Brolucizumab/Beovu®

CRTH258B2301 (KESTREL) and CRTH258B2302 (KITE)

AMNOG Analysis

Week 52

Date: 11th March 2022

Document status: Final

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1 Patient disposition and baseline characteristics

Table 1.1 Patient disposition and compliance (RAN, FAS, SAF), week 52

	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)	**18 (9.5)**	**15 (8.0)**	**33 (8.8)**	**17 (9.5)**	**12 (6.6)**	**29 (8.1)**
Reason for study discontinuation						
Adverse event	2 (1.1)	5 (2.7)	7 (1.9)	4 (2.2)	3 (1.7)	7 (1.9)
Death	5 (2.6)	2 (1.1)	7 (1.9)	3 (1.7)	2 (1.1)	5 (1.4)
Lost to follow-up	1 (0.5)	3 (1.6)	4 (1.1)	1 (0.6)	1 (0.6)	2 (0.6)
Physician decision	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	2 (1.1)	3 (0.8)
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	9 (4.8)	4 (2.1)	13 (3.5)	8 (4.5)	4 (2.2)	12 (3.3)
Study drug discontinuation (FAS)	**25 (13.2)**	**18 (9.6)**	**43 (11.4)**	**19 (10.6)**	**15 (8.3)**	**34 (9.4)**
Received alternative Anti-VEGF treatment	1 (0.5)	1 (0.5)	2 (0.5)	1 (0.6)	0 (0.0)	1 (0.3)
Reason for study drug discontinuation						
Adverse event	4 (2.1)	6 (3.2)	10 (2.7)	7 (3.9)	7 (3.9)	14 (3.9)
Death	3 (1.6)	2 (1.1)	5 (1.3)	3 (1.7)	1 (0.6)	4 (1.1)
Lost to follow-up	3 (1.6)	3 (1.6)	6 (1.6)	1 (0.6)	1 (0.6)	2 (0.6)
Physician decision	2 (1.1)	0 (0.0)	2 (0.5)	2 (1.1)	0 (0.0)	2 (0.6)
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)	2 (1.1)	3 (0.8)
Subject decision	10 (5.3)	5 (2.7)	15 (4.0)	5 (2.8)	4 (2.2)	9 (2.5)

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, 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)

N: Number of patients
n (%): Number and percentage of patients with event
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Table 1.6 Protocol deviations (FAS), week 52

	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	**65 (34.4)**	**76 (40.6)**	**141 (37.5)**	**53 (29.6)**	**54 (29.8)**	**107 (29.7)**
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	30 (15.9)	34 (18.2)	64 (17.0)	26 (14.5)	38 (21.0)	64 (17.8)
Other	54 (28.6)	60 (32.1)	114 (30.3)	45 (25.1)	37 (20.4)	82 (22.8)
Subjects with at least one protocol deviation not related to Covid-19	**20 (10.6)**	**33 (17.6)**	**53 (14.1)**	**14 (7.8)**	**27 (14.9)**	**41 (11.4)**
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	15 (7.9)	18 (9.6)	33 (8.8)	8 (4.5)	17 (9.4)	25 (6.9)
Other	6 (3.2)	12 (6.4)	18 (4.8)	5 (2.8)	6 (3.3)	11 (3.1)
Subjects with at least one protocol deviation related to Covid-19	**50 (26.5)**	**51 (27.3)**	**101 (26.9)**	**40 (22.3)**	**33 (18.2)**	**73 (20.3)**
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	17 (9.0)	20 (10.7)	37 (9.8)	19 (10.6)	23 (12.7)	42 (11.7)
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	16 (8.5)	20 (10.7)	36 (9.6)	19 (10.6)	23 (12.7)	42 (11.7)
Other	50 (26.5)	51 (27.3)	101 (26.9)	40 (22.3)	33 (18.2)	73 (20.3)
Missed visit	41 (21.7)	31 (16.6)	72 (19.1)	36 (20.1)	32 (17.7)	68 (18.9)
Missed BCVA assessment	1 (0.5)	1 (0.5)	2 (0.5)	1 (0.6)	2 (1.1)	3 (0.8)
Missed disease activity assessment	0 (0.0)	1 (0.5)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Missed IOP assessment	10 (5.3)	16 (8.6)	26 (6.9)	0 (0.0)	3 (1.7)	3 (0.8)

