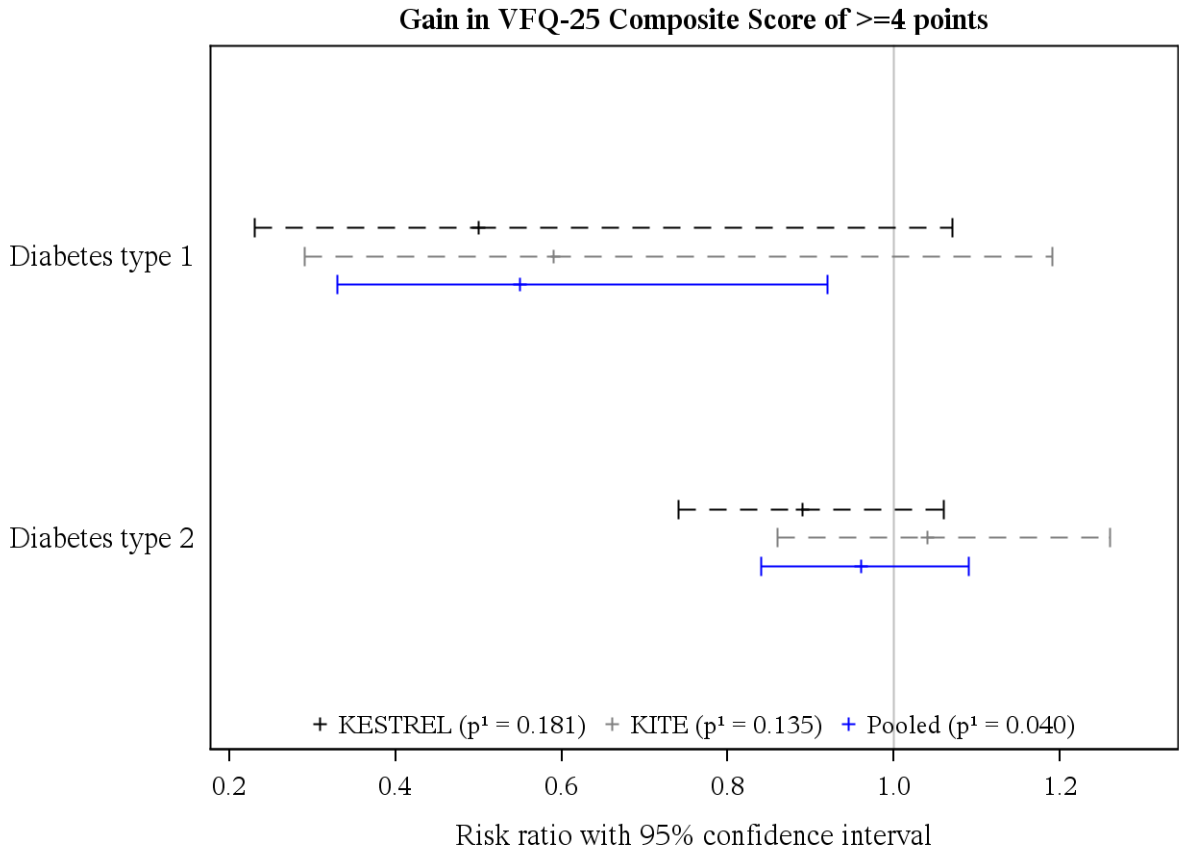
Figure 9.1.5.1 VFQ - Gain of 4 respectively 15 points by region (FAS), forest plot, week 52, gain of >=15 points



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.231$

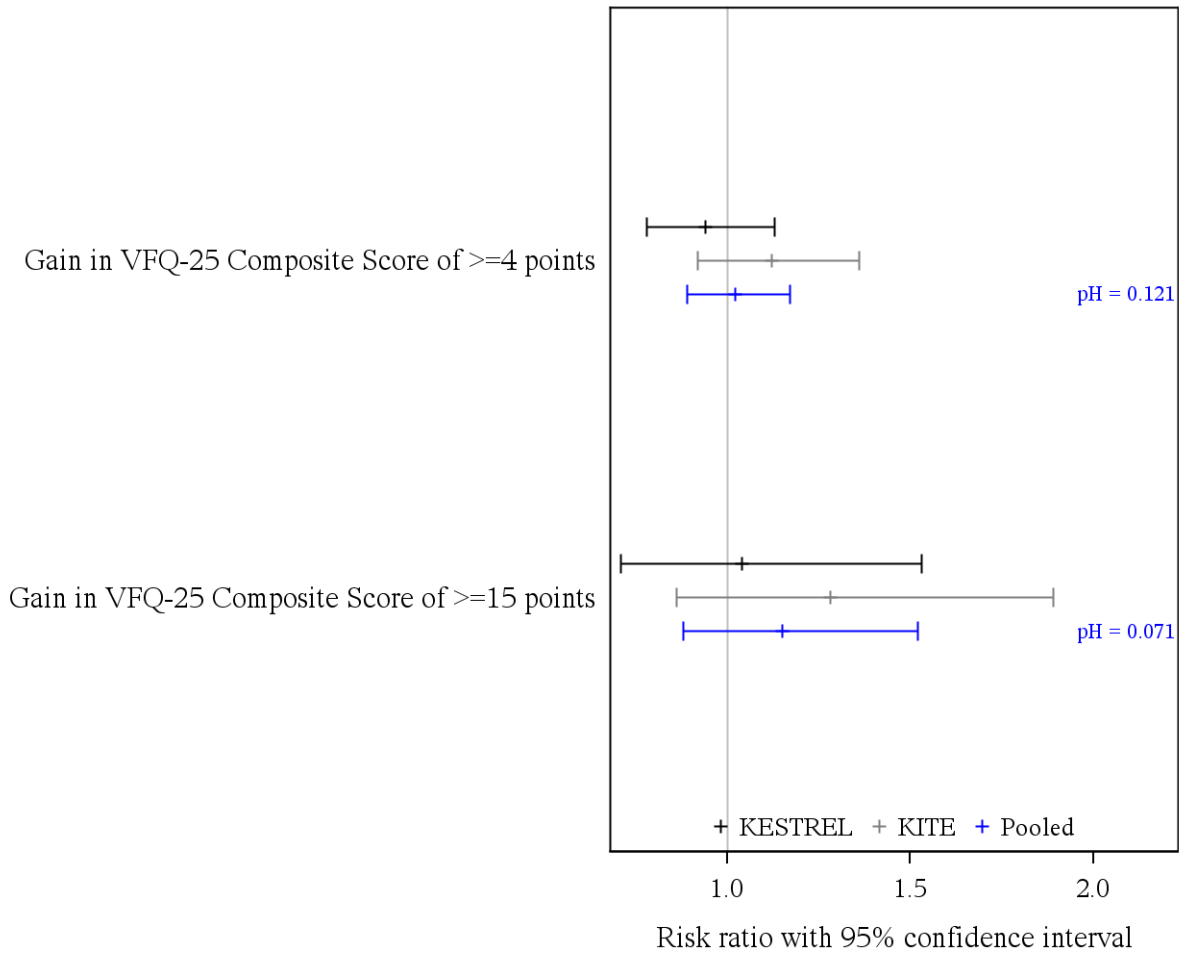
Figure 9.1.6 VFQ - Gain of 4 respectively 15 points by diabetes type (FAS), forest plot, week 52

Figure 9.1.6.1 VFQ - Gain of 4 respectively 15 points by diabetes type (FAS), forest plot, week 52, gain of >=4 points



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.178$

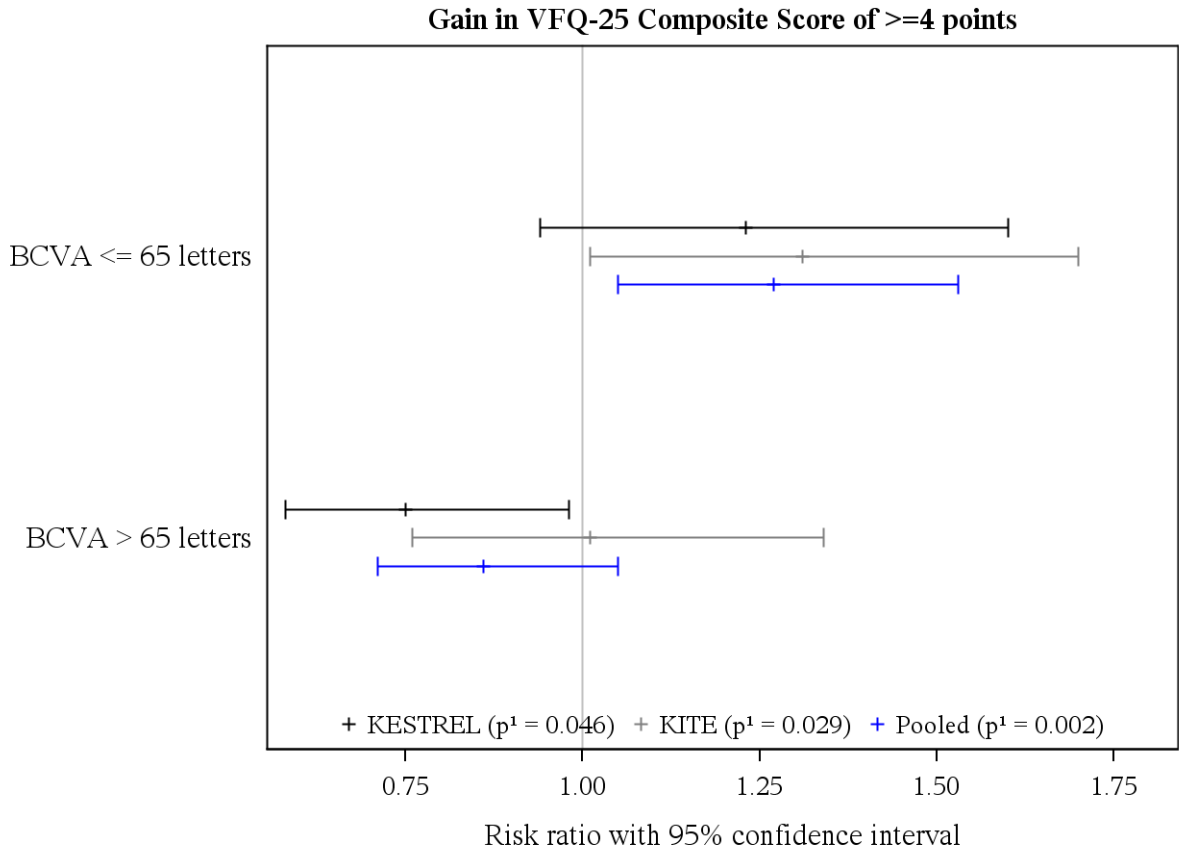
Figure 9.2.1 VFQ - Gain of 4 respectively 15 points (FAS), forest plot, week 100



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 9.2.4 VFQ - Gain of 4 respectively 15 points by BCVA (FAS), forest plot, week 100

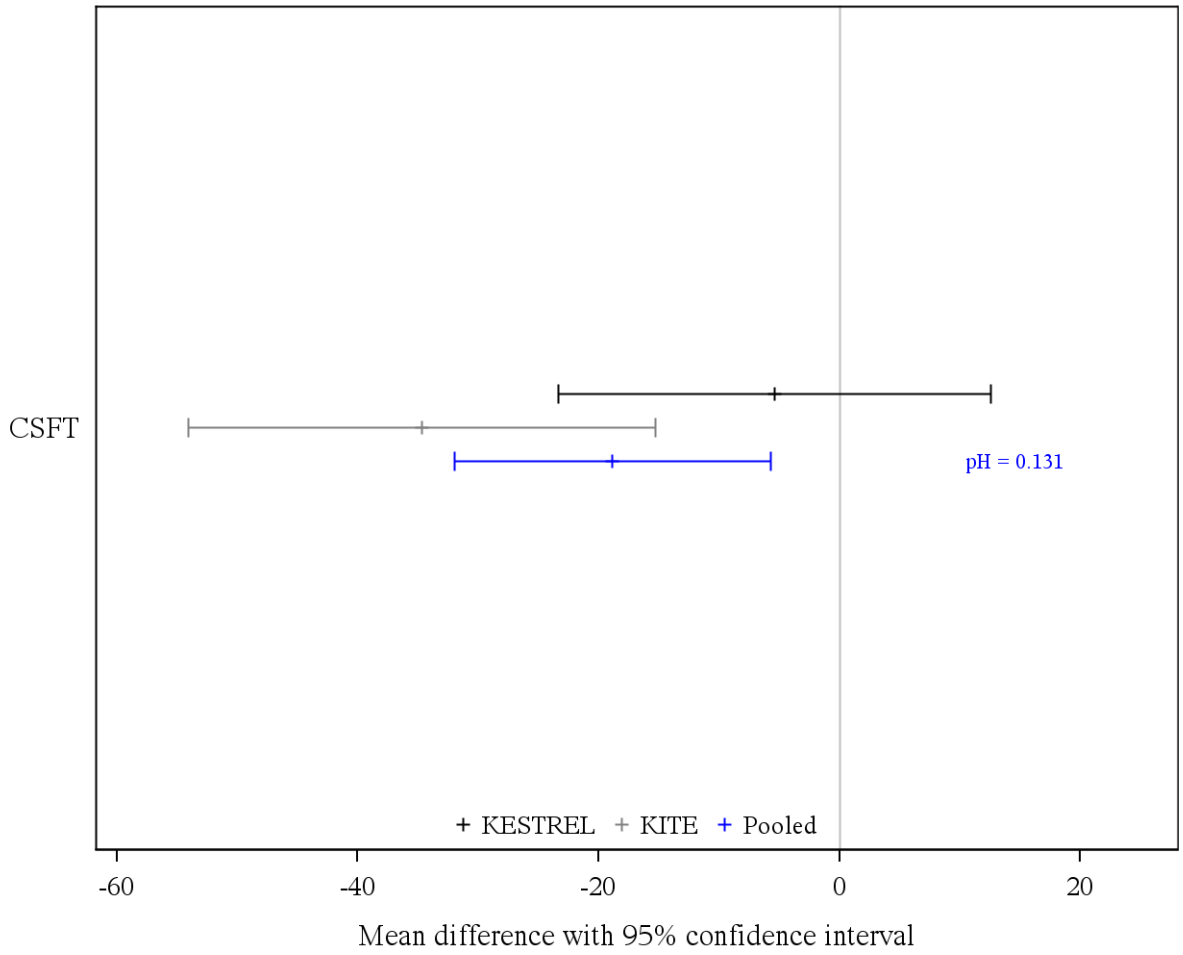
Figure 9.2.4.1 VFQ - Gain of 4 respectively 15 points by BCVA (FAS), forest plot, week 100, gain of >=4 points



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.121$

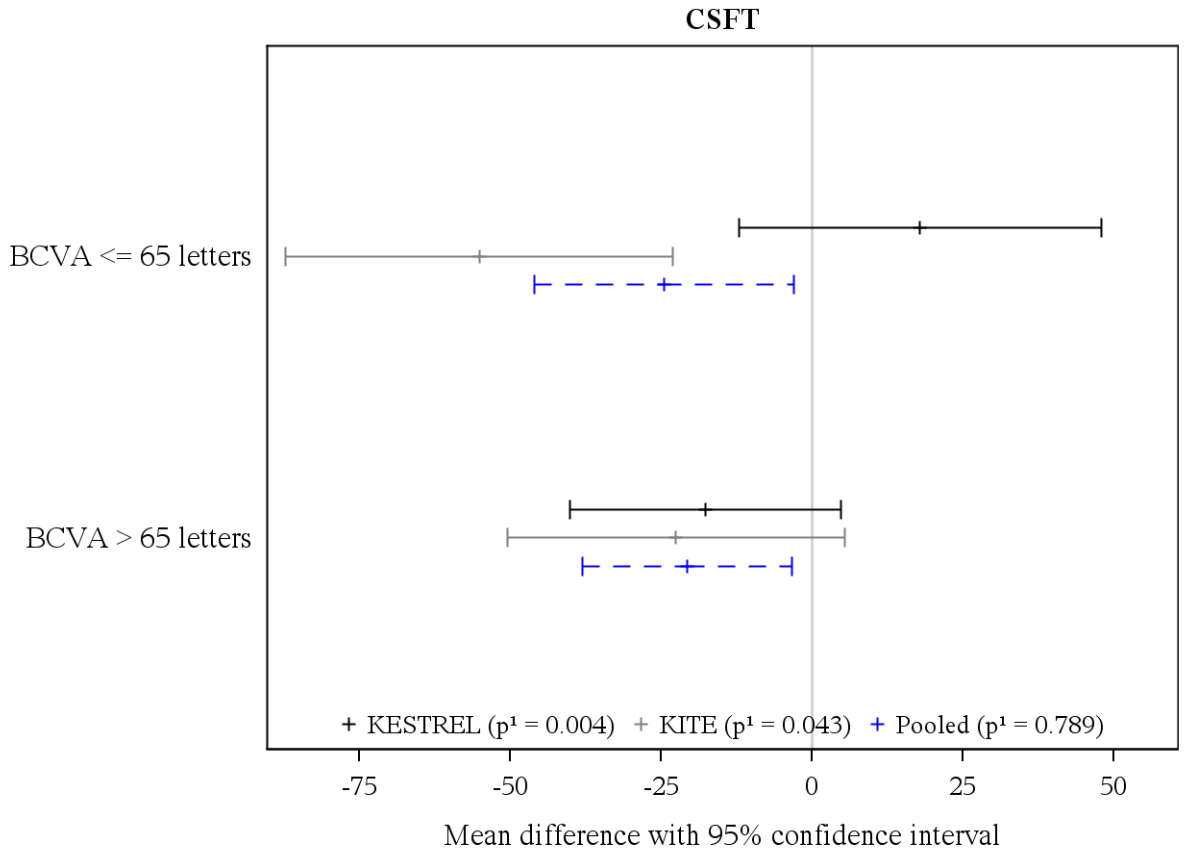
10 CSFT: Continuous analysis

Figure 10.1.1 CSFT (FAS), forest plot, week 52



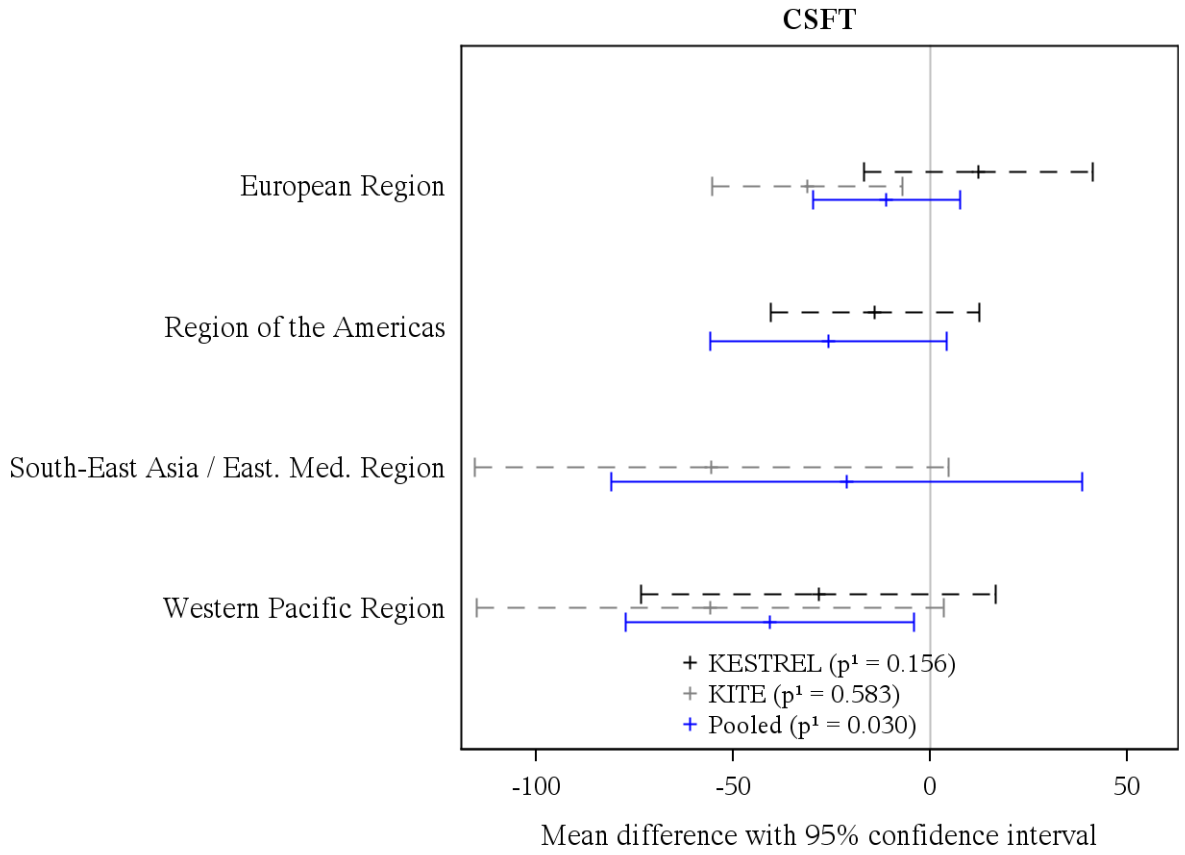
p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 10.1.4 CSFT by BCVA (FAS), forest plot, week 52



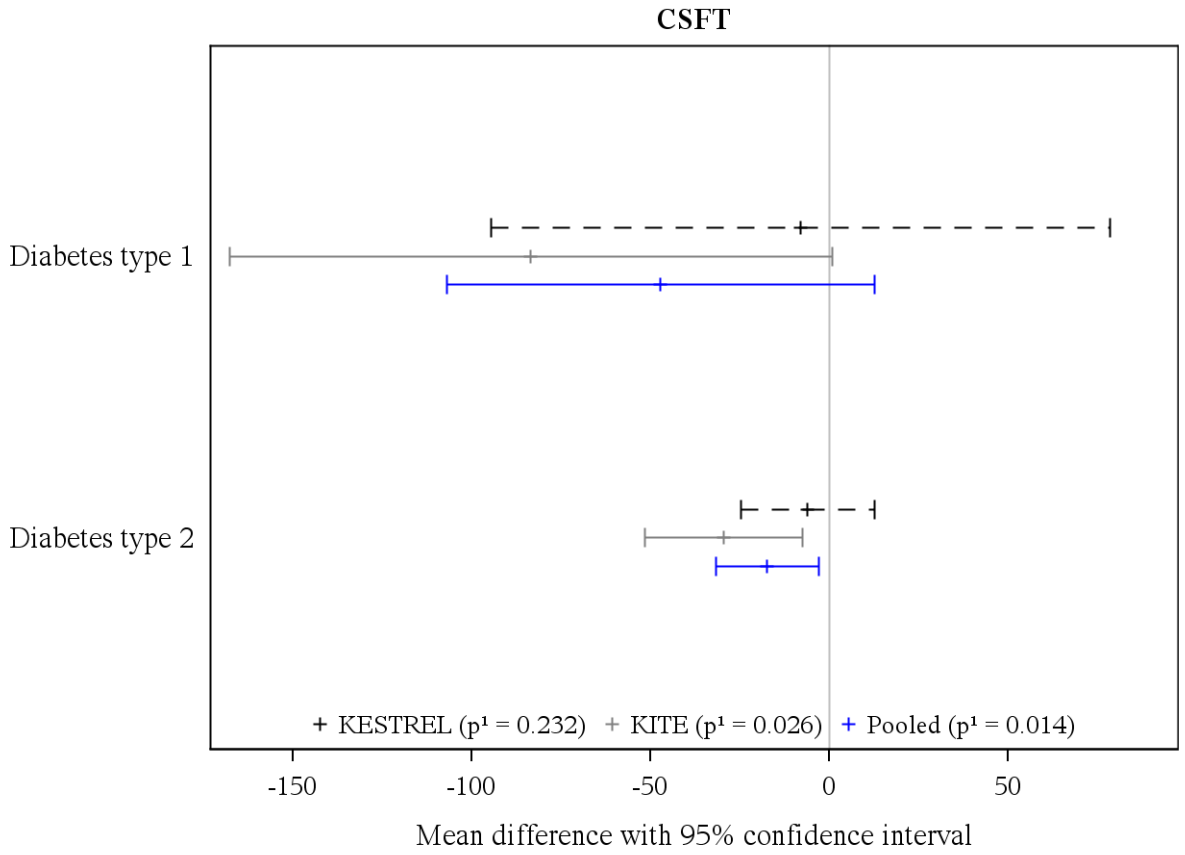
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.131$

Figure 10.1.5 CSFT by region (FAS), forest plot, week 52



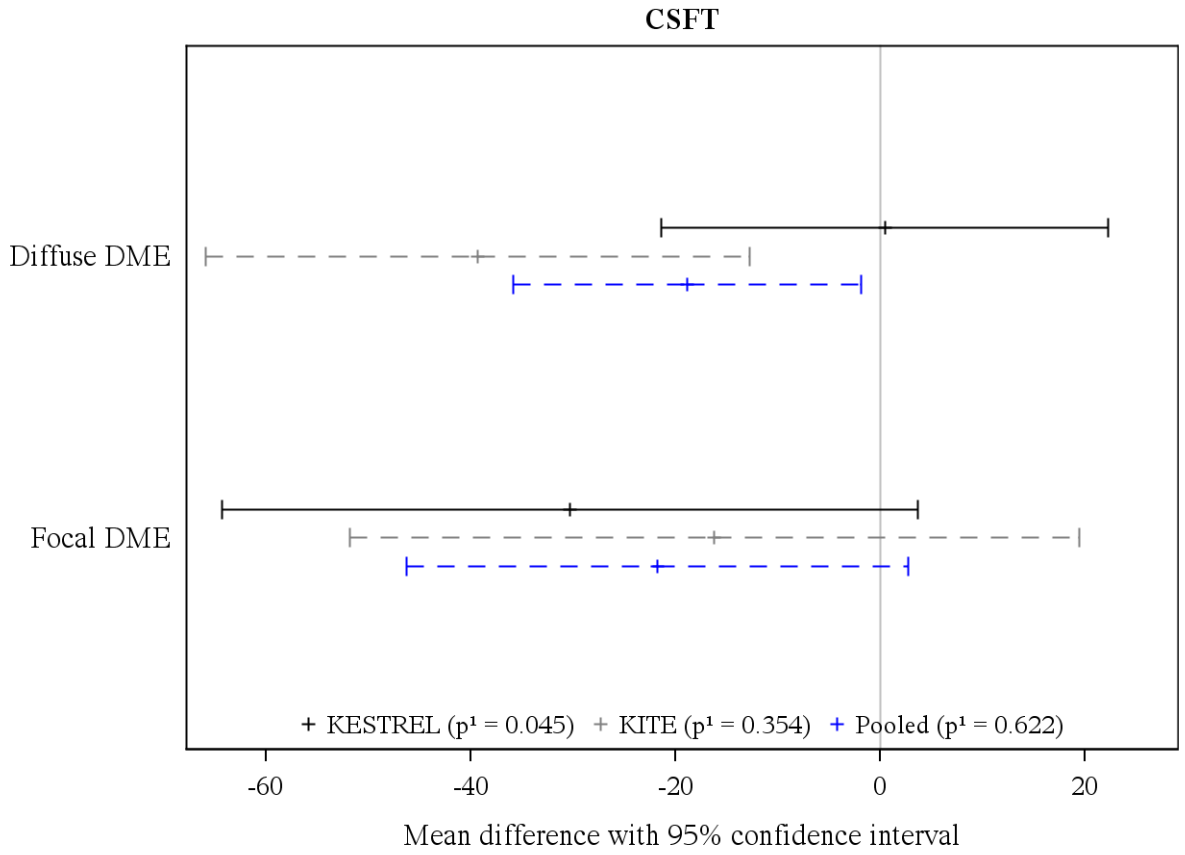
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.131$

Figure 10.1.6 CSFT by diabetes type (FAS), forest plot, week 52



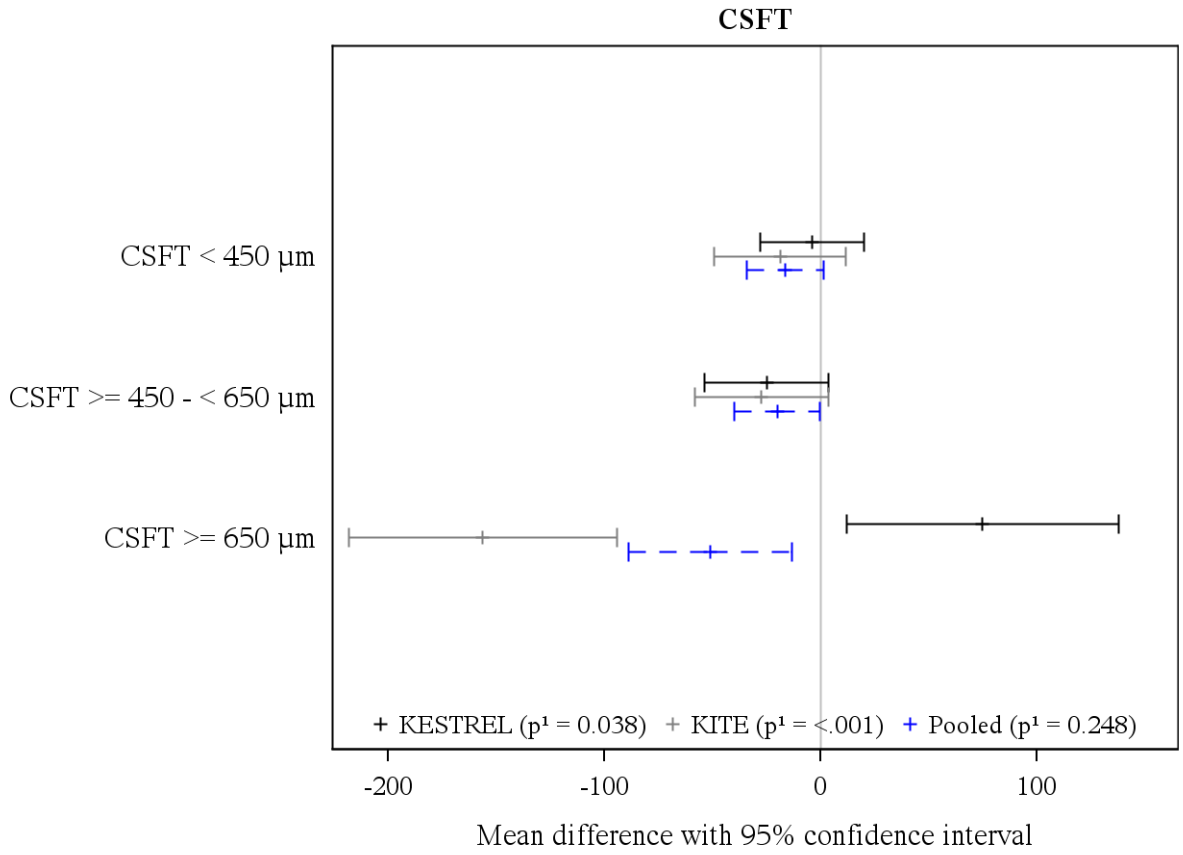
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.131$

Figure 10.1.9 CSFT by DME type (FAS), forest plot, week 52



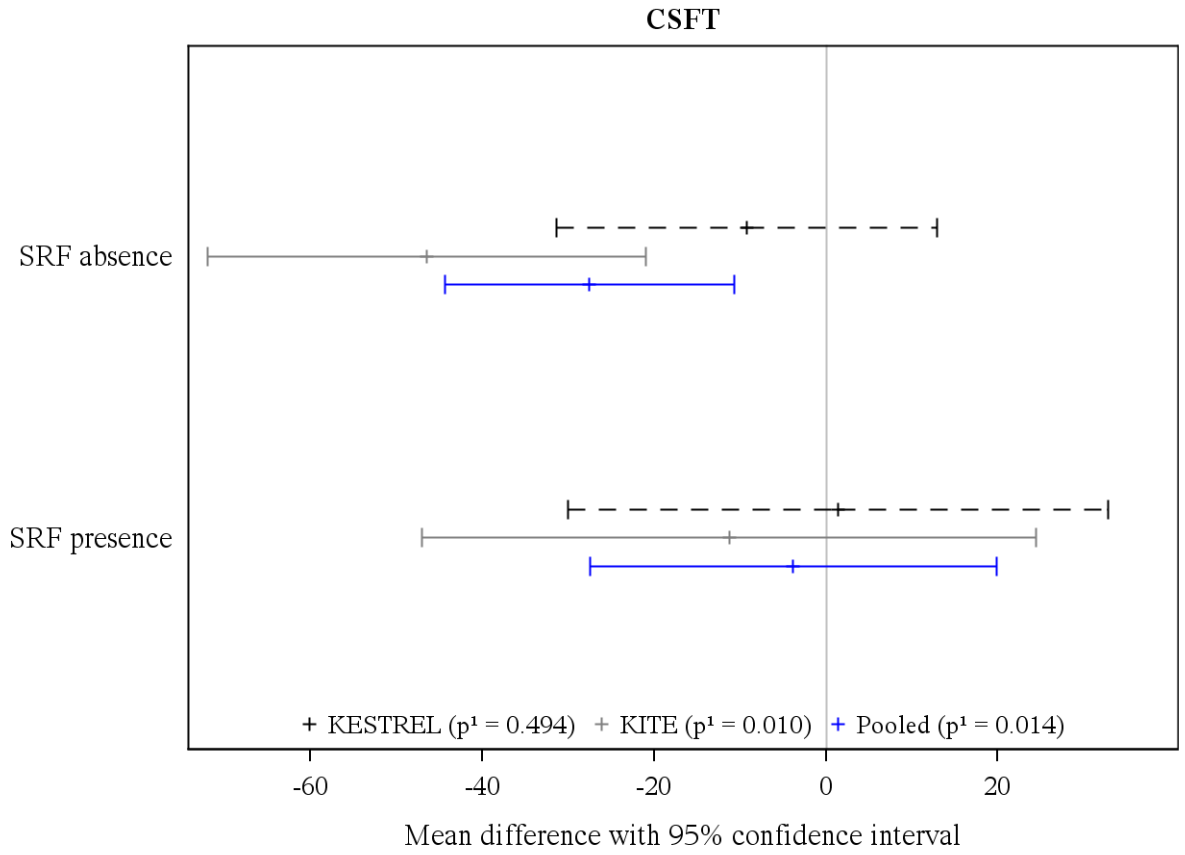
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.131$

Figure 10.1.10 CSFT by CSFT (FAS), forest plot, week 52



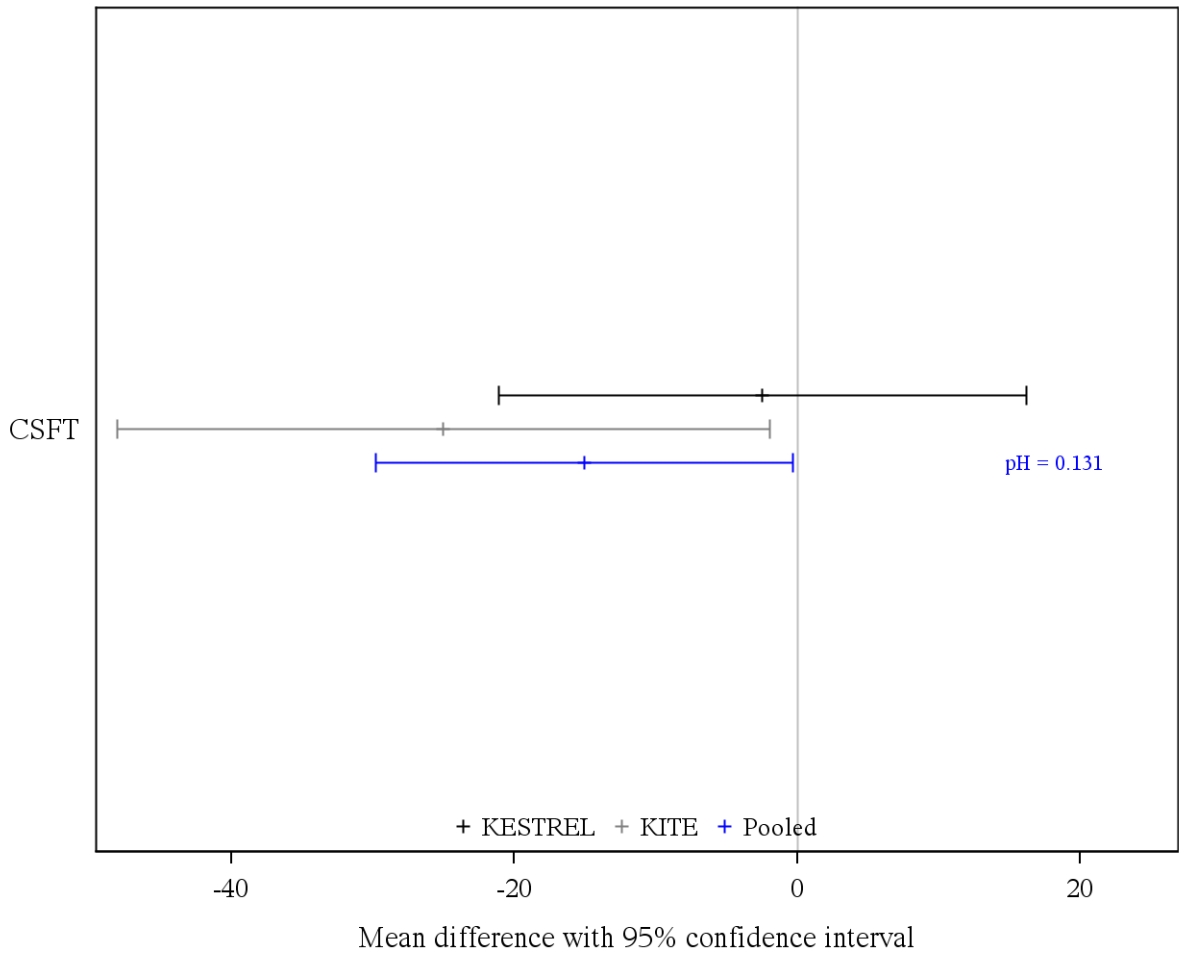
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.131$

Figure 10.1.11 CSFT by status of SRF (FAS), forest plot, week 52



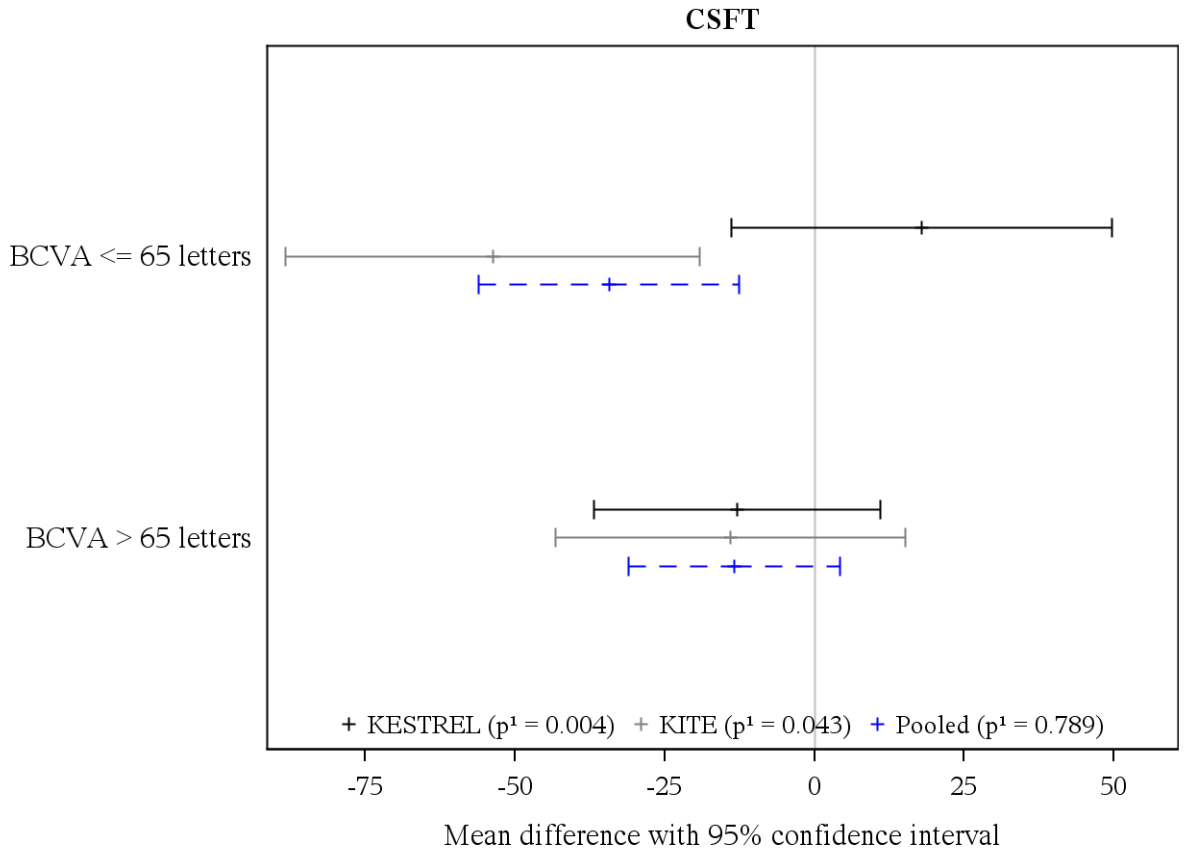
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.131$

Figure 10.2.1 CSFT (FAS), forest plot, week 100



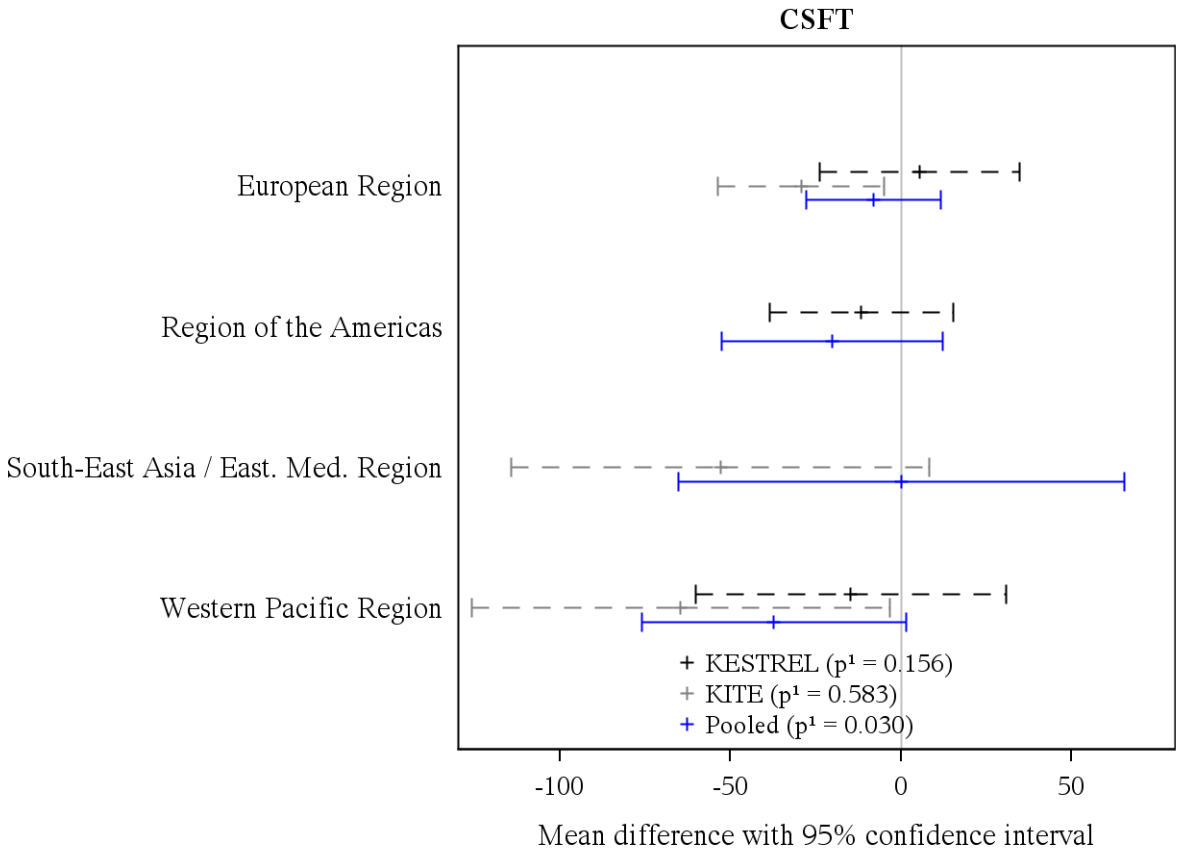
p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 10.2.4 CSFT by BCVA (FAS), forest plot, week 100



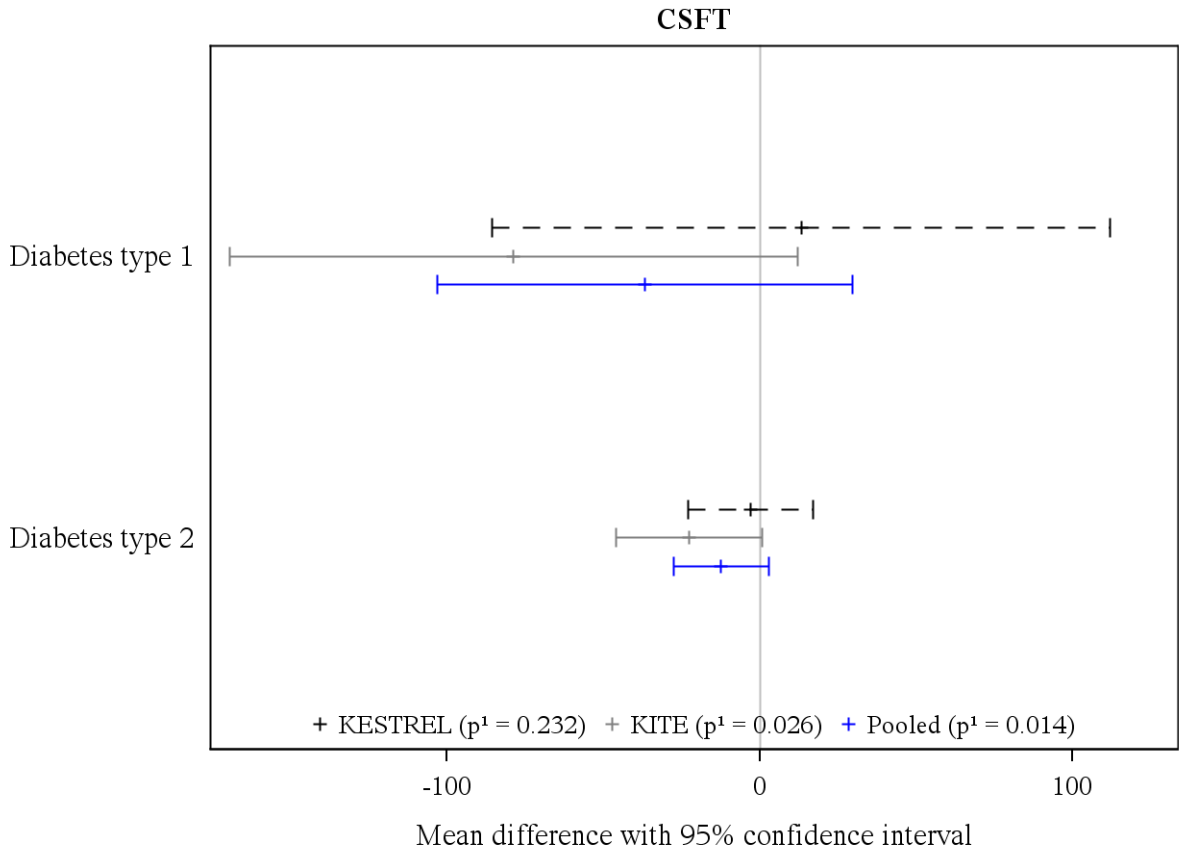
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.131$

Figure 10.2.5 CSFT by region (FAS), forest plot, week 100



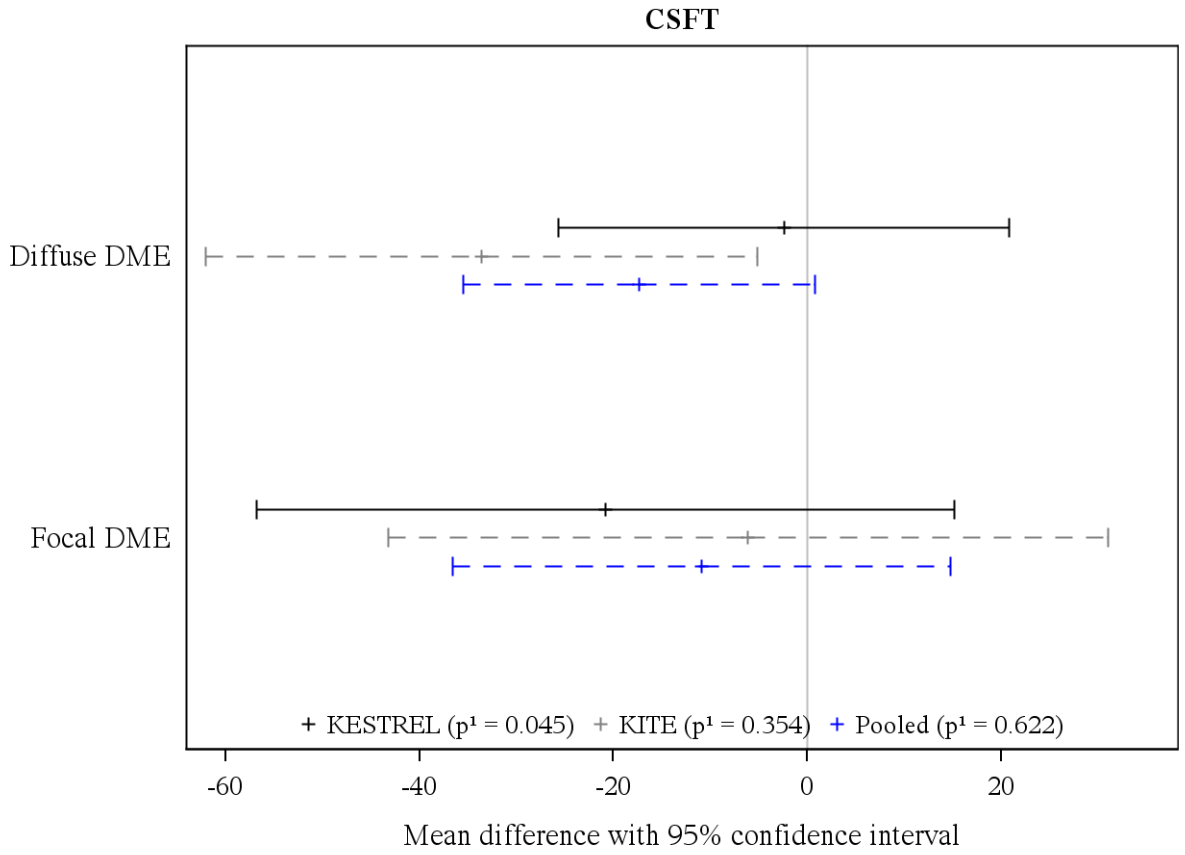
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.131$

Figure 10.2.6 CSFT by diabetes type (FAS), forest plot, week 100



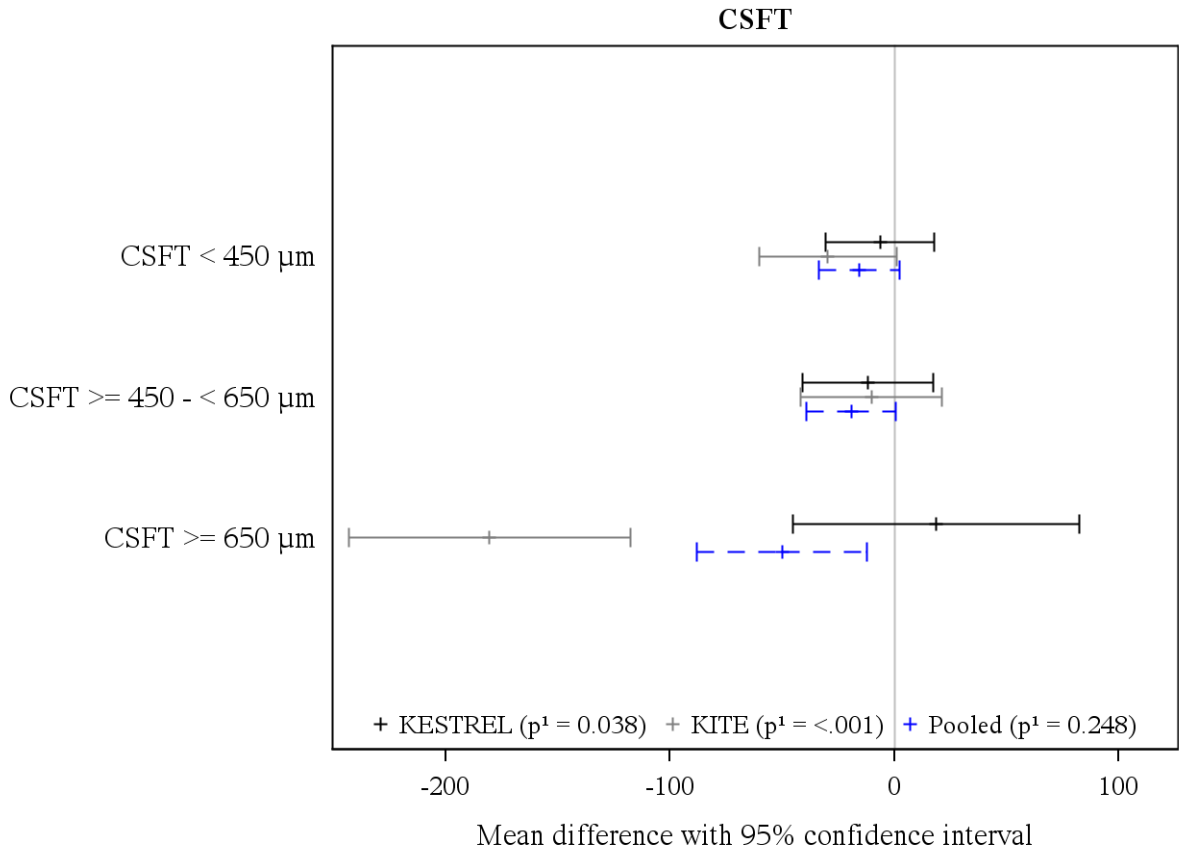
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.131$