	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 (%)**
Missed laboratory assessment	4 (2.1)	11 (5.9)	15 (4.0)	0 (0.0)	1 (0.6)	1 (0.3)
Missed ophthalmic imaging	4 (2.1)	8 (4.3)	12 (3.2)	3 (1.7)	1 (0.6)	4 (1.1)
Missed PK/ADA assessment	6 (3.2)	17 (9.1)	23 (6.1)	2 (1.1)	2 (1.1)	4 (1.1)
Missed VFQ-25 assessment	1 (0.5)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Missed vital signs assessment	3 (1.6)	10 (5.3)	13 (3.5)	1 (0.6)	3 (1.7)	4 (1.1)
Study discontinuation	1 (0.5)	0 (0.0)	1 (0.3)	1 (0.6)	0 (0.0)	1 (0.3)

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

Table 1.7 Duration of study participation (FAS), week 52

	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)	358.4 ± 39.3	355.4 ± 53.9	356.9 ± 47.1	353.7 ± 55.6	356.8 ± 51.9	355.3 ± 53.7
Median (in days)	365.0	365.0	365.0	365.0	366.0	365.0
Range (in days)	39 to 393	27 to 387	27 to 393	30 to 386	71 to 388	30 to 388
Patients ≥ 52 weeks in study, n (%)	171 (90.5)	172 (92.0)	343 (91.2)	162 (90.5)	169 (93.4)	331 (91.9)
Patients < 52 weeks in study, n (%)	18 (9.5)	15 (8.0)	33 (8.8)	17 (9.5)	12 (6.6)	29 (8.1)
Duration of study participation on study drug						
Mean ± SD (in days)	352.6 ± 52.5	352.1 ± 60.0	352.4 ± 56.3	352.2 ± 57.7	354.6 ± 55.0	353.4 ± 56.3
Median (in days)	365.0	365.0	365.0	365.0	365.0	365.0
Range (in days)	29 to 393	1 to 387	1 to 393	30 to 386	57 to 388	30 to 388
Patients ≥ 52 weeks in study, n (%)	164 (86.8)	169 (90.4)	333 (88.6)	160 (89.4)	166 (91.7)	326 (90.6)
Patients < 52 weeks in study, n (%)	25 (13.2)	18 (9.6)	43 (11.4)	19 (10.6)	15 (8.3)	34 (9.4)

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

2 Mortality

Table 2.1 All-cause mortality (FAS), binary analysis, week 52

	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 (%)	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
p_H=0.689					

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.
RR and RD calculated directly (with Wald CI and p-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 52

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

Table 2.3 All-cause mortality by gender (FAS), binary analysis, week 52

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

Table 2.4 All-cause mortality by BCVA (FAS), binary analysis, week 52

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

Table 2.5 All-cause mortality by region (FAS), binary analysis, week 52

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

Table 2.6 All-cause mortality by diabetes type (FAS), binary analysis, week 52

	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

	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 (%)	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

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 + 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, KITE: logit(proportion) = treatment [by diabetes type].
Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 2.7 All-cause mortality by HbA1c (FAS), binary analysis, week 52

	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

	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 (%)	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

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, KITE: logit(proportion) = treatment [by HbA1c].
Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by HbA1c].

Table 2.8 All-cause mortality by duration of DME (FAS), binary analysis, week 52

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

Table 2.9 All-cause mortality by DME type (FAS), binary analysis, week 52

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

Table 2.10 All-cause mortality by CSFT (FAS), binary analysis, week 52

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

Table 2.11 All-cause mortality by status of SRF (FAS), binary analysis, week 52

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

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

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

3 BCVA: Continuous analysis

Table 3.0 BCVA (FAS), return rates, Week 52

	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)
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)
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)

	Treatment Groups		
BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Total**
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)
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)
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)