Figure 10.2.9 CSFT by DME type (FAS), forest plot, week 100



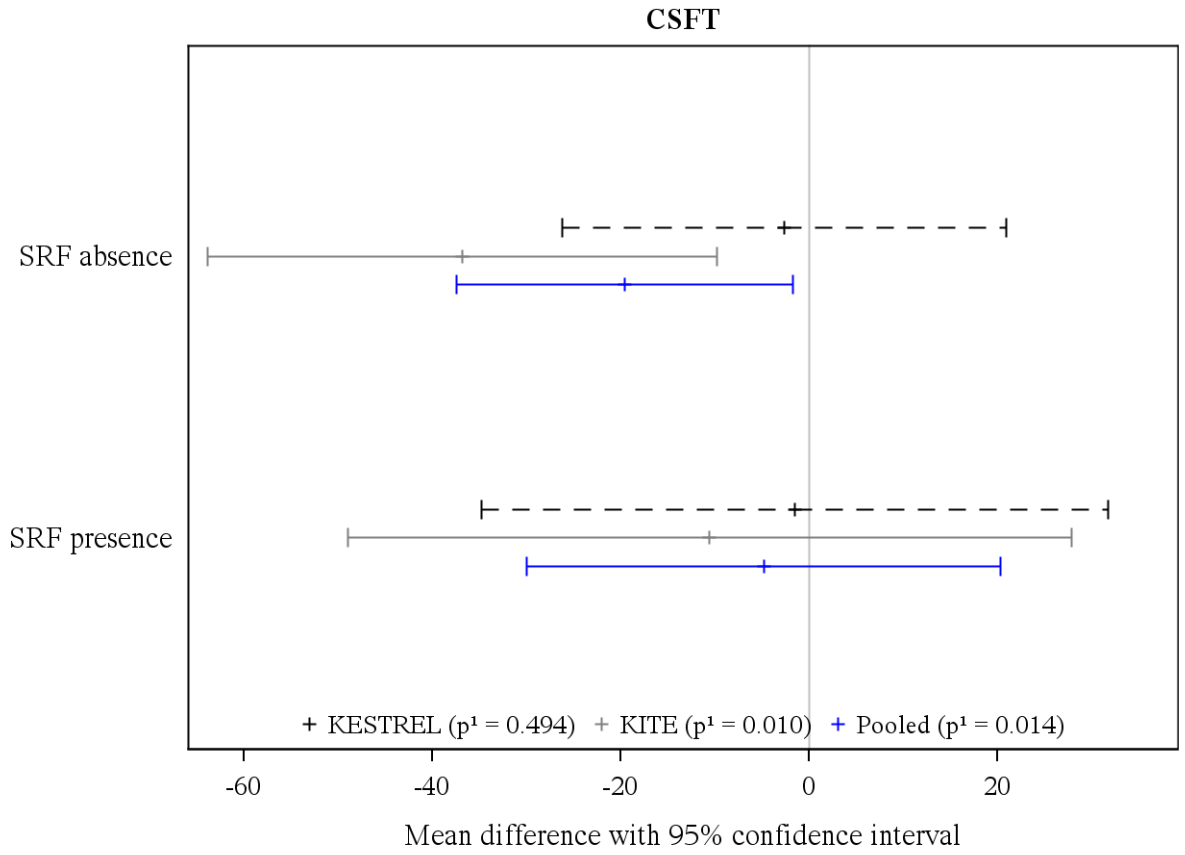
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.131$

Figure 10.2.10 CSFT by CSFT (FAS), forest plot, week 100



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.131$

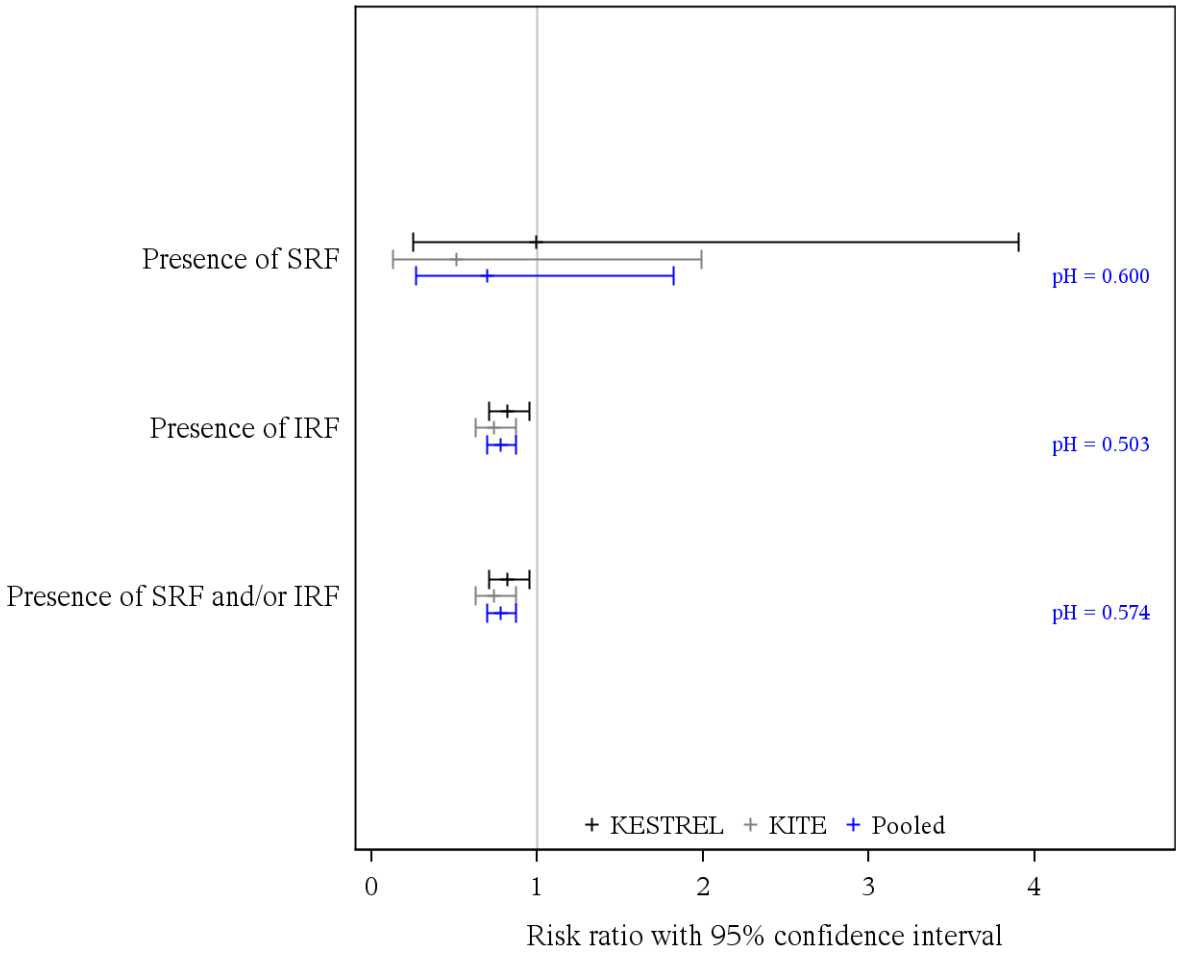
Figure 10.2.11 CSFT by status of SRF (FAS), forest plot, week 100



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.131$

11 Presence of SRF and/or IRF in the study eye: Binary analysis

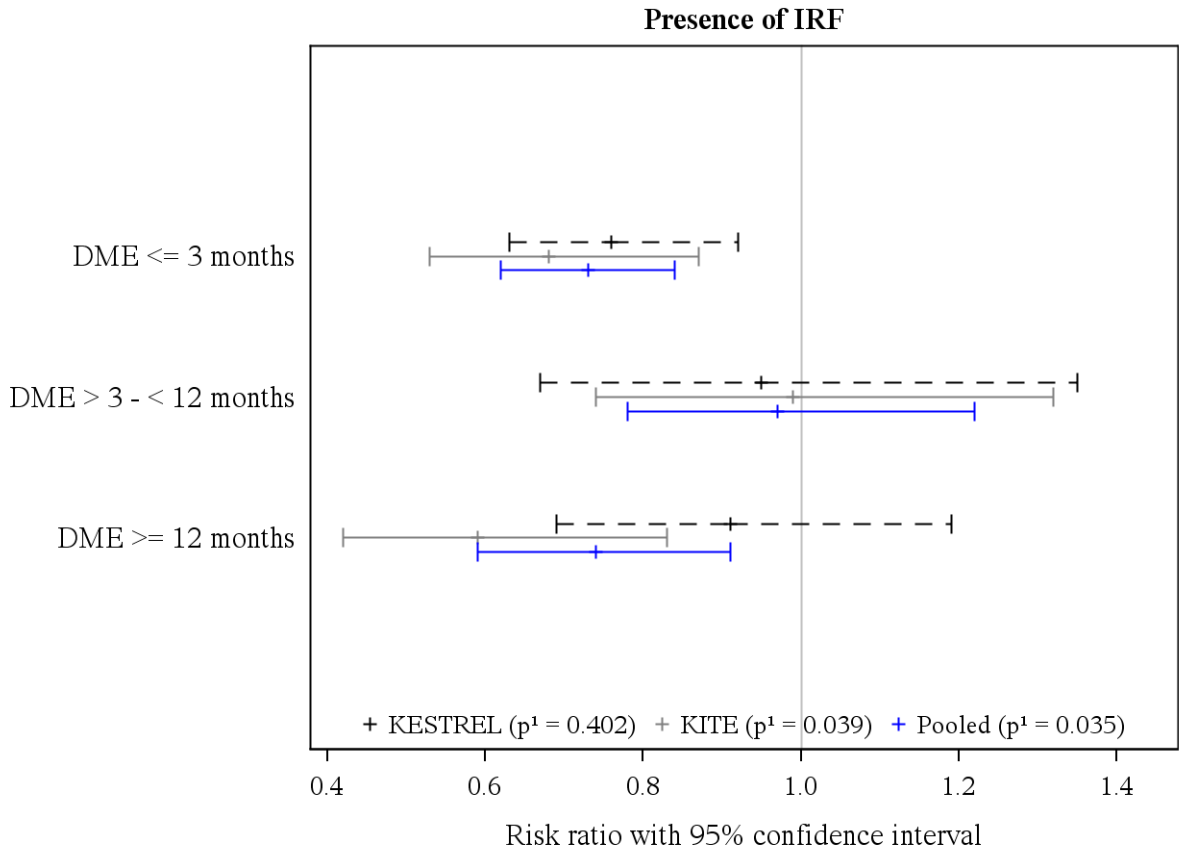
Figure 11.1.1 Presence of SRF and/or IRF in the study eye (FAS), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 11.1.8 Presence of SRF and/or IRF in the study eye by duration of DME (FAS), forest plot, week 52

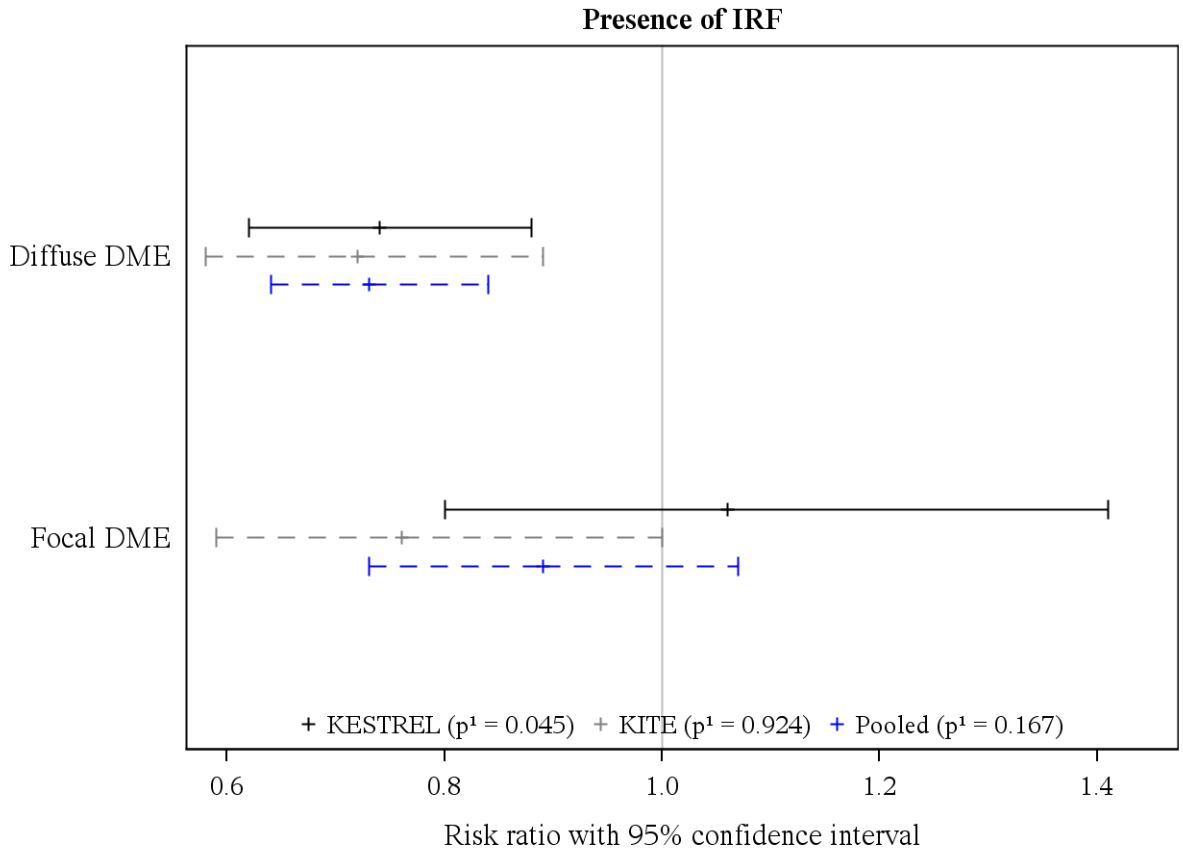
Figure 11.1.8.1 Presence of SRF and/or IRF in the study eye by duration of DME (FAS), forest plot, week 52, Presence of IRF



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.503$

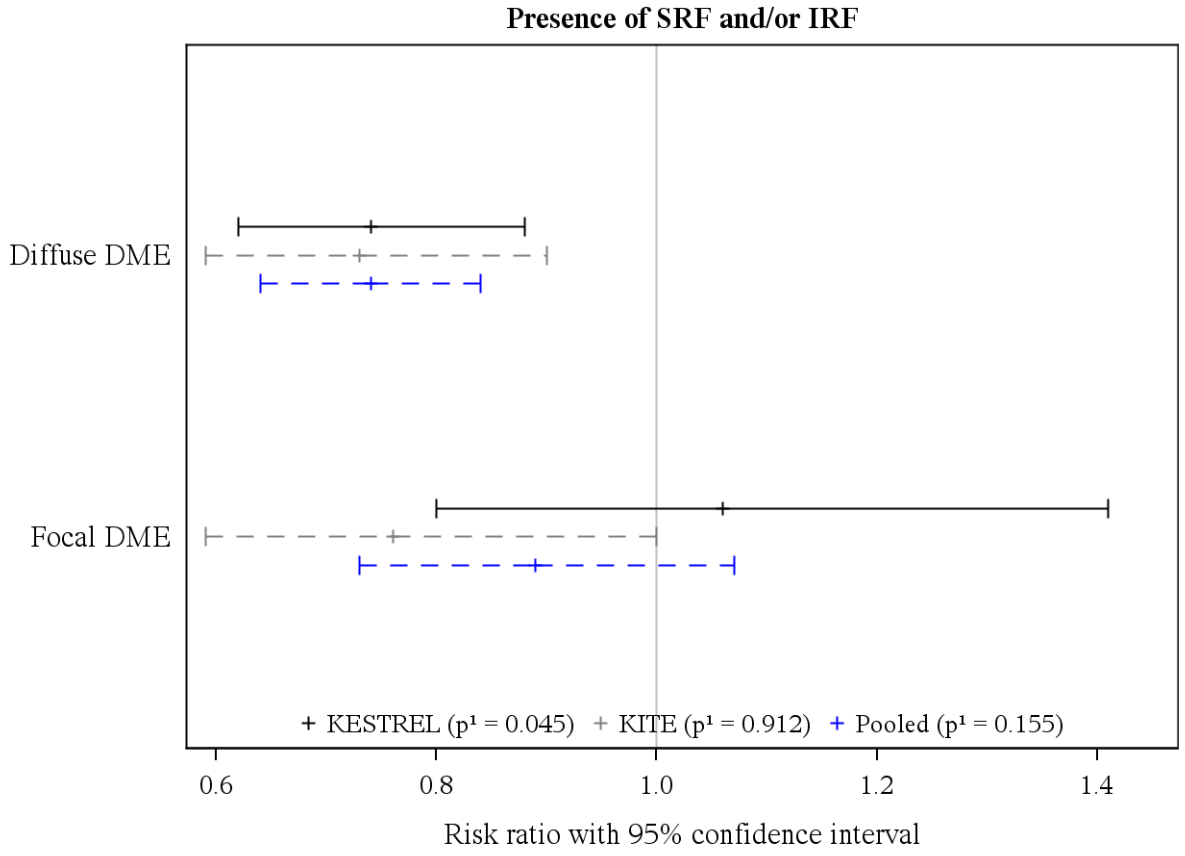
Figure 11.1.9 Presence of SRF and/or IRF in the study eye by DME type (FAS), forest plot, week 52

Figure 11.1.9.1 Presence of SRF and/or IRF in the study eye by DME type (FAS), forest plot, week 52, Presence of IRF



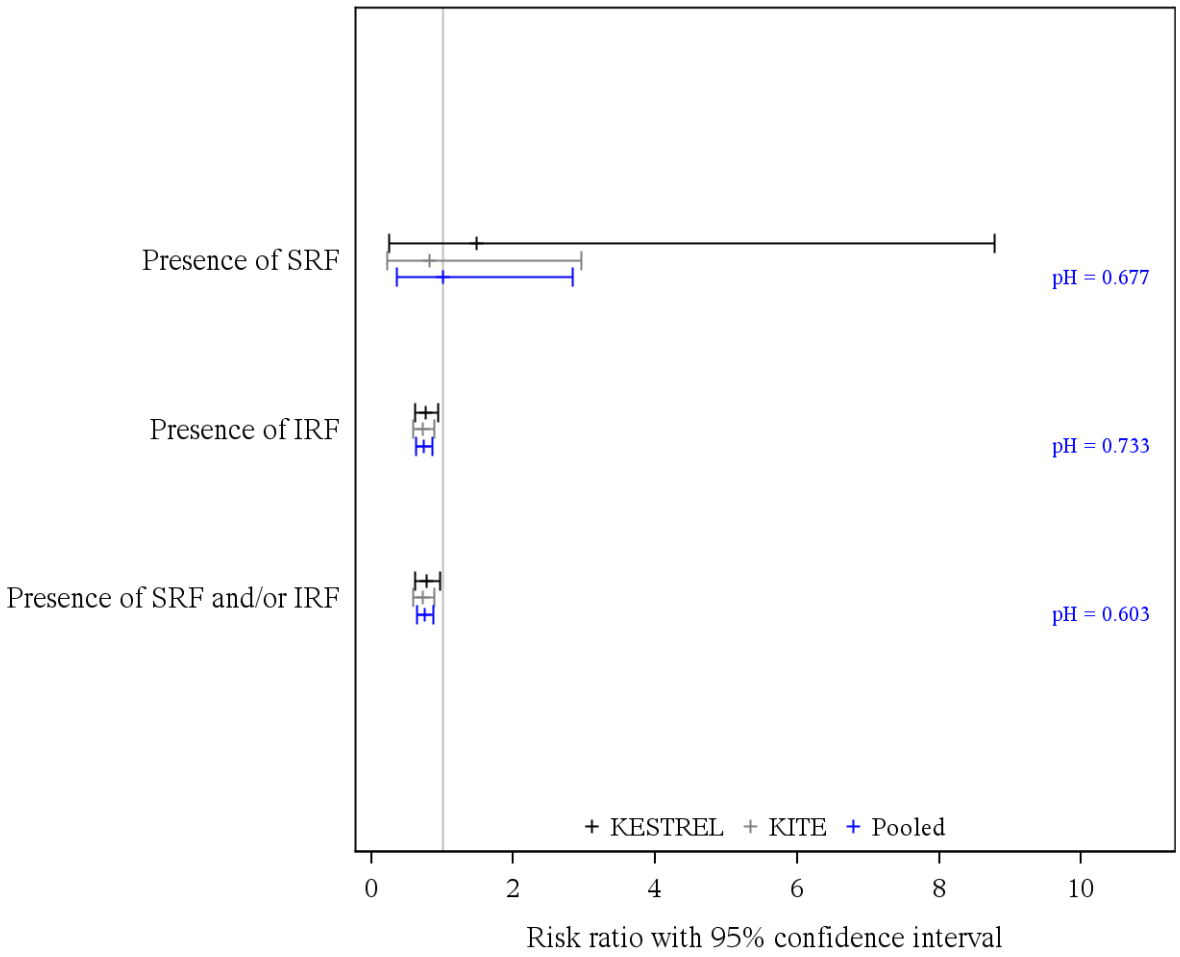
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.503$

Figure 11.1.9.2 Presence of SRF and/or IRF in the study eye by DME type (FAS), forest plot, week 52, Presence of SRF and/or IRF



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.574$

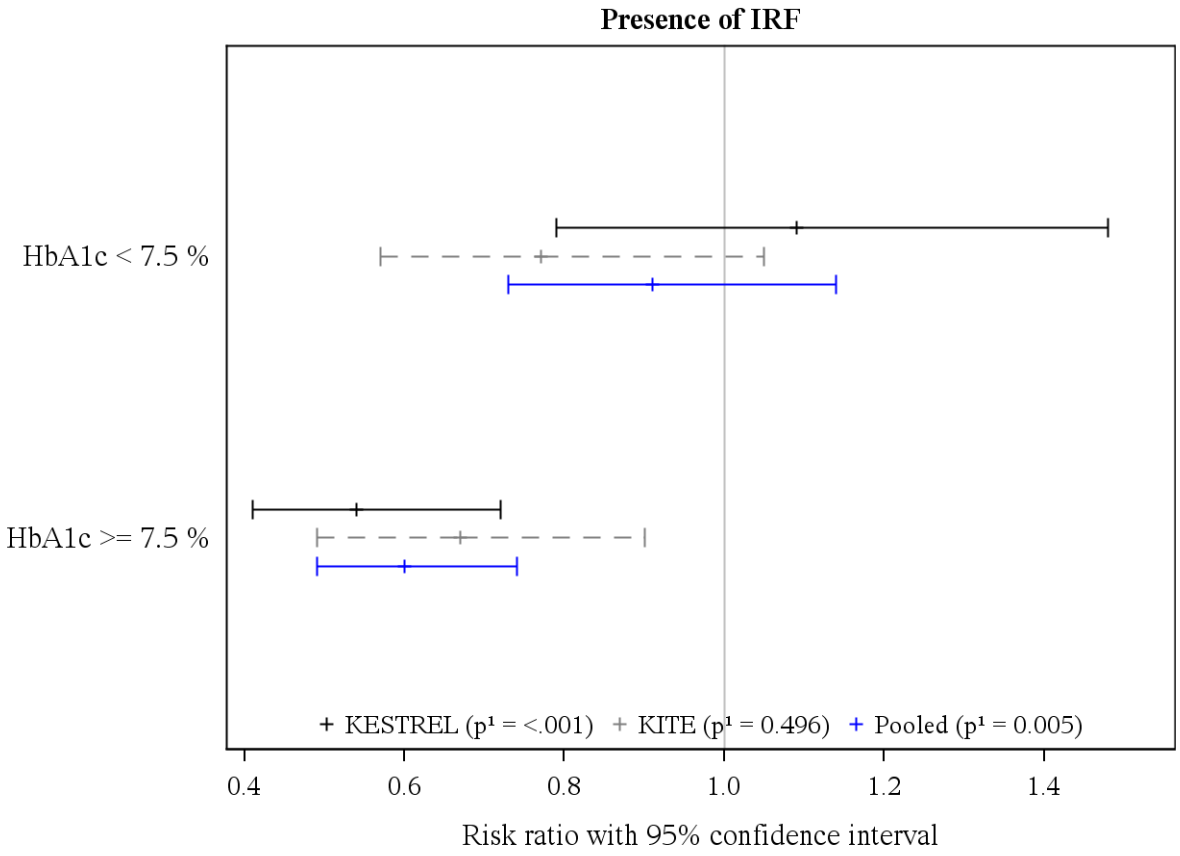
Figure 11.2.1 Presence of SRF and/or IRF in the study eye (FAS), forest plot, week 100



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

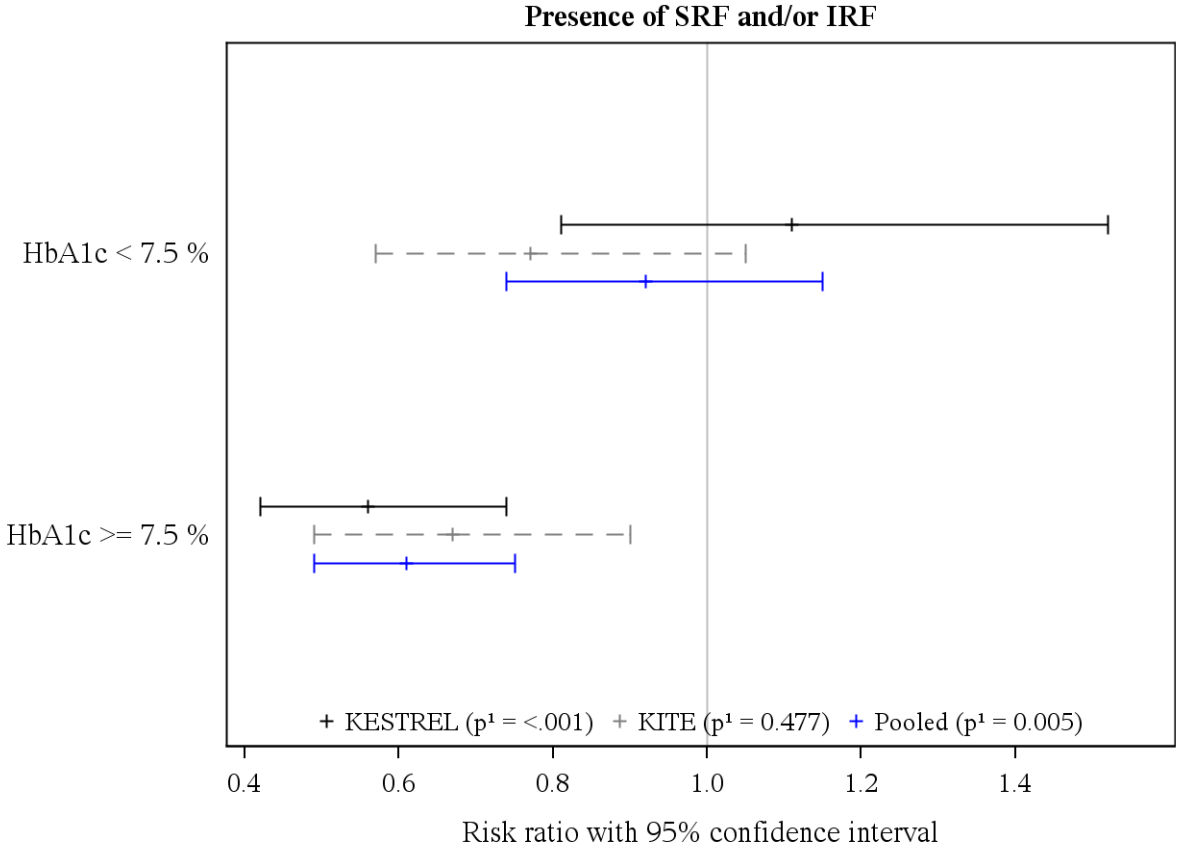
Figure 11.2.7 Presence of SRF and/or IRF in the study eye by HbA1c (FAS), forest plot, week 100

Figure 11.2.7.1 Presence of SRF and/or IRF in the study eye by HbA1c (FAS), forest plot, week 100, Presence of IRF



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.733$

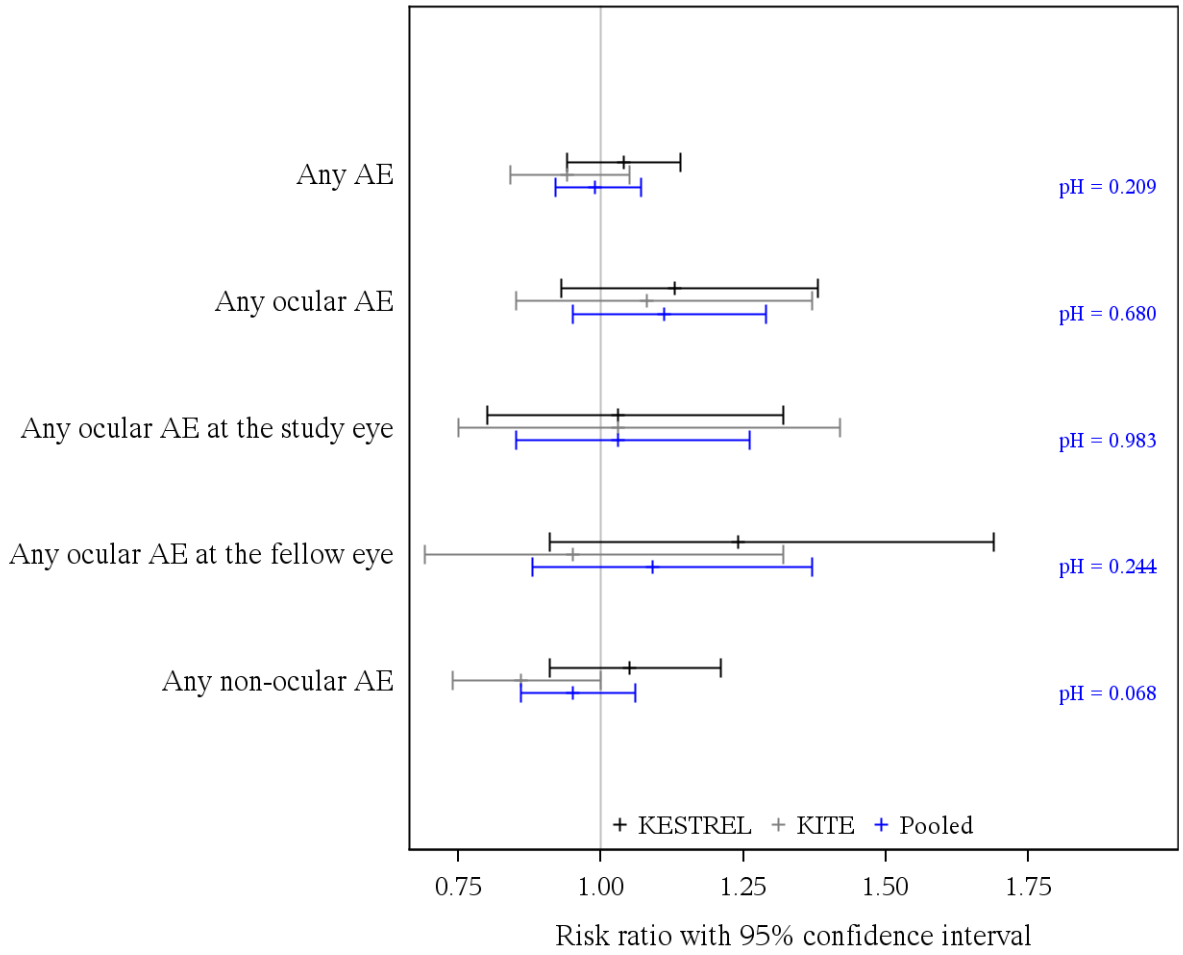
Figure 11.2.7.2 Presence of SRF and/or IRF in the study eye by HbA1c (FAS), forest plot, week 100, Presence of SRF and/or IRF



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.603$

12 Safety analysis: Any adverse event

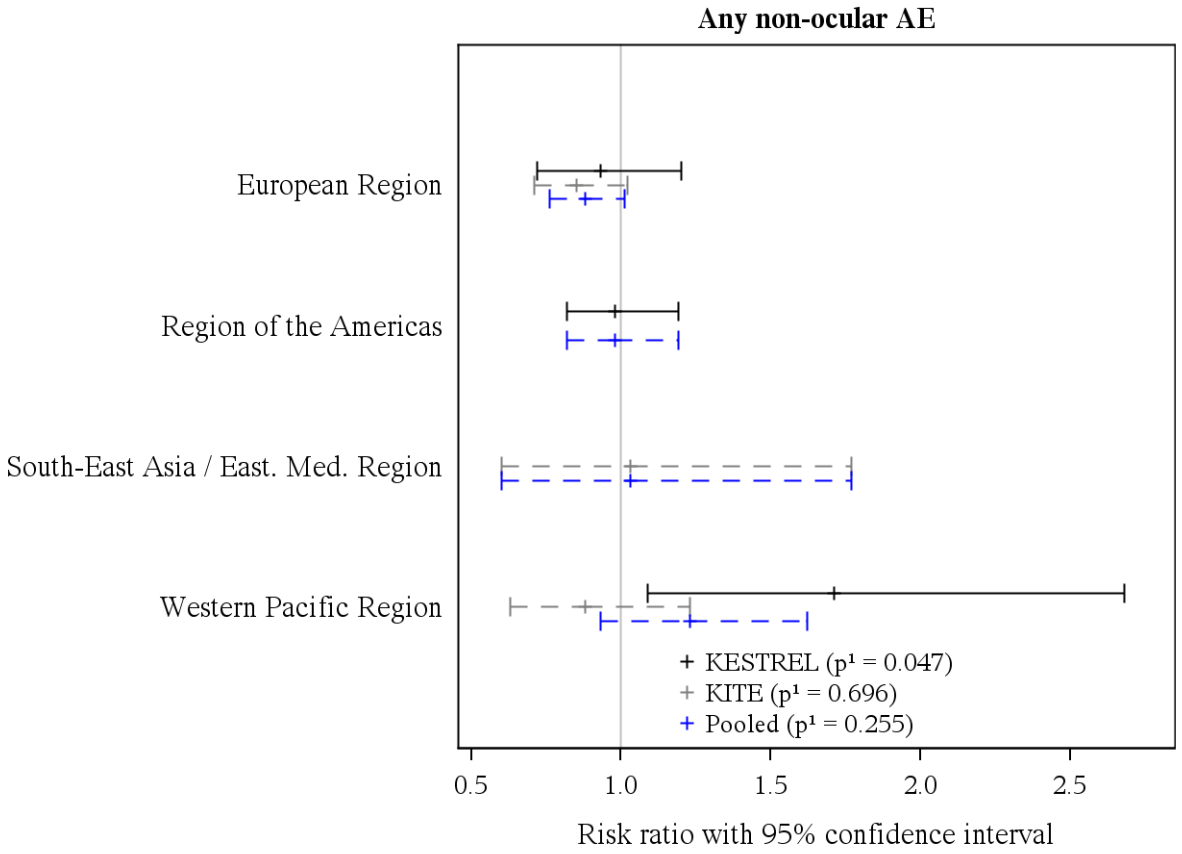
Figure 12.1.1 Any adverse event (SAF), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 12.1.5 Any adverse event by region (SAF), forest plot, week 52

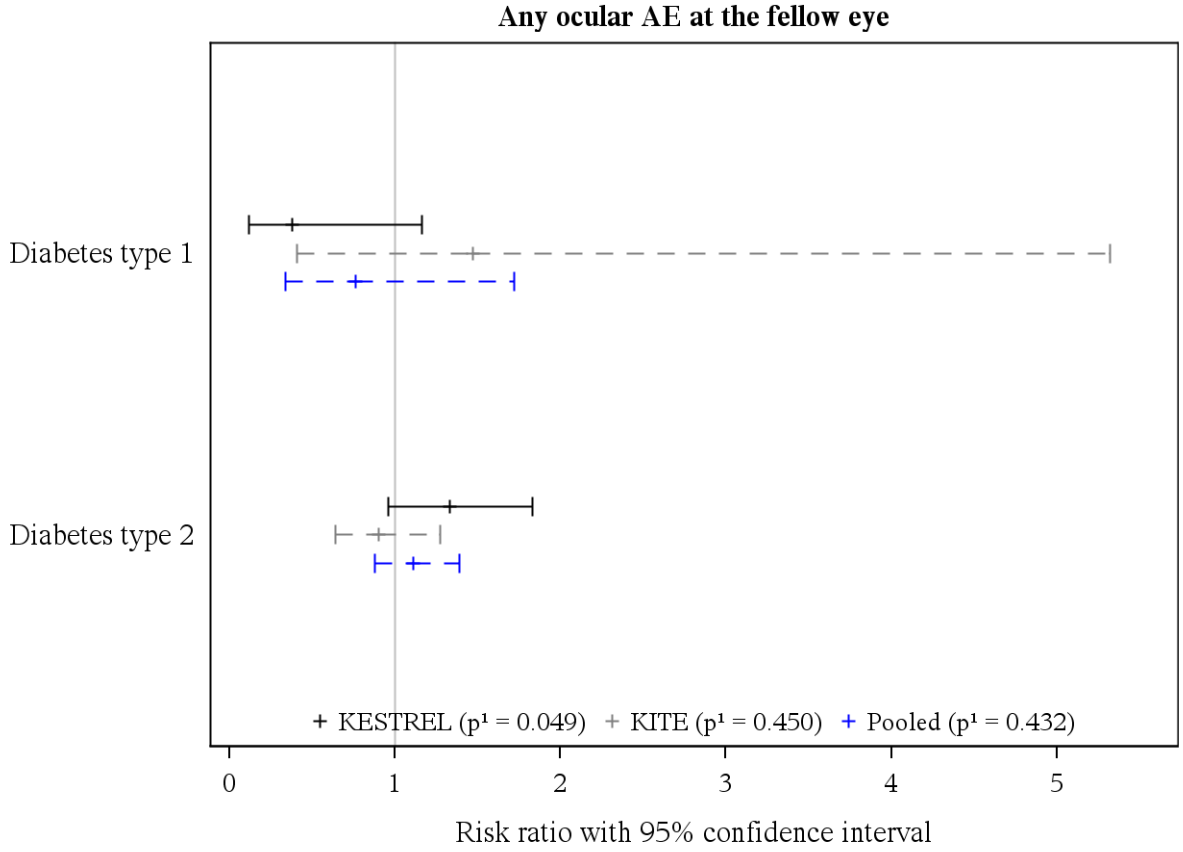
Figure 12.1.5.1 Any adverse event by region (SAF), forest plot, week 52, any non-ocular AE



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.068$

Figure 12.1.6 Any adverse event by diabetes type (SAF), forest plot, week 52

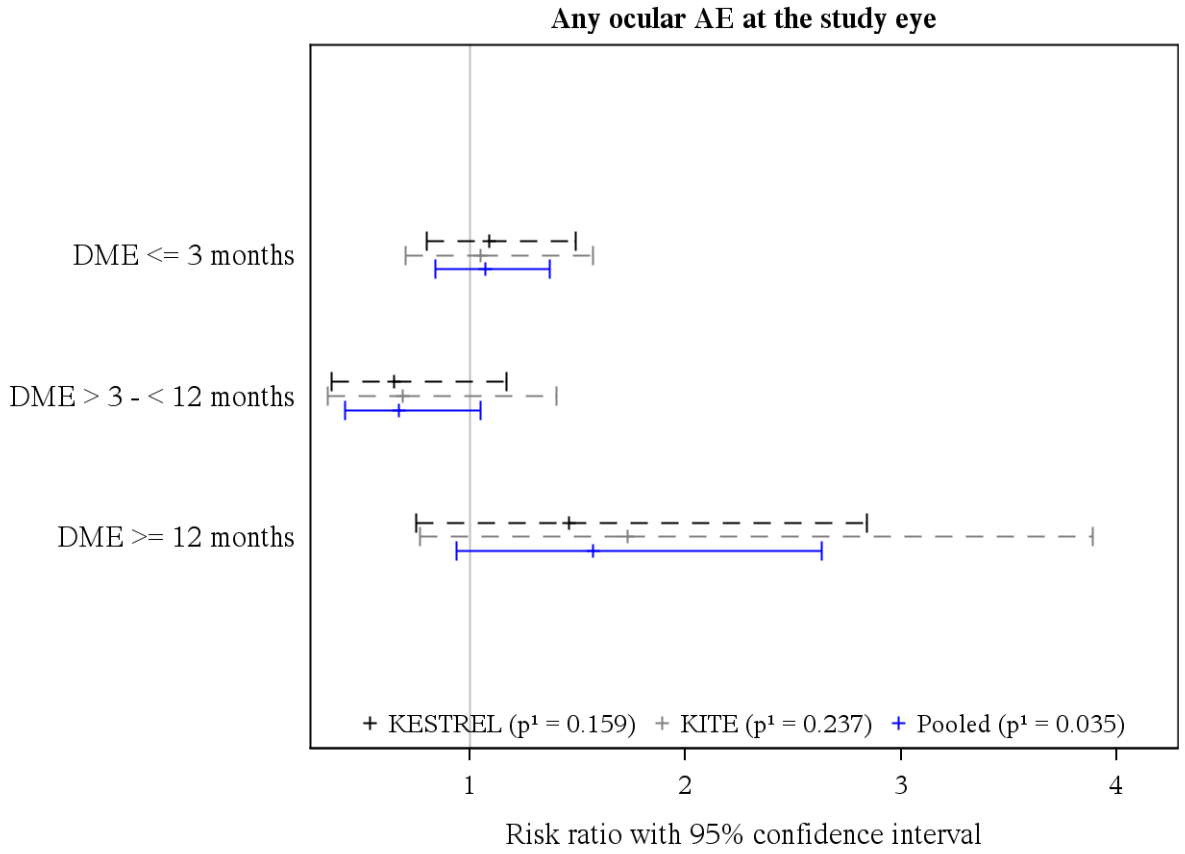
Figure 12.1.6.1 Any adverse event by diabetes type (SAF), forest plot, week 52, any ocular AE at the fellow eye



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.244$

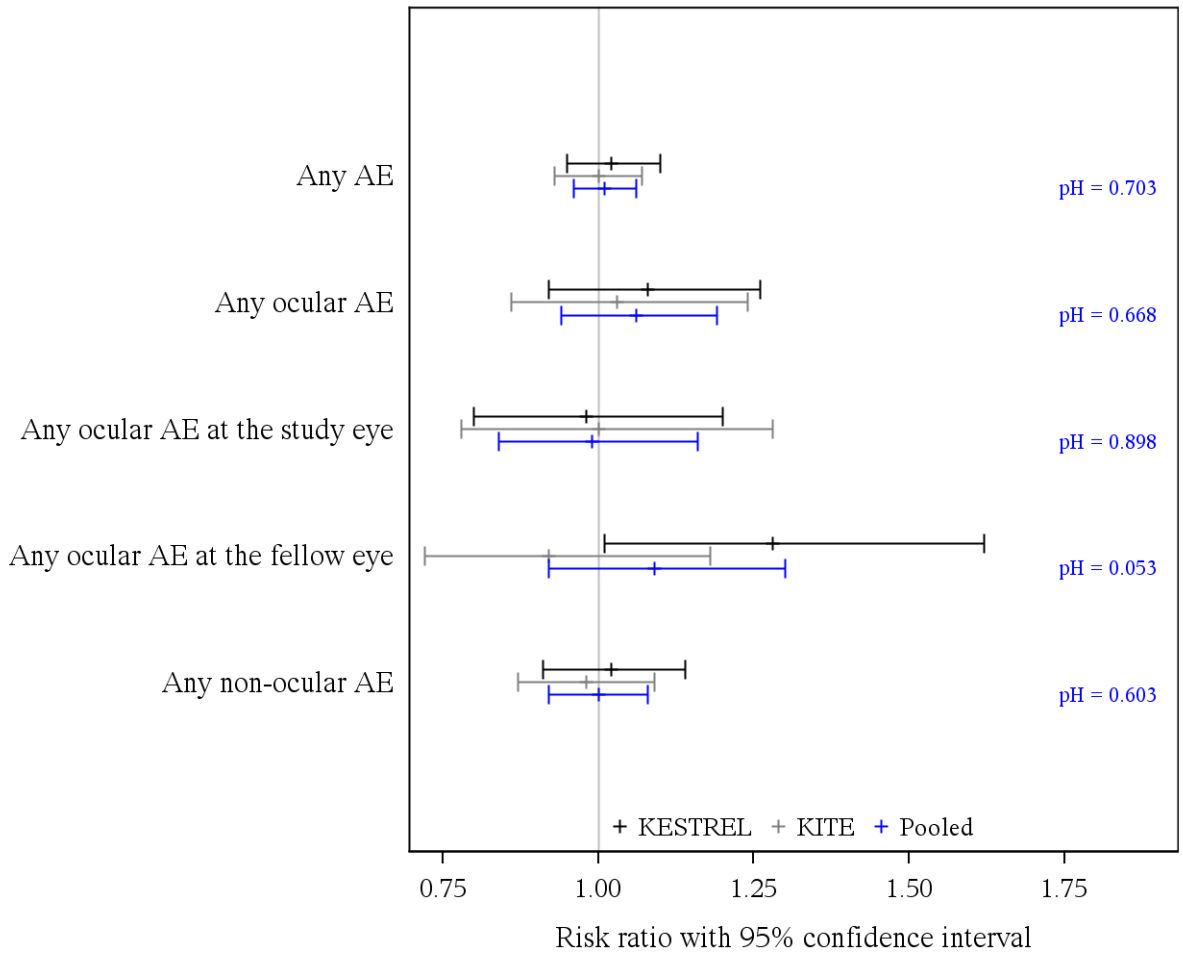
Figure 12.1.8 Any adverse event by duration of DME (SAF), forest plot, week 52

Figure 12.1.8.1 Any adverse event by duration of DME (SAF), forest plot, week 52, any ocular AE at the study eye



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.983$

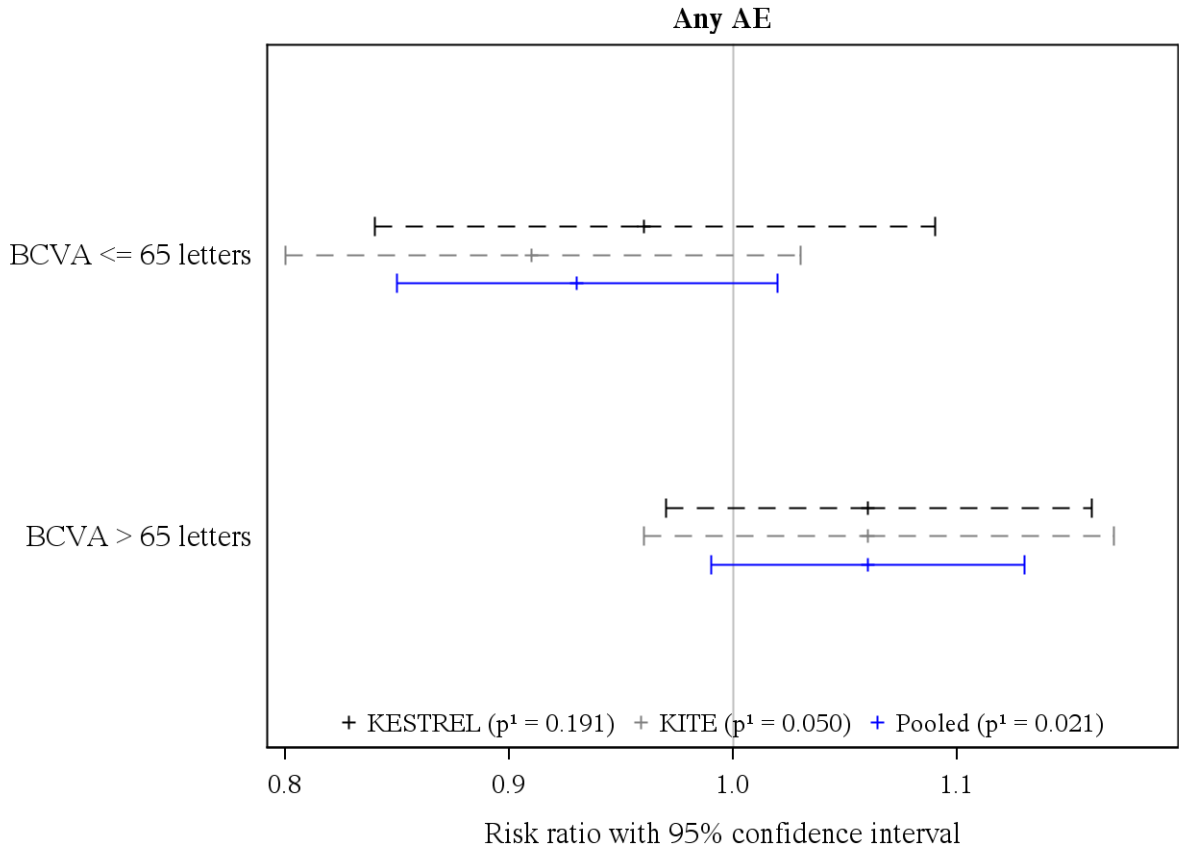
Figure 12.2.1 Any adverse event (SAF), forest plot, week 100



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

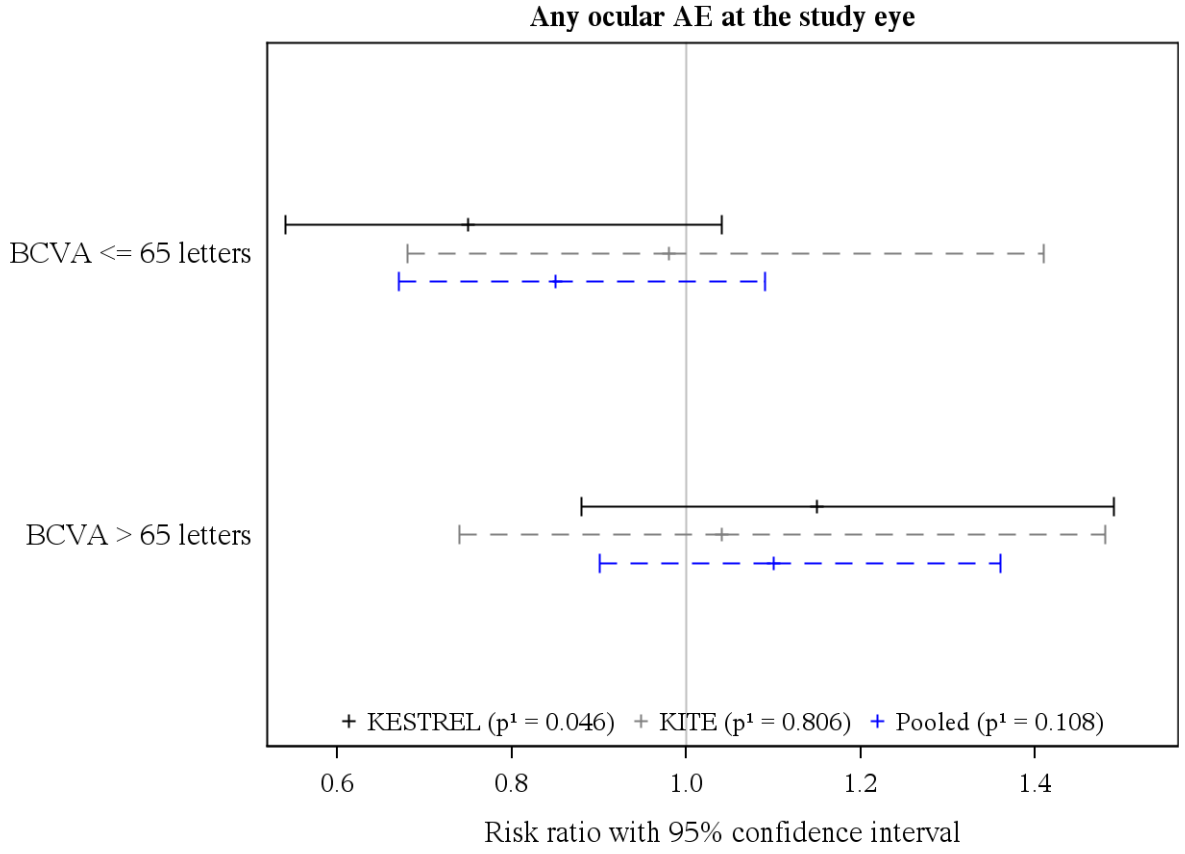
Figure 12.2.4 Any adverse event by BCVA (SAF), forest plot, week 100

Figure 12.2.4.1 Any adverse event by BCVA (SAF), forest plot, week 100, any AE



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.703$

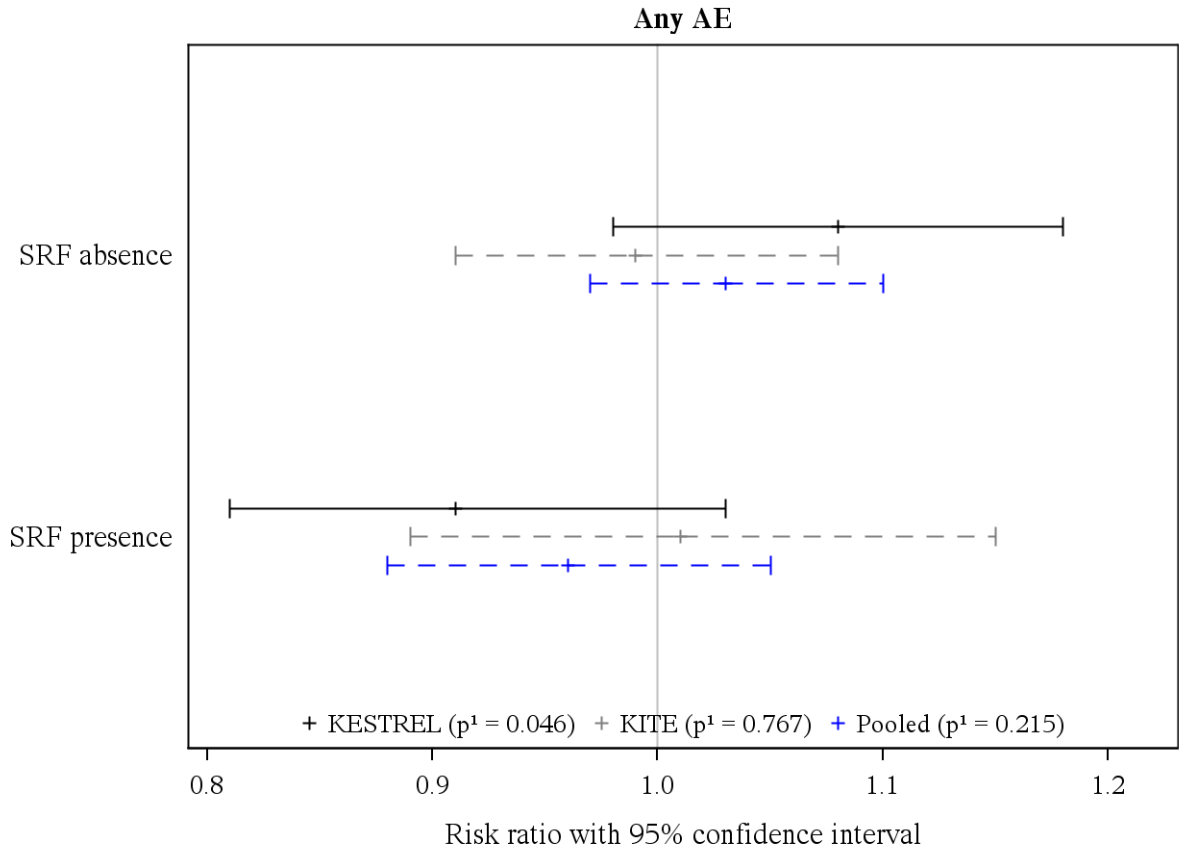
Figure 12.2.4.2 Any adverse event by BCVA (SAF), forest plot, week 100, any ocular AE at the study eye