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 52

	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 52: Adjusted Mean Change (SE)	9.54 (0.57)	10.69 (0.57)	-1.15 [-2.75; 0.45]	0.158
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 52: Adjusted Mean Change (SE)	11.24 (0.61)	9.54 (0.61)	1.70 [-0.00; 3.40]	0.050
Pooled Analysis: Best Corrected Visual Acuity - Study Eye p_H=0.014 *				
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 52: Adjusted Mean Change (SE)	10.34 (0.42)	10.12 (0.42)	0.22 [-0.94; 1.38]	0.708

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.
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 52

	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=0.014 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.022 *			
< 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 52: Adjusted Mean Change (SE)	12.21 (0.77)	11.22 (0.80)	0.99 [-1.19; 3.17]	0.371
≥ 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 52: Adjusted Mean Change (SE)	6.42 (0.85)	10.04 (0.81)	-3.63 [-5.94; -1.32]	0.002 *
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.331			
< 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 52: Adjusted Mean Change (SE)	12.53 (0.83)	10.80 (0.81)	1.73 [-0.55; 4.02]	0.137
≥ 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 52: Adjusted Mean Change (SE)	9.60 (0.91)	7.93 (0.92)	1.68 [-0.87; 4.22]	0.196
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.022 *			
< 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 52: Adjusted Mean Change (SE)	12.35 (0.56)	11.01 (0.57)	1.34 [-0.23; 2.90]	0.095

	Treatment Groups		Comparison	
BCVA by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 52: Adjusted Mean Change (SE)	7.93 (0.62)	9.07 (0.61)	-1.14 [-2.85; 0.57]	0.190

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.

Table 3.3 BCVA by gender (FAS), continuous analysis, week 52

	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=0.014 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.897			
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 52: Adjusted Mean Change (SE)	10.34 (0.75)	11.36 (0.70)	-1.02 [-3.04; 1.01]	0.323
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 52: Adjusted Mean Change (SE)	8.46 (0.88)	9.37 (0.99)	-0.90 [-3.50; 1.69]	0.494
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.427			
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 52: Adjusted Mean Change (SE)	11.12 (0.75)	8.99 (0.76)	2.13 [0.03; 4.23]	0.047 *
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 52: Adjusted Mean Change (SE)	11.48 (1.07)	10.52 (1.01)	0.96 [-1.94; 3.86]	0.514
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.515			
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 52: Adjusted Mean Change (SE)	10.72 (0.53)	10.24 (0.52)	0.47 [-0.98; 1.93]	0.524

	Treatment Groups		Comparison	
BCVA by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 52: Adjusted Mean Change (SE)	9.74 (0.68)	9.90 (0.70)	-0.16 [-2.09; 1.76]	0.868

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.

Table 3.4 BCVA by BCVA (FAS), continuous analysis, week 52

	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=0.014 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.065			
≤ 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 52: Adjusted Mean Change (SE)	11.91 (0.91)	15.65 (0.96)	-3.75 [-6.35; -1.14]	0.005 *
> 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 52: Adjusted Mean Change (SE)	8.18 (0.72)	7.96 (0.70)	0.22 [-1.75; 2.18]	0.827
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.378			
≤ 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 52: Adjusted Mean Change (SE)	14.96 (1.02)	12.02 (0.85)	2.94 [0.33; 5.56]	0.028 *
> 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 52: Adjusted Mean Change (SE)	8.74 (0.77)	7.53 (0.86)	1.21 [-1.06; 3.48]	0.295
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.603			
≤ 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 52: Adjusted Mean Change (SE)	13.40 (0.68)	13.63 (0.64)	-0.23 [-2.06; 1.61]	0.809

	Treatment Groups		Comparison	
BCVA by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 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 52: Adjusted Mean Change (SE)	8.38 (0.52)	7.71 (0.54)	0.67 [-0.81; 2.16]	0.376

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.