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.898$

Figure 12.2.11 Any adverse event by status of SRF (SAF), forest plot, week 100

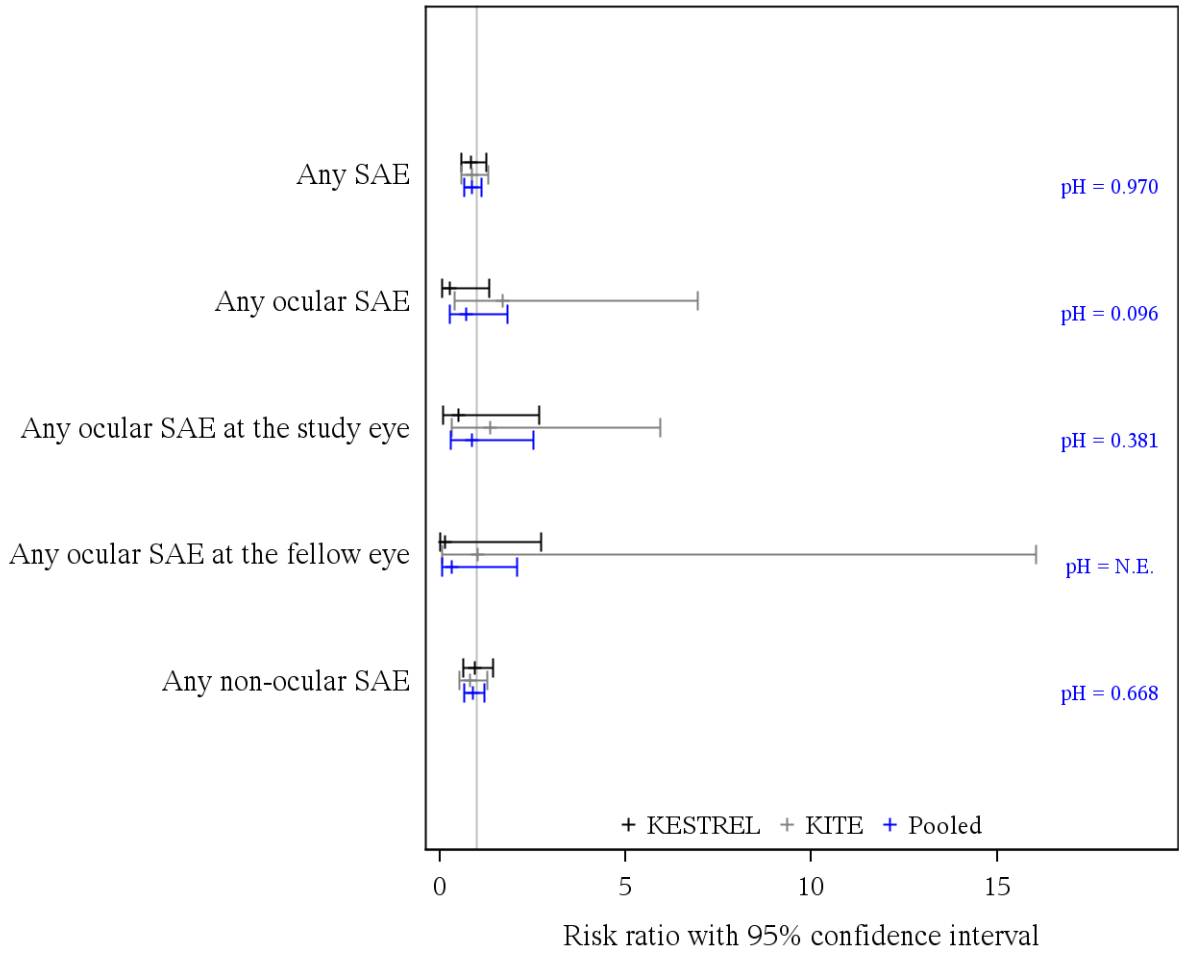
Figure 12.2.11.1 Any adverse event by status of SRF (SAF), forest plot, week 100, any AE



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.703$

13 Safety analysis: Any serious adverse event

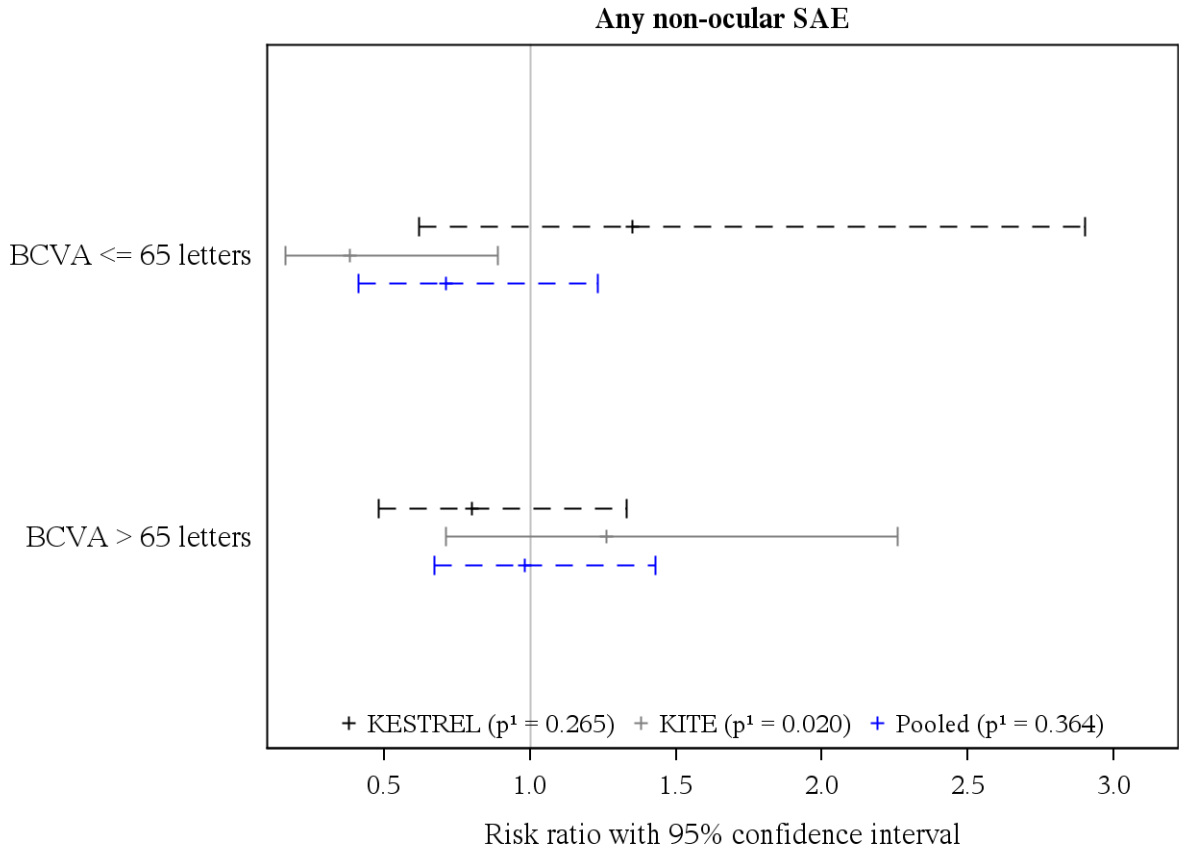
Figure 13.1.1 Any serious adverse event (SAF), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 13.1.4 Any serious adverse event by BCVA (SAF), forest plot, week 52

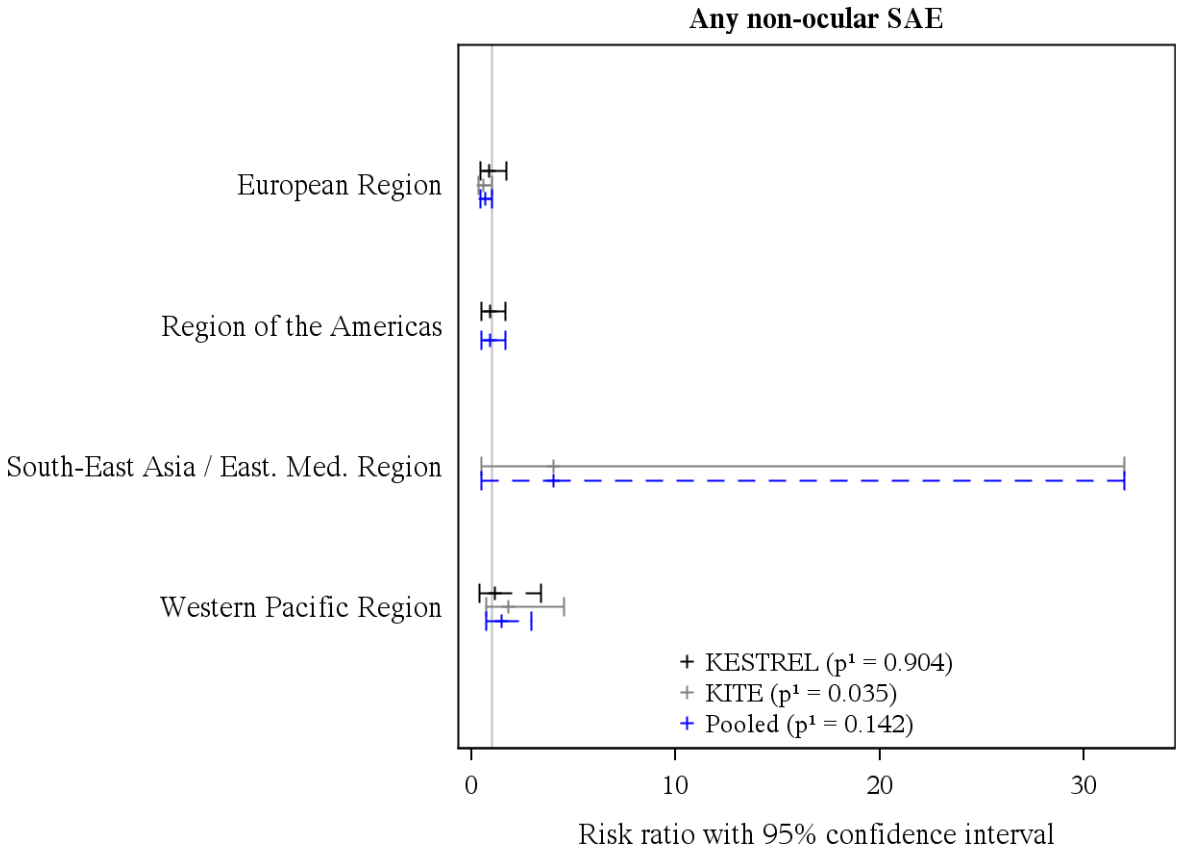
Figure 13.1.4.1 Any serious adverse event by BCVA (SAF), forest plot, week 52, any non-ocular SAE



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.668$

Figure 13.1.5 Any serious adverse event by region (SAF), forest plot, week 52

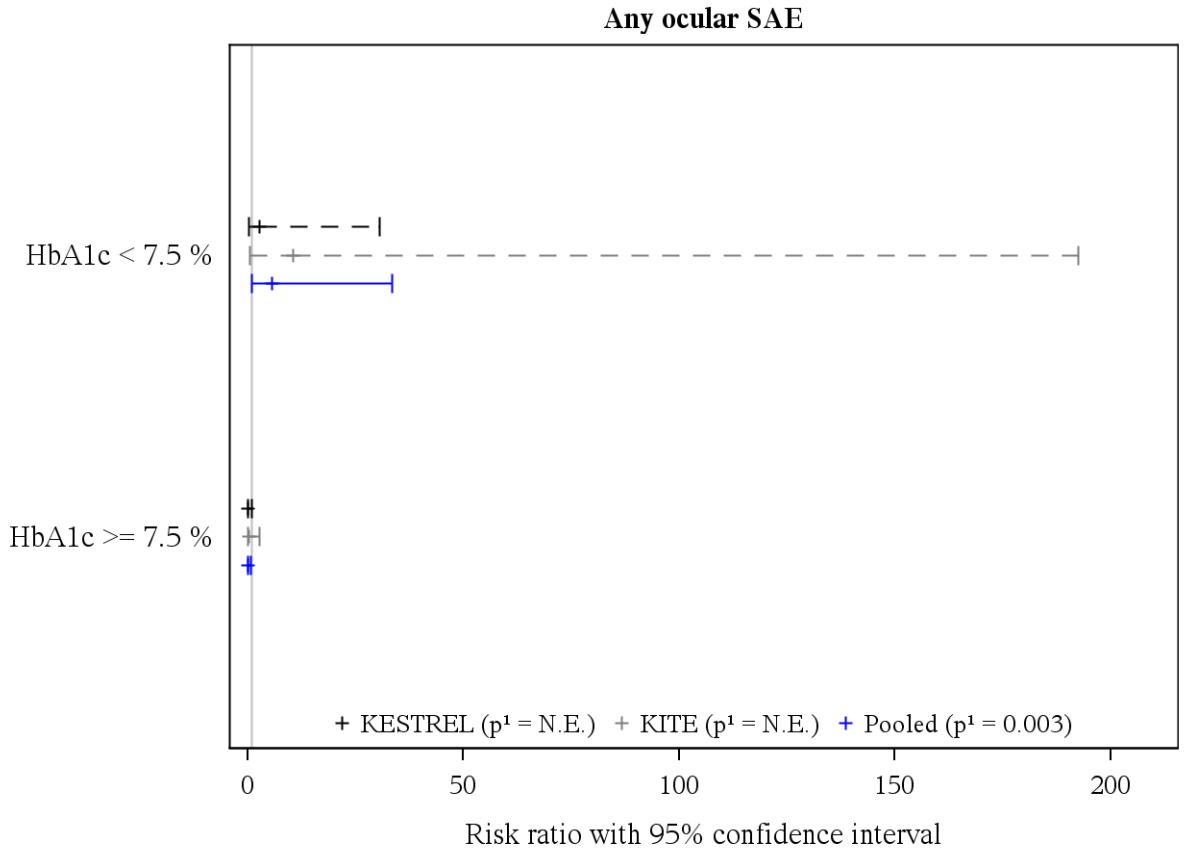
Figure 13.1.5.1 Any serious adverse event by region (SAF), forest plot, week 52, any non-ocular SAE



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.668$

Figure 13.1.7 Any serious adverse event by HbA1c (SAF), forest plot, week 52

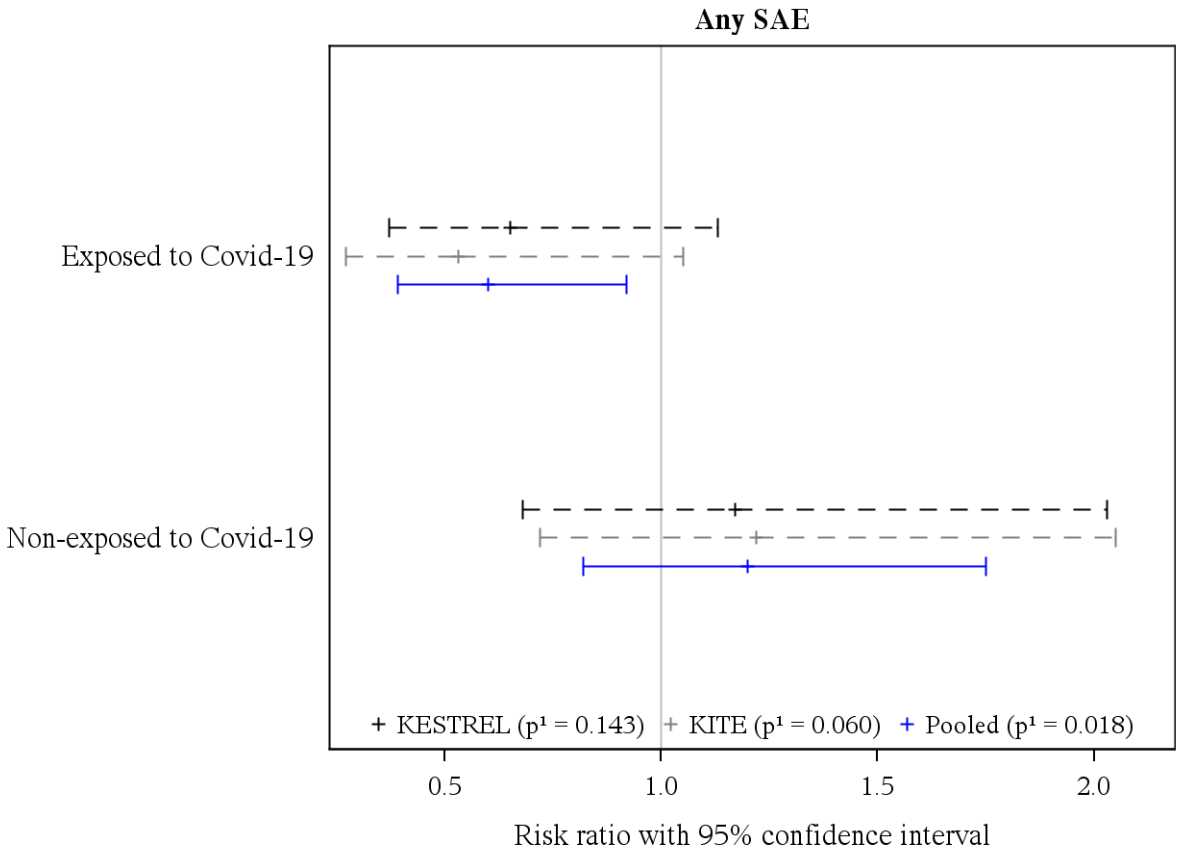
Figure 13.1.7.1 Any serious adverse event by HbA1c (SAF), forest plot, week 52, any ocular SAE



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.096$

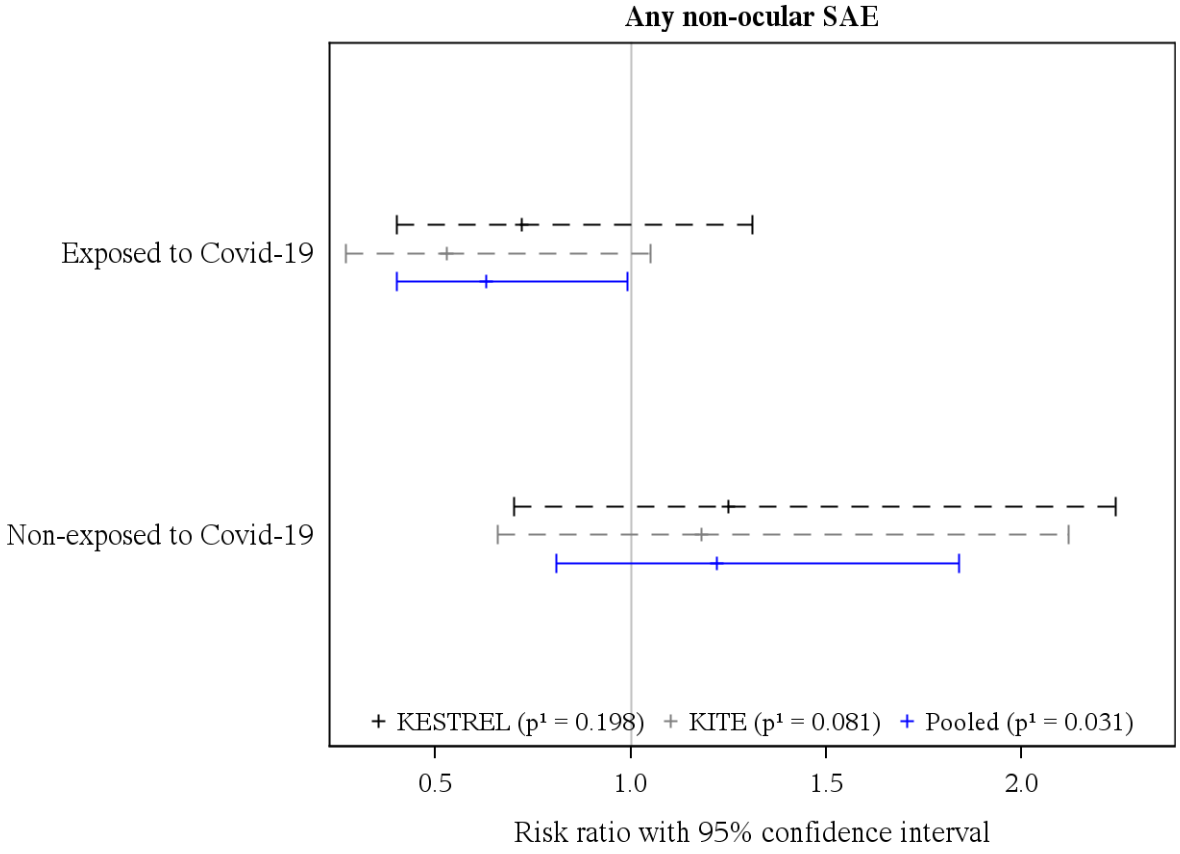
Figure 13.1.12 Any serious adverse event by exposure (week 52) (SAF), forest plot, week 52

Figure 13.1.12.1 Any serious adverse event by exposure (week 52) (SAF), forest plot, week 52, any SAE



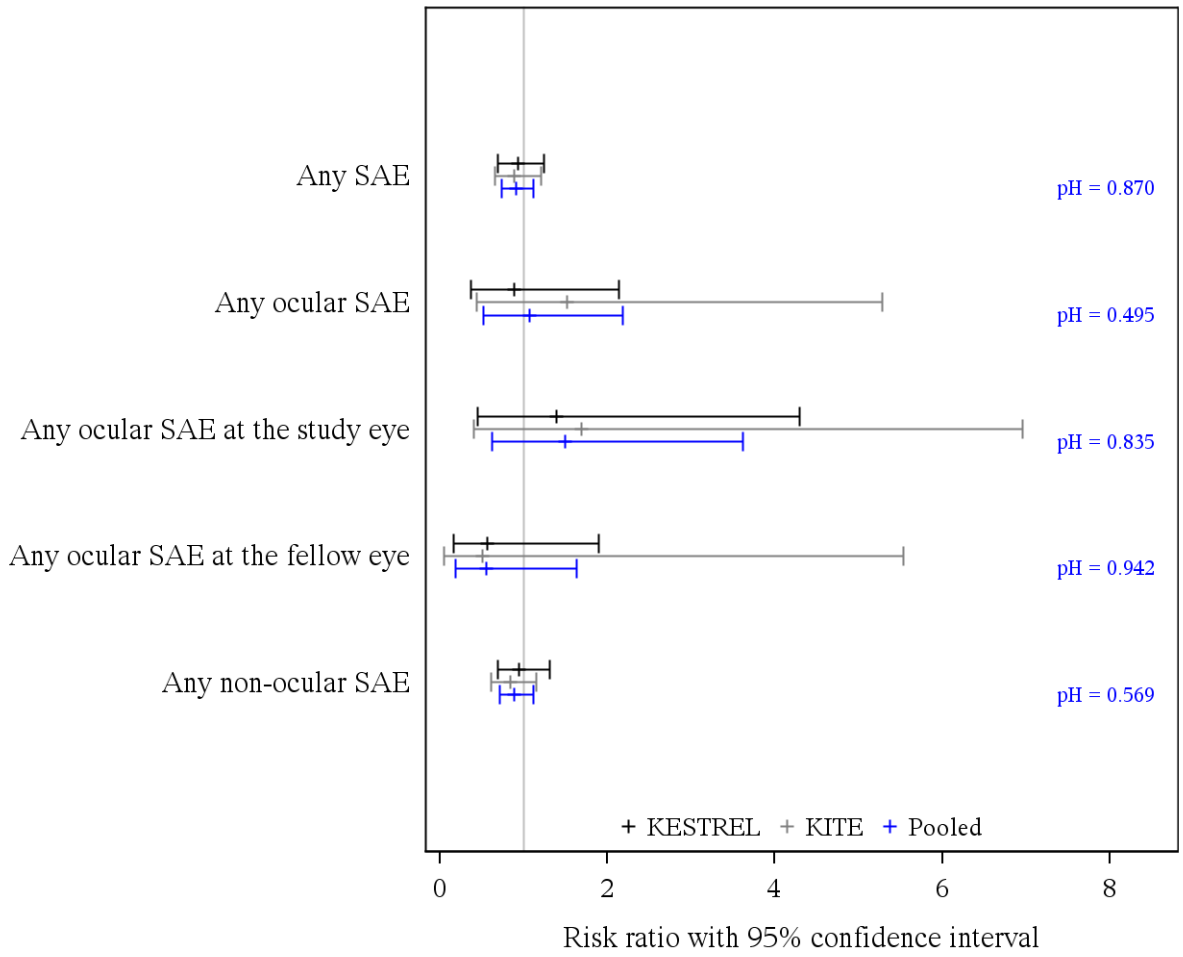
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.970$

Figure 13.1.12.2 Any serious adverse event by exposure (week 52) (SAF), forest plot, week 52, any non-ocular SAE



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.668$

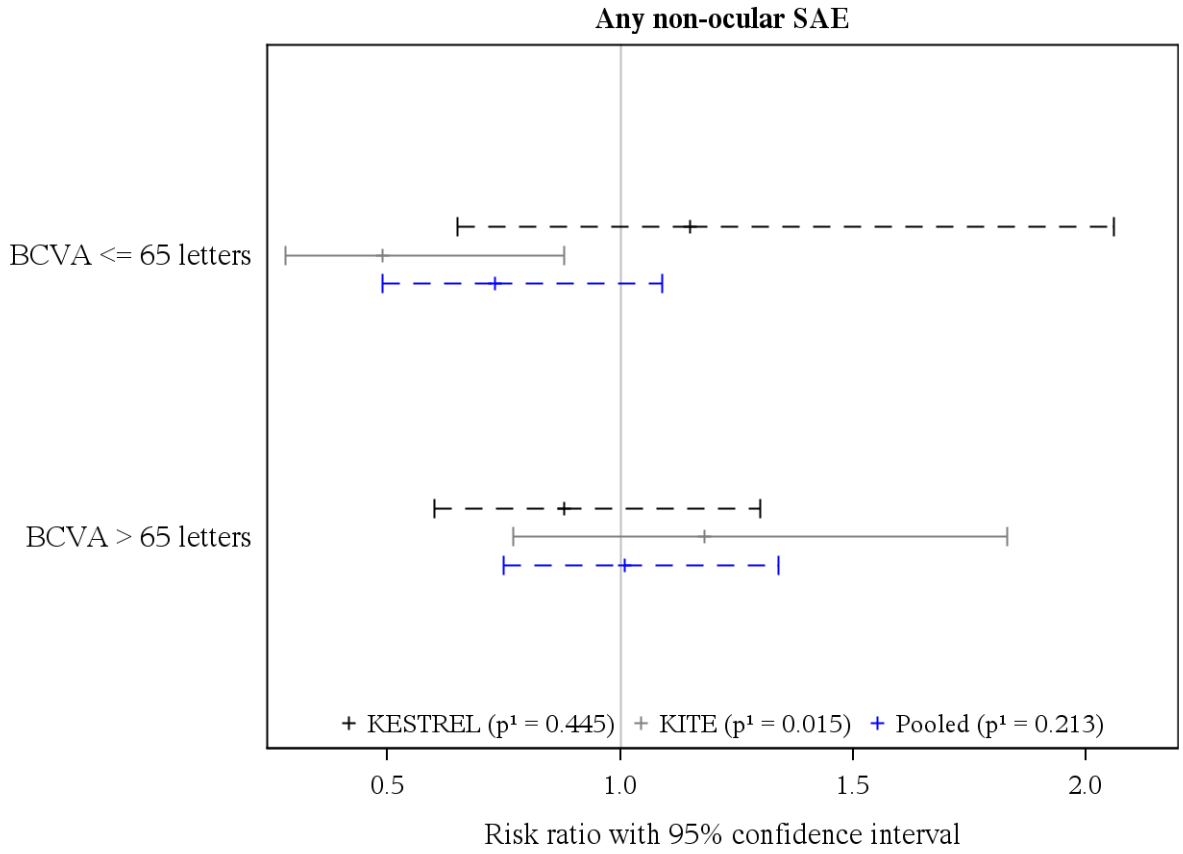
Figure 13.2.1 Any serious adverse event (SAF), forest plot, week 100



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 13.2.4 Any serious adverse event by BCVA (SAF), forest plot, week 100

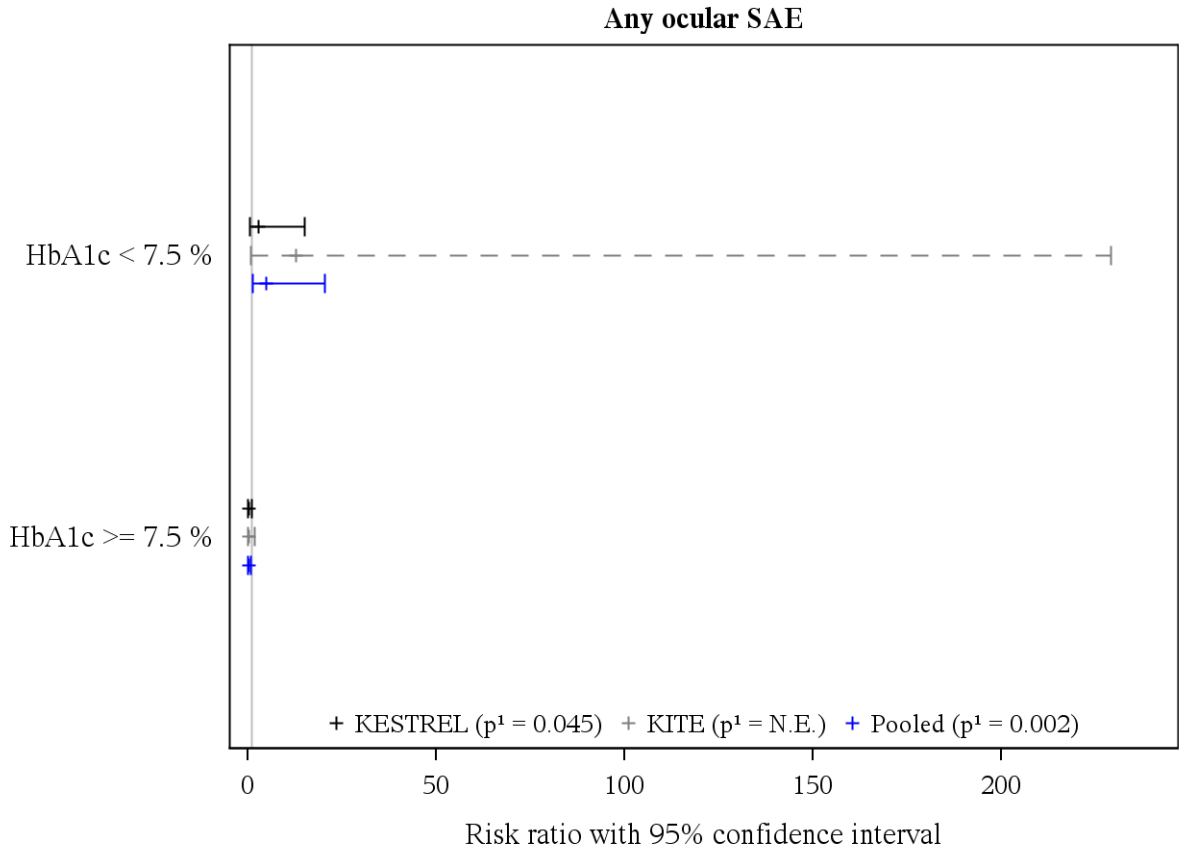
Figure 13.2.4.1 Any serious adverse event by BCVA (SAF), forest plot, week 100, any non-ocular SAE



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.569$

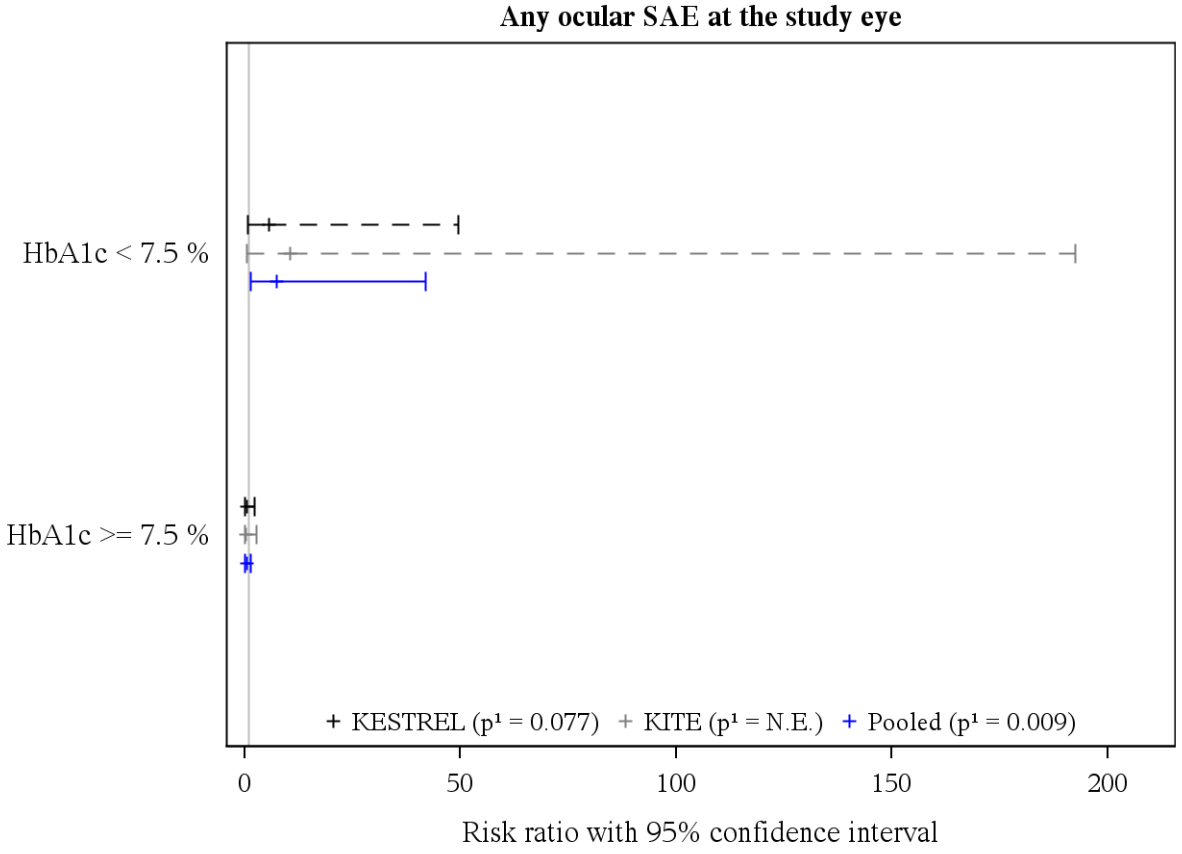
Figure 13.2.7 Any serious adverse event by HbA1c (SAF), forest plot, week 100

Figure 13.2.7.1 Any serious adverse event by HbA1c (SAF), forest plot, week 100, any ocular SAE



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.495$

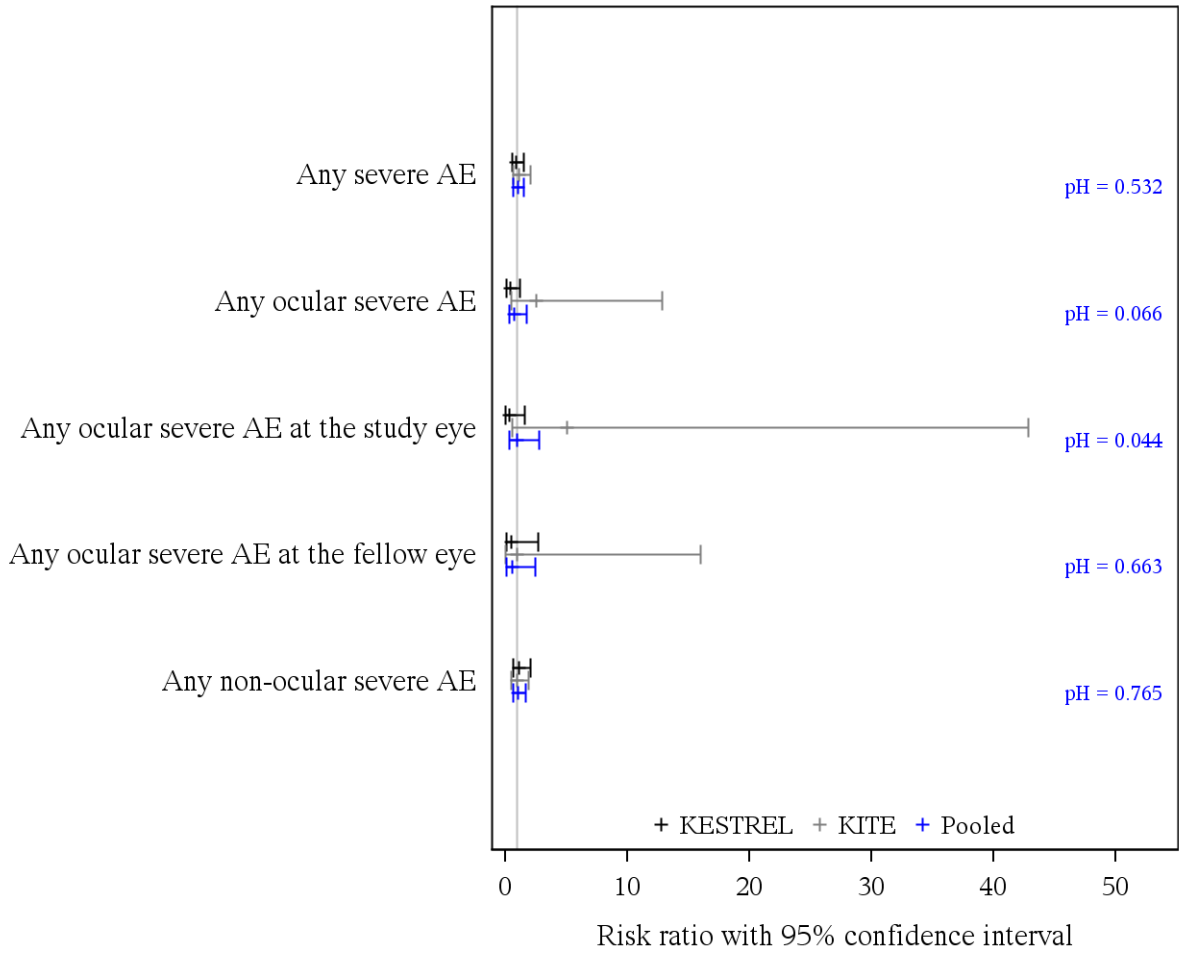
Figure 13.2.7.2 Any serious adverse event by HbA1c (SAF), forest plot, week 100, any ocular SAE at the study eye



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.835$

14 Safety analysis: Any severe adverse event

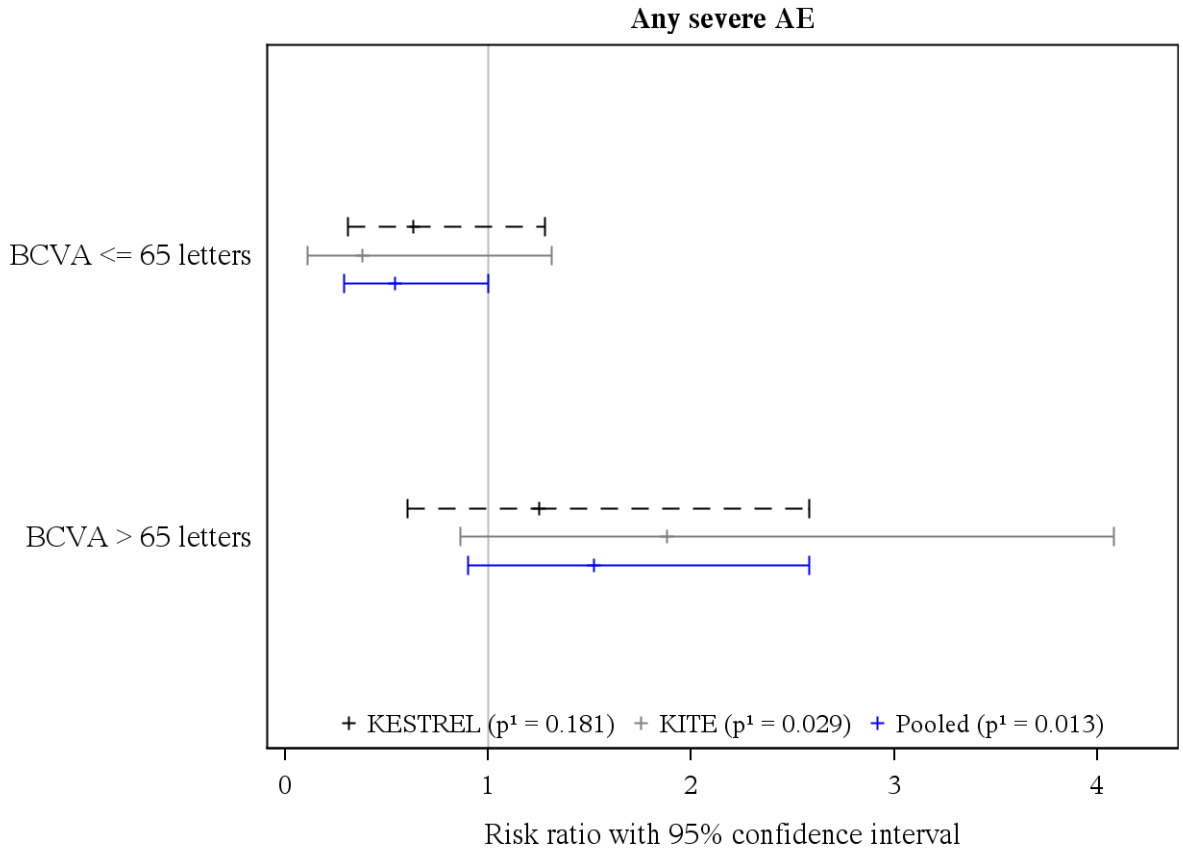
Figure 14.1.1 Any severe adverse event (SAF), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

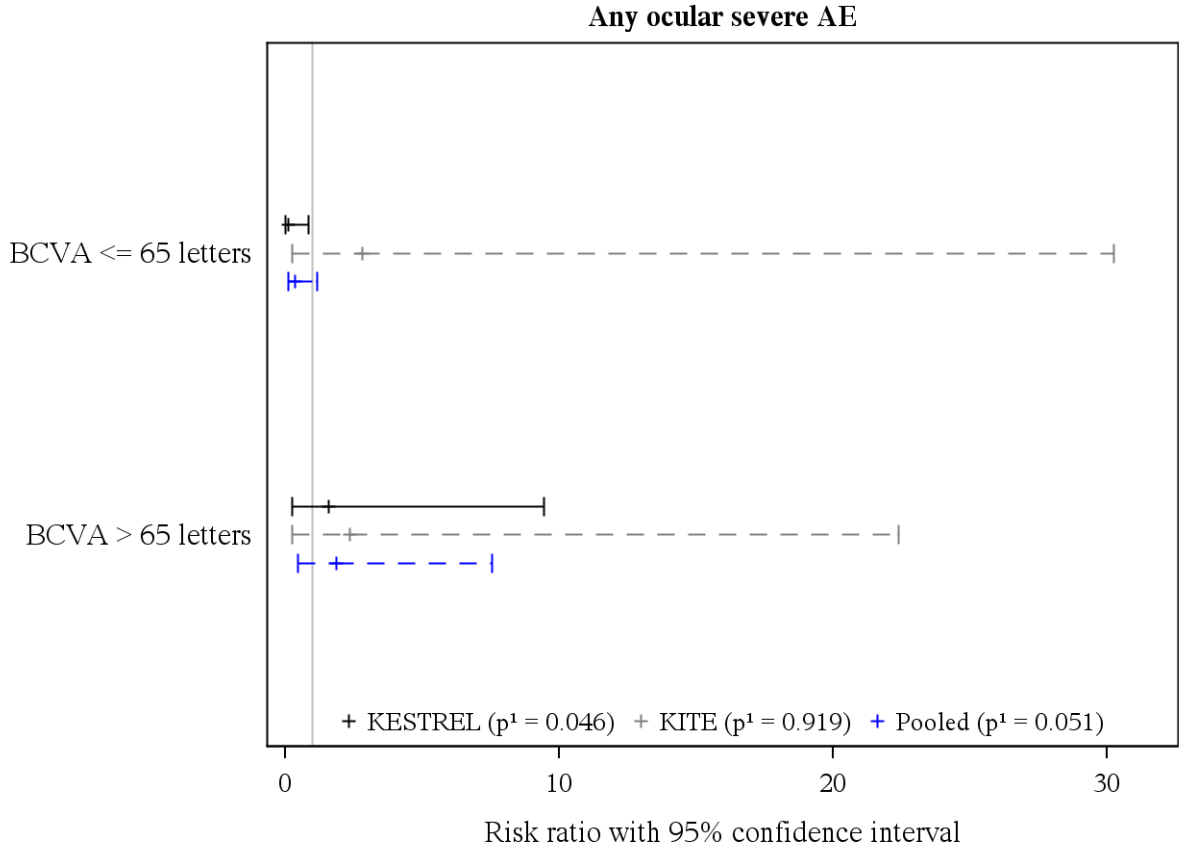
Figure 14.1.4 Any severe adverse event by BCVA (SAF), forest plot, week 52

Figure 14.1.4.1 Any severe adverse event by BCVA (SAF), forest plot, week 52, any severe AE



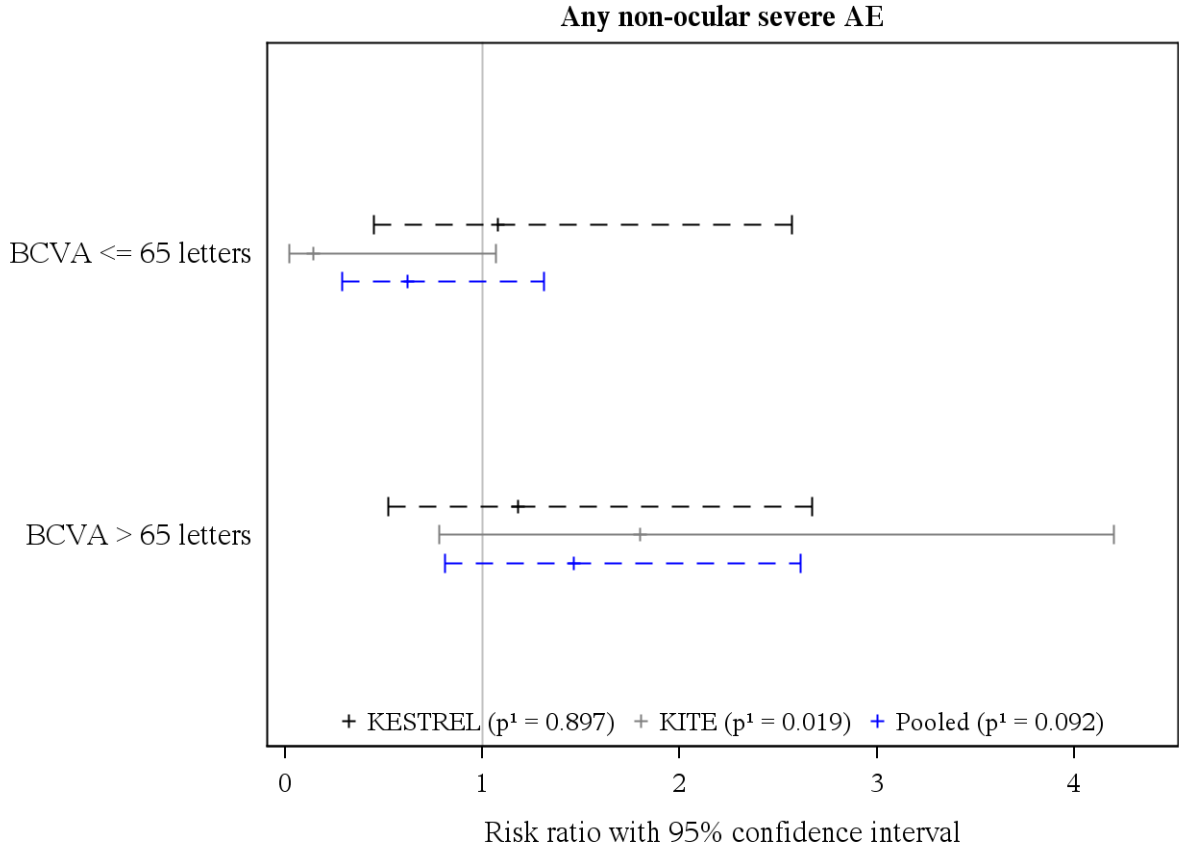
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.532$

Figure 14.1.4.2 Any severe adverse event by BCVA (SAF), forest plot, week 52, any ocular severe AE



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.066$

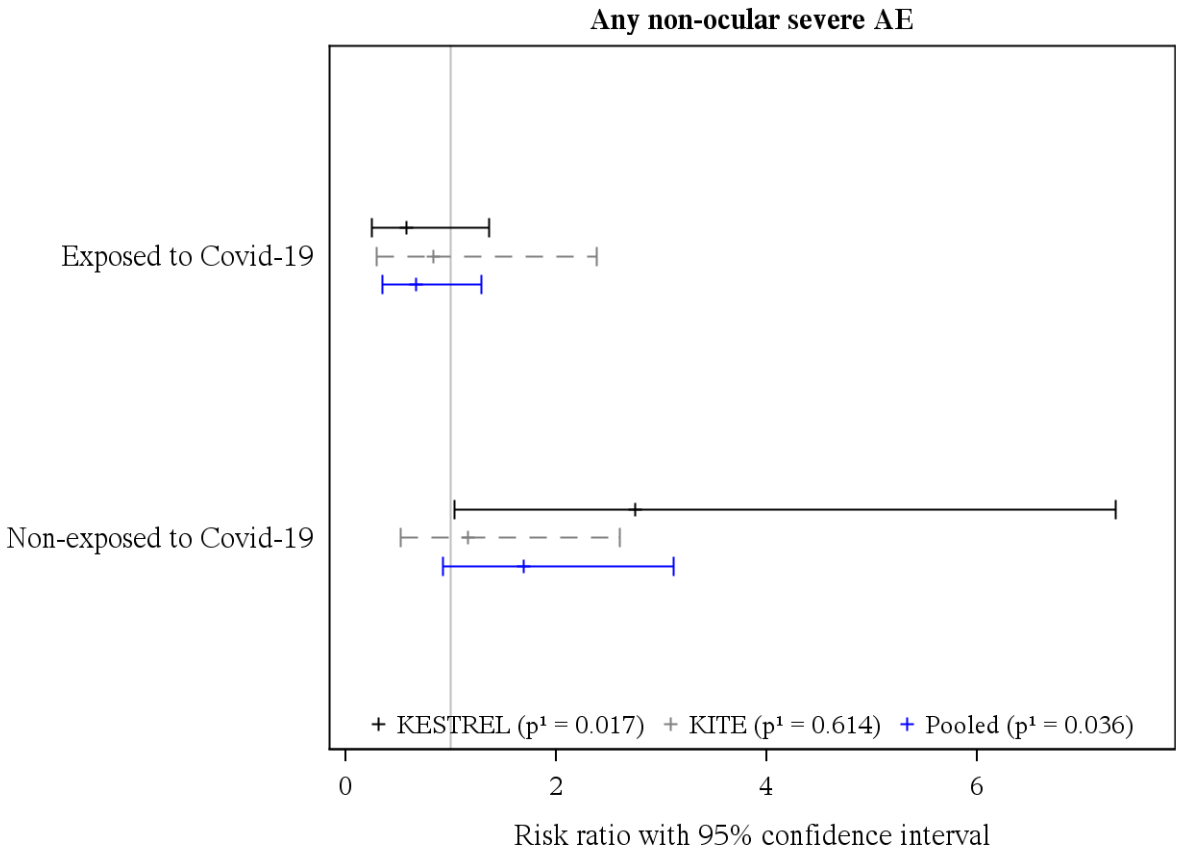
Figure 14.1.4.3 Any severe adverse event by BCVA (SAF), forest plot, week 52, any non-ocular severe AE



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.765$

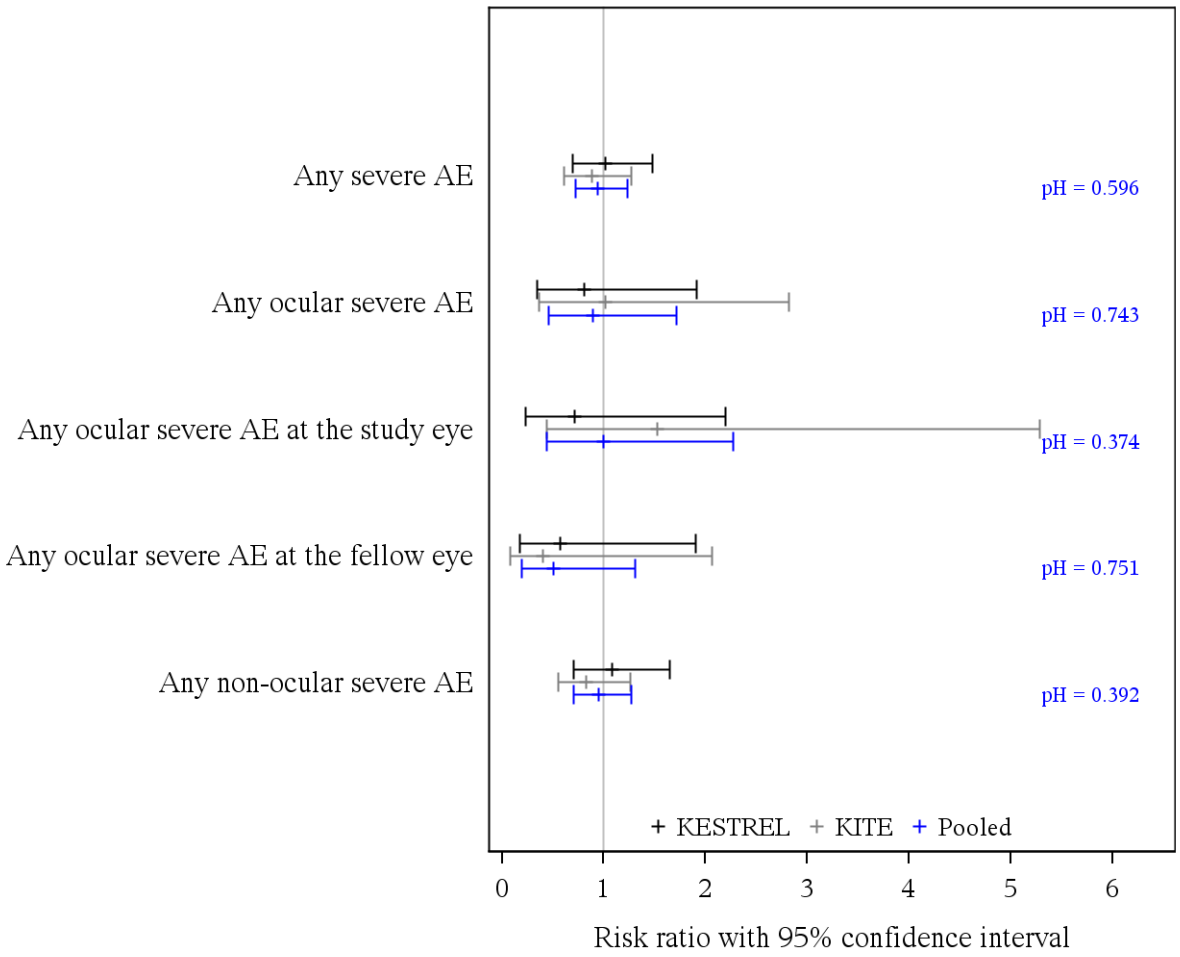
Figure 14.1.12 Any severe adverse event by exposure (week 52) (SAF), forest plot, week 52

Figure 14.1.12.1 Any severe adverse event by exposure (week 52) (SAF), forest plot, week 52, any non-ocular severe AE



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.765$

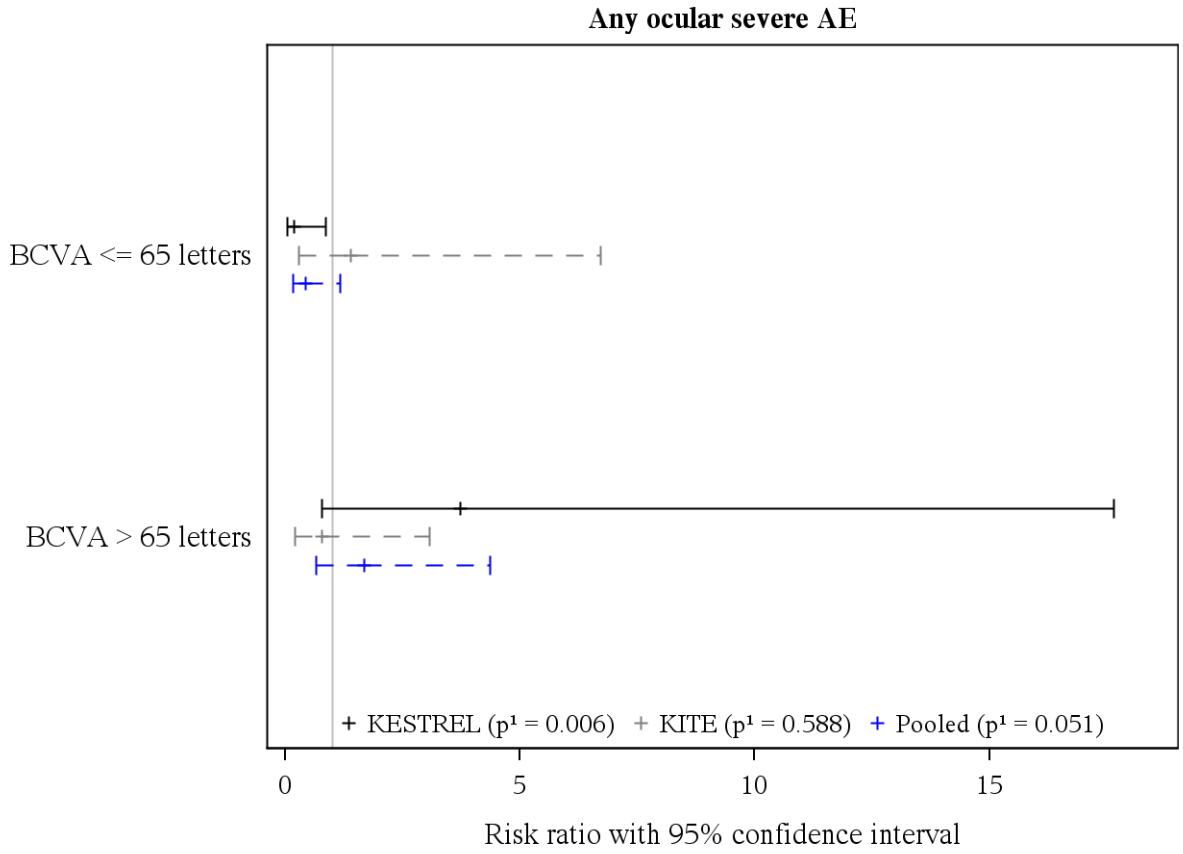
Figure 14.2.1 Any severe adverse event (SAF), forest plot, week 100



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

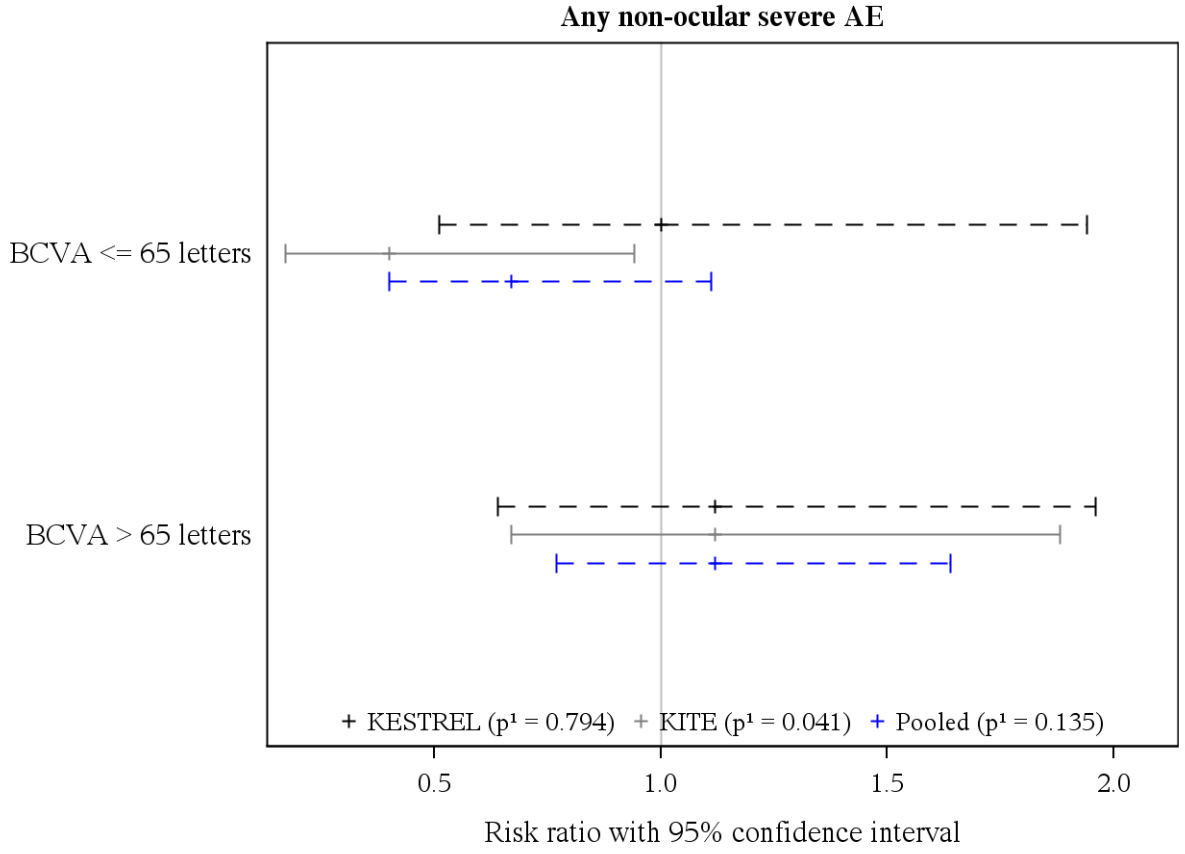
Figure 14.2.4 Any severe adverse event by BCVA (SAF), forest plot, week 100

Figure 14.2.4.1 Any severe adverse event by BCVA (SAF), forest plot, week 100, any ocular severe AE



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.743$

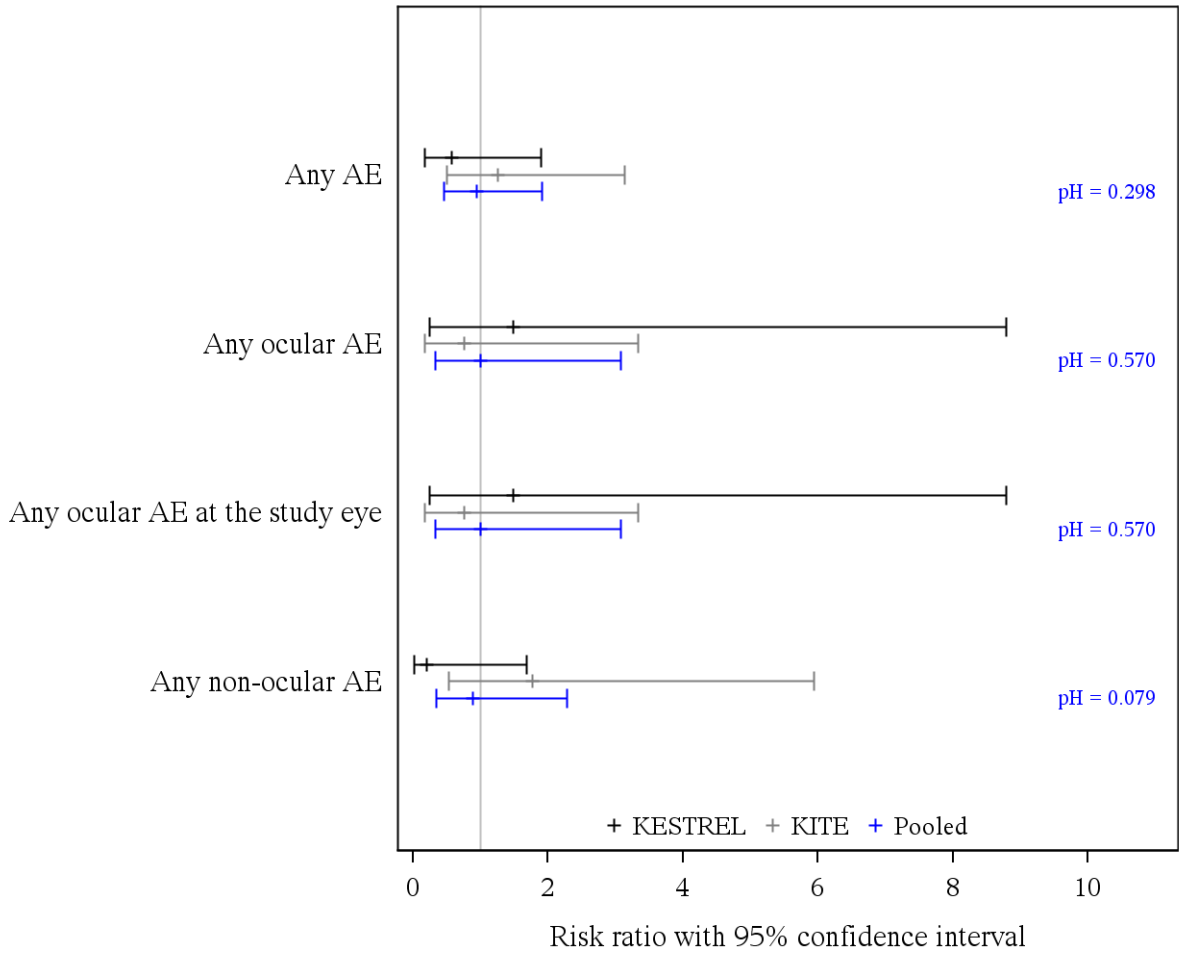
Figure 14.2.4.2 Any severe adverse event by BCVA (SAF), forest plot, week 100, any non-ocular severe AE



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.392$

15 Safety analysis: Any adverse event leading to study drug discontinuation

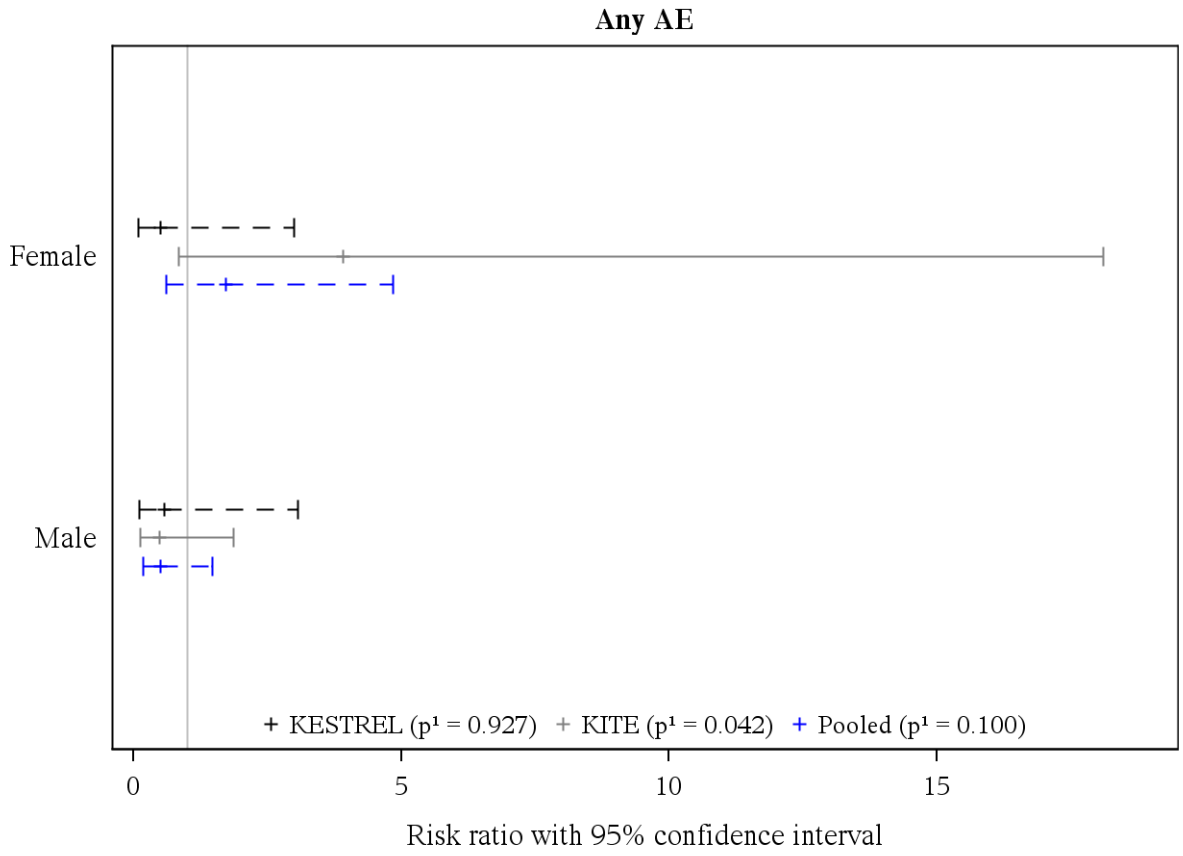
Figure 15.1.1 Any adverse event leading to study drug discontinuation (SAF), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

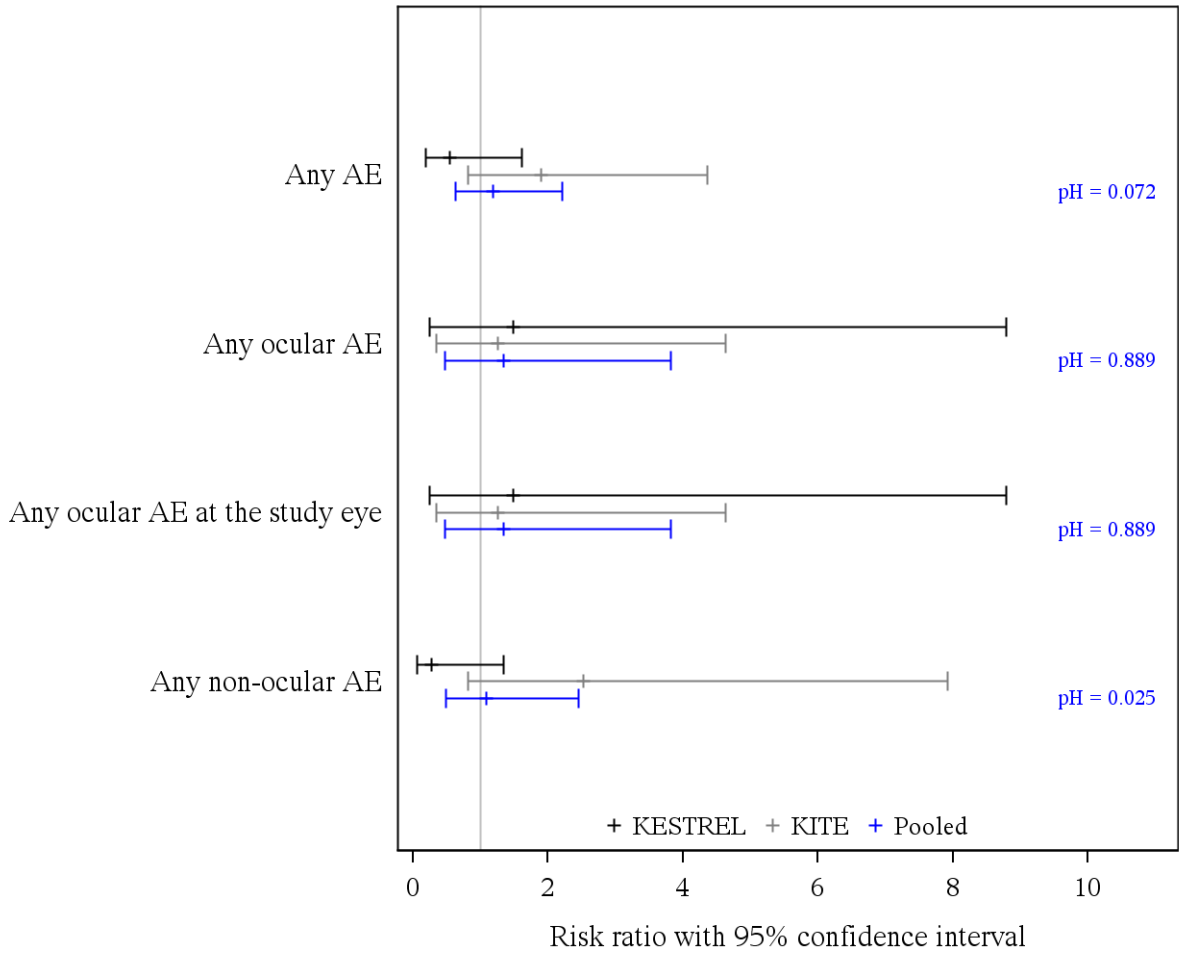
Figure 15.1.3 Any adverse event leading to study drug discontinuation by gender (SAF), forest plot, week 52

Figure 15.1.3.1 Any adverse event leading to study drug discontinuation by gender (SAF), forest plot, week 52, any AE



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.298$

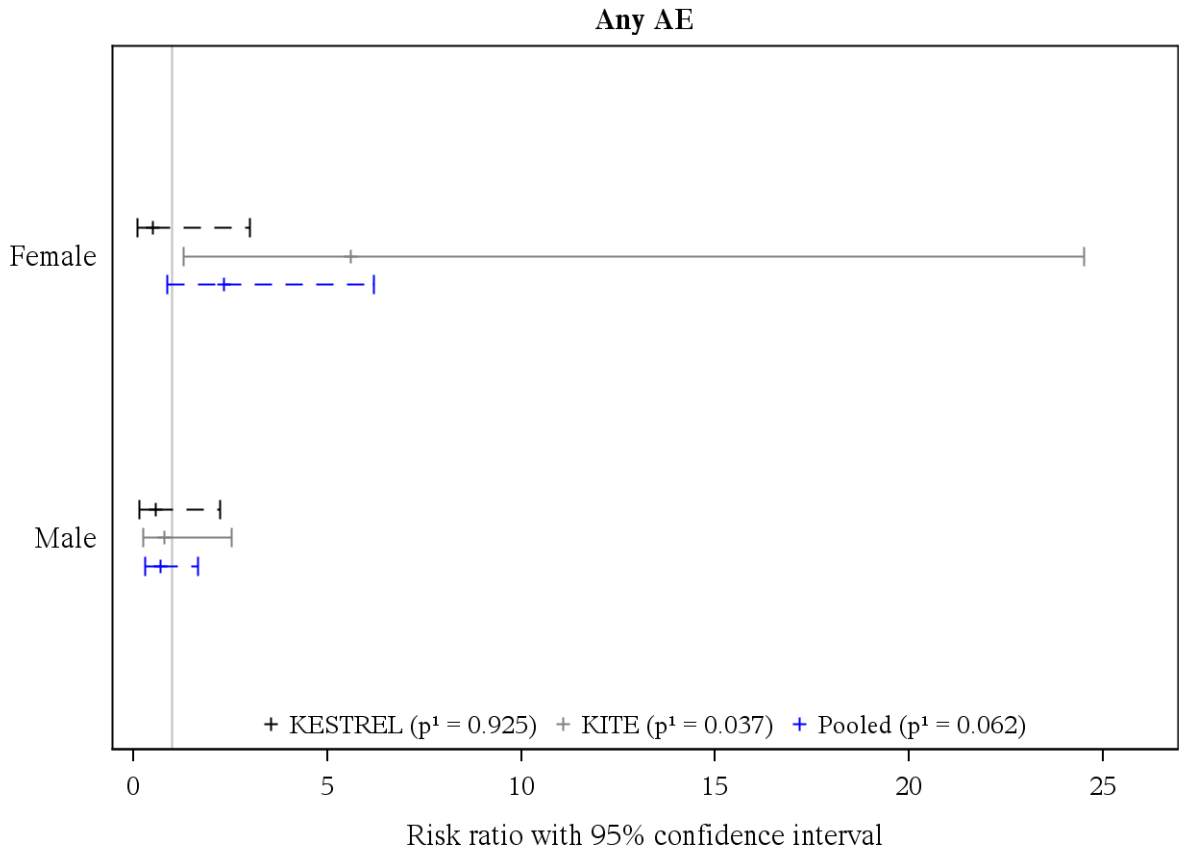
Figure 15.2.1 Any adverse event leading to study drug discontinuation (SAF), forest plot, week 100



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 15.2.3 Any adverse event leading to study drug discontinuation by gender (SAF), forest plot, week 100

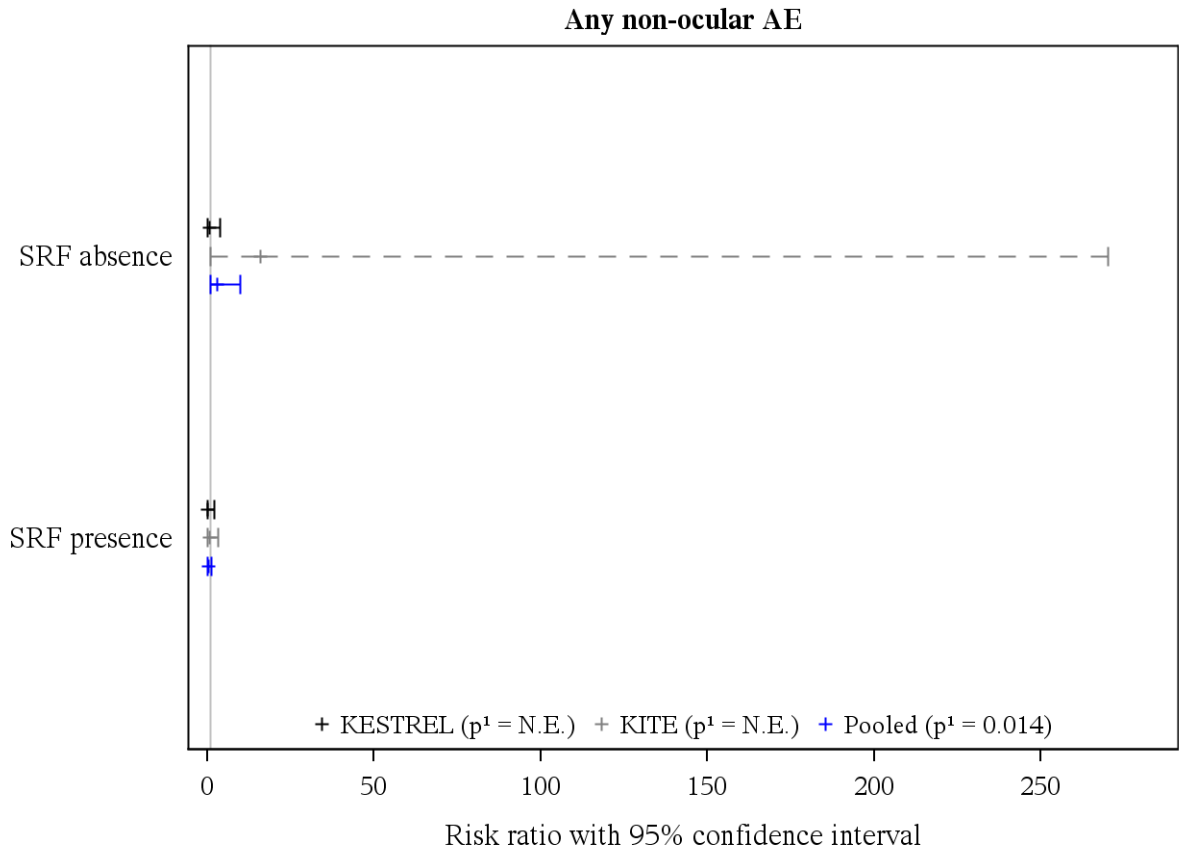
Figure 15.2.3.1 Any adverse event leading to study drug discontinuation by gender (SAF), forest plot, week 100, any AE



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.072$

Figure 15.2.11 Any adverse event leading to study drug discontinuation by status of SRF (SAF), forest plot, week 100

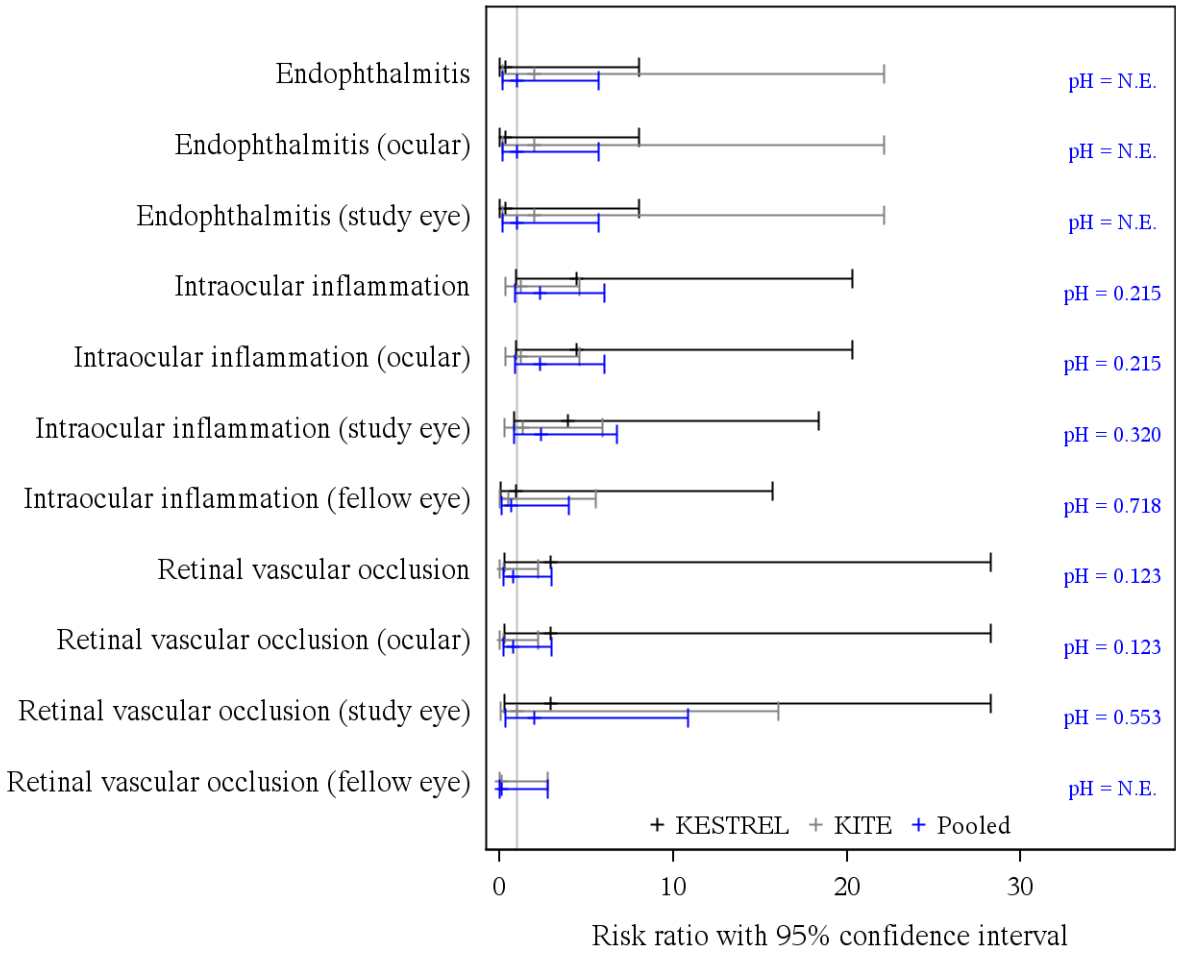
Figure 15.2.11.1 Any adverse event leading to study drug discontinuation by status of SRF (SAF), forest plot, week 100, any non-ocular AE



p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.025$

20 Safety analysis: Any adverse event of special interest

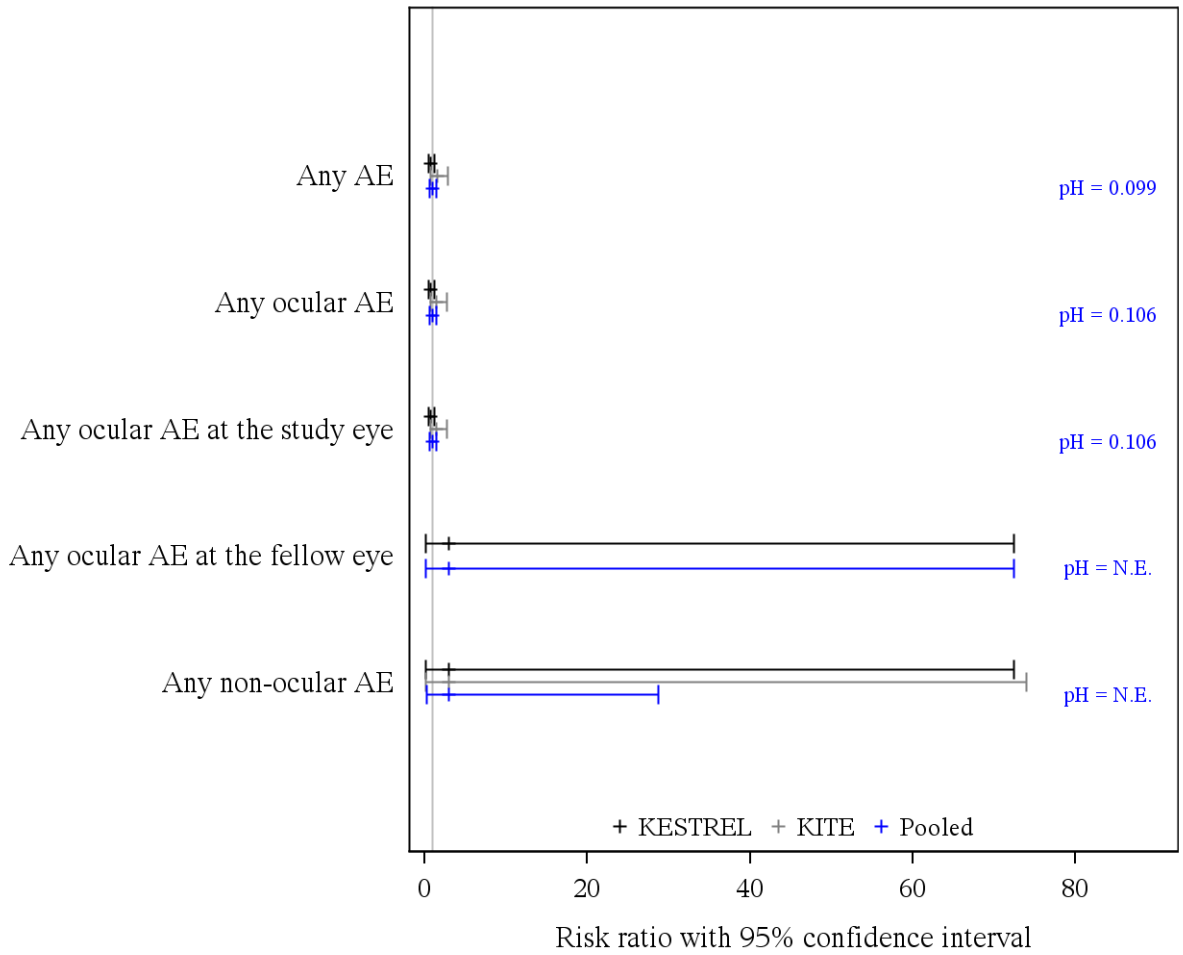
Figure 20.2.1 Any adverse event of special interest (SAF), forest plot, week 100



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

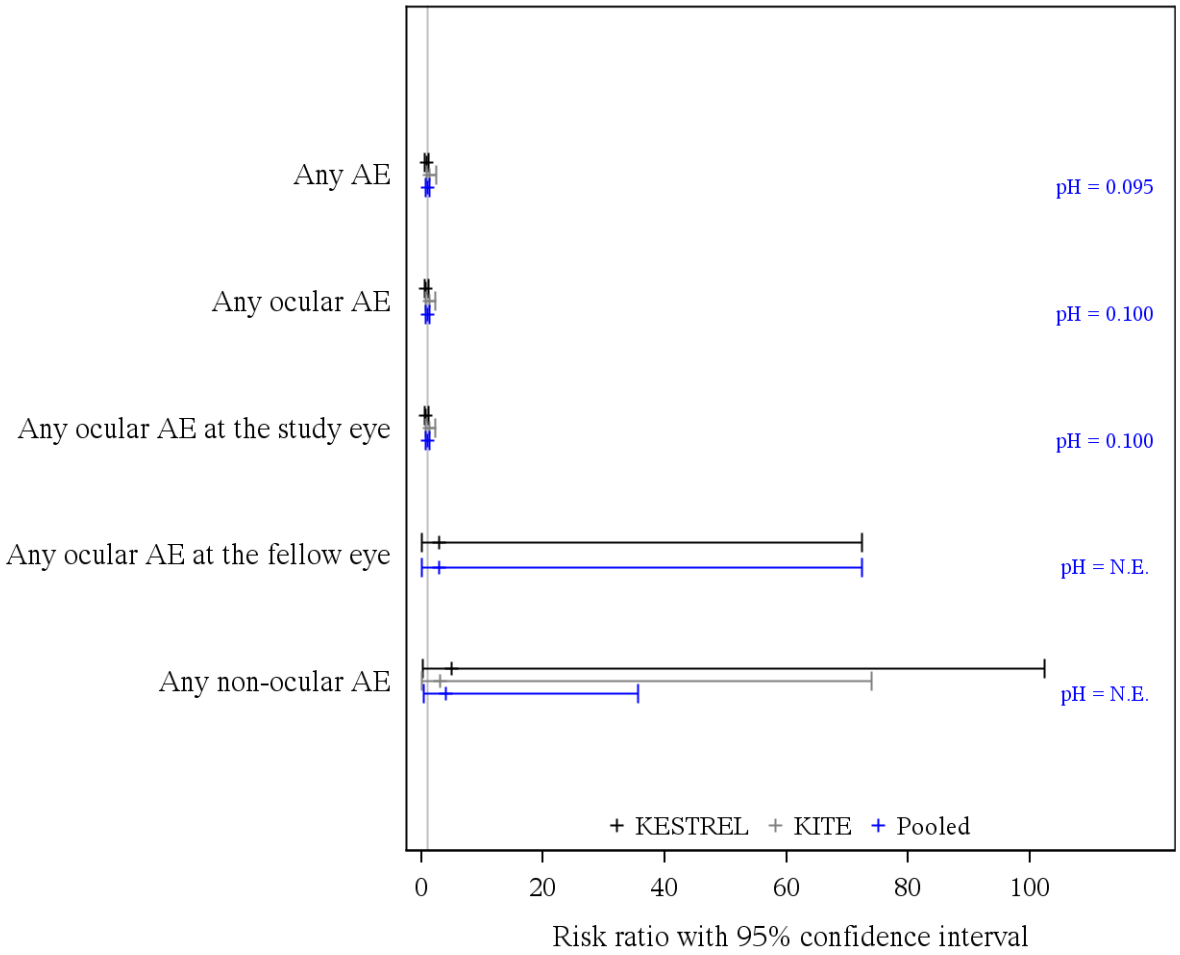
21 Safety analysis: Any adverse event of potential relevance to intravitreal anti-VEGF injection

Figure 21.1.1 Any adverse event of potential relevance to intravitreal anti-VEGF injection (SAF), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

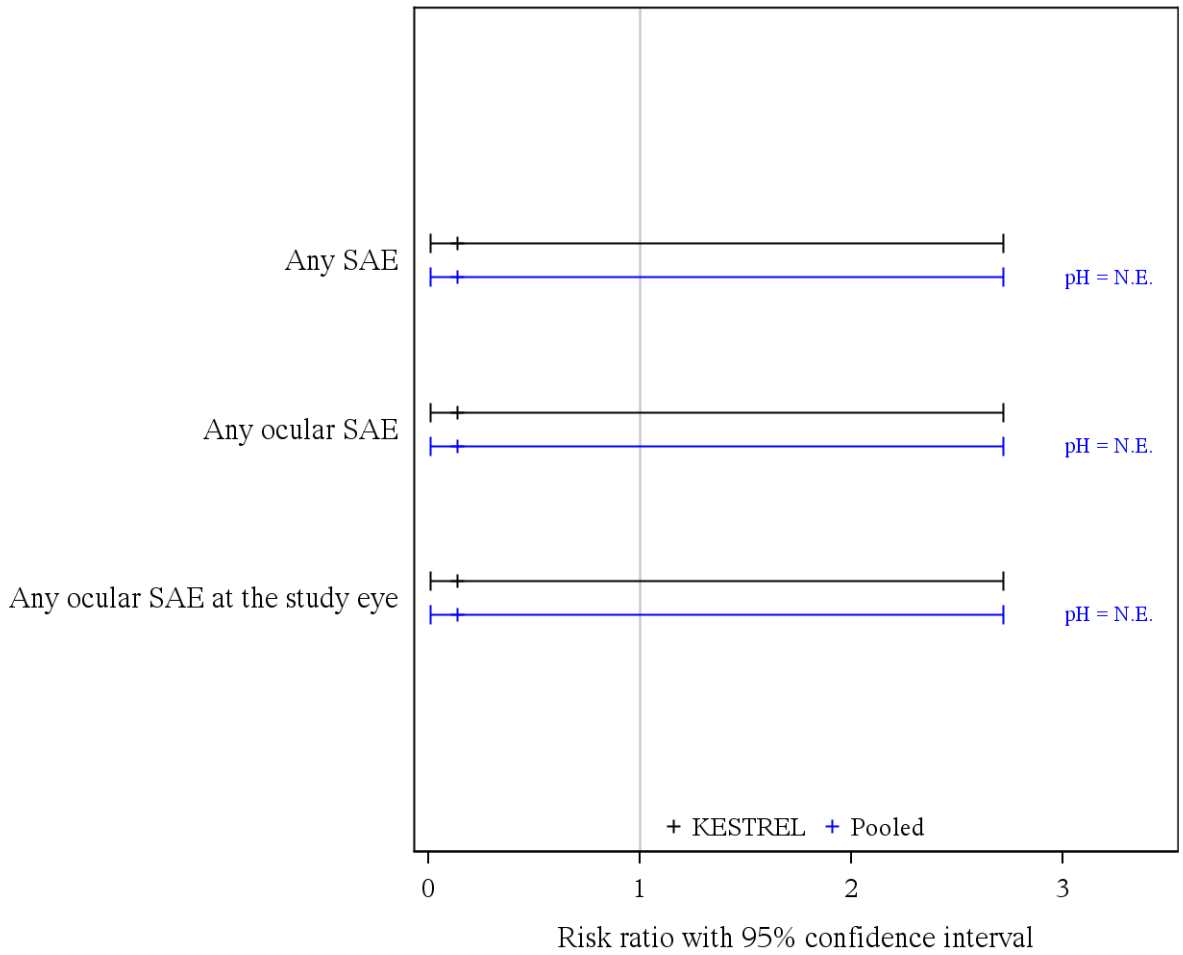
Figure 21.2.1 Any adverse event of potential relevance to intravitreal anti-VEGF injection (SAF), forest plot, week 100



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

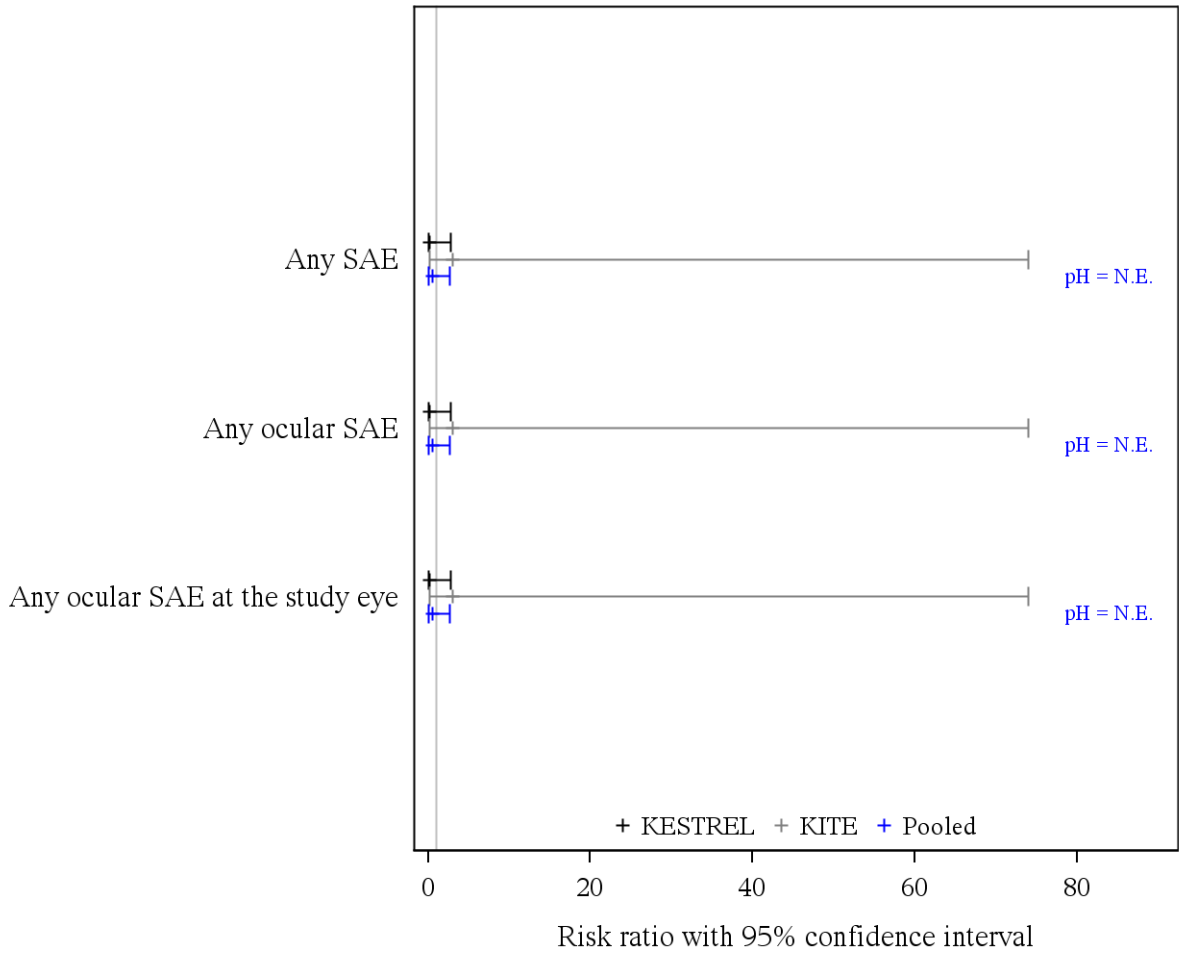
22 Safety analysis: Any serious adverse event of potential relevance to intravitreal anti-VEGF injection

Figure 22.1.1 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection (SAF), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

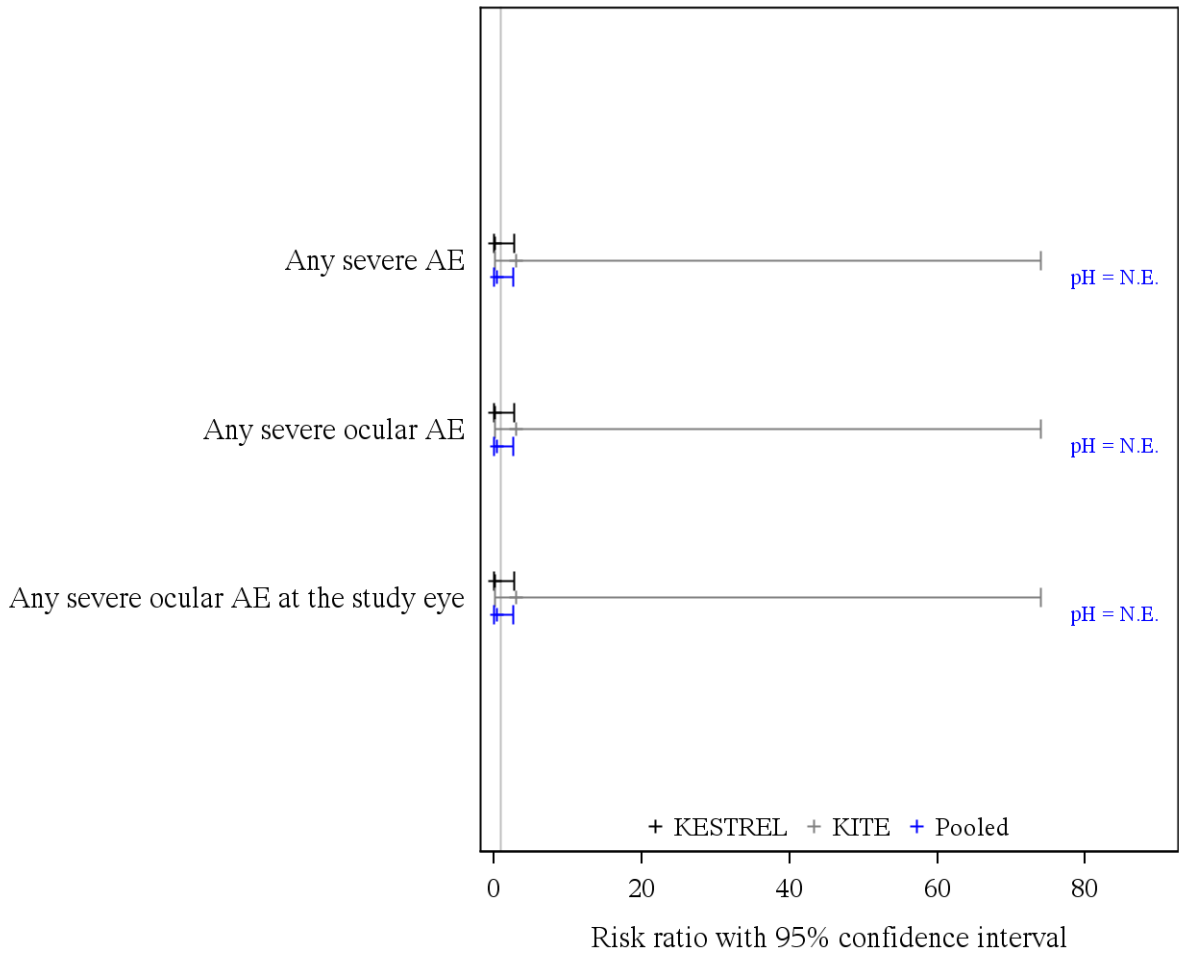
Figure 22.2.1 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection (SAF), forest plot, week 100



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

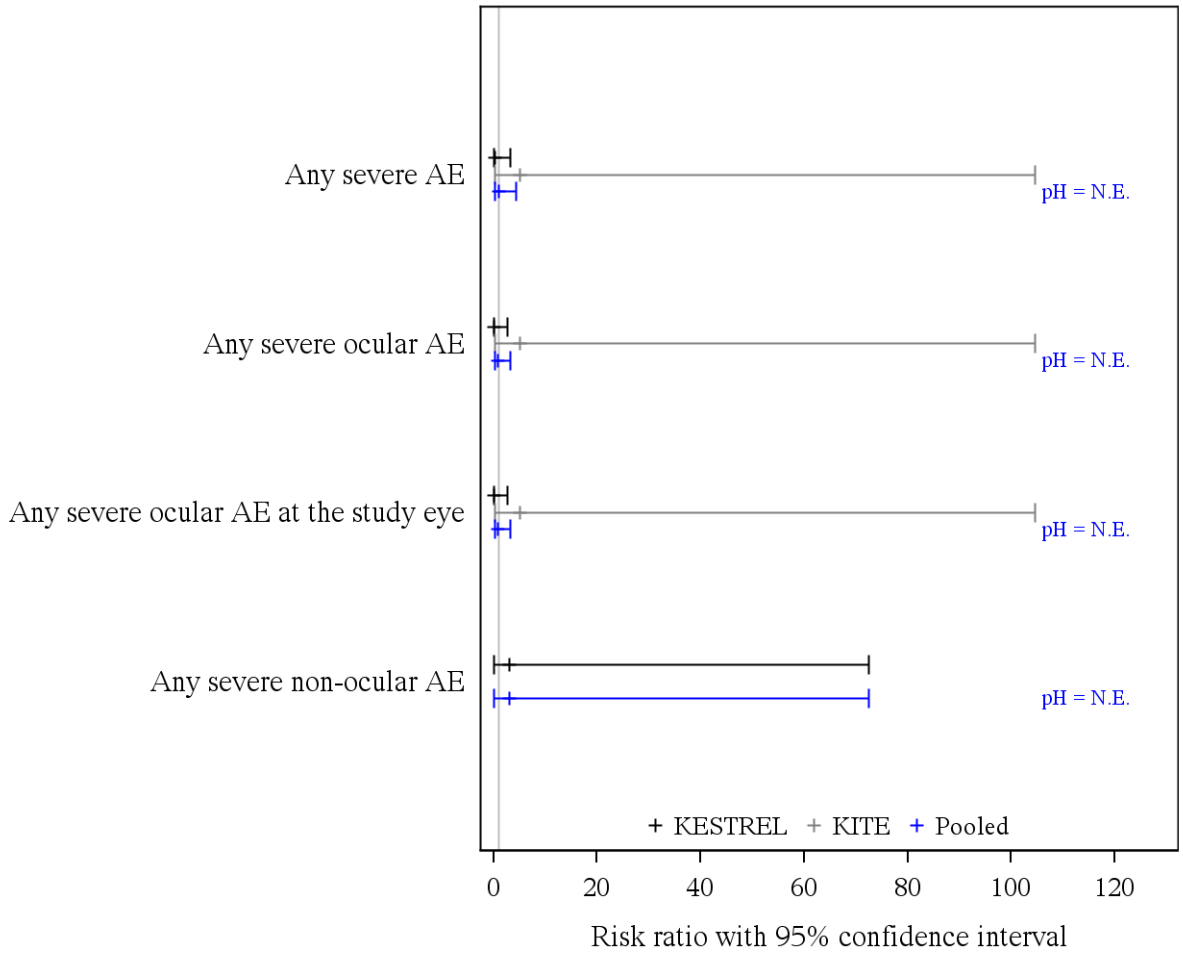
23 Safety analysis: Any severe adverse event of potential relevance to intravitreal anti-VEGF injection

Figure 23.1.1 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection (SAF), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 23.2.1 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection (SAF), forest plot, week 100



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.