Table 3.5 BCVA by region (FAS), continuous analysis, week 52

	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=0.014 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.640			
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 52: Adjusted Mean Change (SE)	8.92 (0.84)	10.02 (0.86)	-1.10 [-3.45; 1.26]	0.360
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 52: Adjusted Mean Change (SE)	10.74 (0.95)	11.12 (0.92)	-0.38 [-2.98; 2.22]	0.775
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 52: Adjusted Mean Change (SE)	8.60 (1.44)	11.47 (1.46)	-2.87 [-6.90; 1.15]	0.162
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.328			
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 52: Adjusted Mean Change (SE)	9.99 (1.67)	9.80 (1.84)	0.20 [-4.69; 5.08]	0.936
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 52: Adjusted Mean Change (SE)	11.72 (0.70)	9.18 (0.71)	2.53 [0.57; 4.49]	0.011 *

	Treatment Groups		Comparison	
BCVA by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 52: Adjusted Mean Change (SE)	9.00 (1.91)	11.10 (1.55)	-2.10 [-6.93; 2.73]	0.393
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.439			
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 52: Adjusted Mean Change (SE)	9.40 (0.91)	9.60 (0.93)	-0.20 [-2.76; 2.36]	0.879
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 52: Adjusted Mean Change (SE)	9.46 (1.69)	10.78 (1.84)	-1.32 [-6.22; 3.58]	0.598
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 52: Adjusted Mean Change (SE)	11.18 (0.57)	10.02 (0.56)	1.16 [-0.41; 2.74]	0.148
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 52: Adjusted Mean Change (SE)	8.85 (1.15)	11.11 (1.06)	-2.27 [-5.34; 0.81]	0.148

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.

Table 3.6 BCVA by diabetes type (FAS), continuous analysis, week 52

	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=0.014 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.157			
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 52: Adjusted Mean Change (SE)	10.28 (2.31)	9.11 (3.12)	1.16 [-6.48; 8.81]	0.765
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 52: Adjusted Mean Change (SE)	9.49 (0.60)	10.73 (0.59)	-1.24 [-2.88; 0.40]	0.138
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.531			
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 52: Adjusted Mean Change (SE)	12.63 (1.85)	10.82 (3.01)	1.81 [-5.13; 8.75]	0.609
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 52: Adjusted Mean Change (SE)	11.07 (0.65)	9.48 (0.62)	1.59 [-0.19; 3.37]	0.079
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.158			
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 52: Adjusted Mean Change (SE)	11.42 (1.43)	10.06 (2.15)	1.35 [-3.72; 6.43]	0.601

	Treatment Groups		Comparison	
BCVA by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 52: Adjusted Mean Change (SE)	10.25 (0.44)	10.12 (0.43)	0.13 [-1.07; 1.33]	0.832

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.

Table 3.7 BCVA by HbA1c (FAS), continuous analysis, week 52

	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=0.014 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.896			
< 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 52: Adjusted Mean Change (SE)	9.08 (0.90)	10.72 (0.76)	-1.65 [-3.96; 0.67]	0.162
≥ 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 52: Adjusted Mean Change (SE)	9.90 (0.75)	10.65 (0.89)	-0.76 [-3.05; 1.53]	0.517
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.224			
< 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 52: Adjusted Mean Change (SE)	12.41 (0.91)	8.97 (0.83)	3.44 [1.02; 5.86]	0.005 *
≥ 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 52: Adjusted Mean Change (SE)	10.27 (0.83)	10.17 (0.88)	0.10 [-2.28; 2.48]	0.932
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.451			
< 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 52: Adjusted Mean Change (SE)	10.67 (0.64)	9.90 (0.56)	0.77 [-0.90; 2.44]	0.366

	Treatment Groups		Comparison	
BCVA by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 52: Adjusted Mean Change (SE)	10.12 (0.56)	10.41 (0.63)	-0.29 [-1.93; 1.36]	0.731

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.

Table 3.8 BCVA by duration of DME (FAS), continuous analysis, week 52

	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=0.014 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.785			
≤ 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 52: Adjusted Mean Change (SE)	10.53 (0.71)	11.63 (0.74)	-1.10 [-3.11; 0.91]	0.282
> 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 52: Adjusted Mean Change (SE)	9.69 (1.43)	10.35 (1.26)	-0.66 [-4.40; 3.08]	0.730
≥ 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 52: Adjusted Mean Change (SE)	6.20 (1.29)	8.32 (1.26)	-2.12 [-5.66; 1.41]	0.238
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.117			
≤ 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 52: Adjusted Mean Change (SE)	11.40 (0.89)	8.29 (0.85)	3.11 [0.68; 5.54]	0.012 *
> 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 52: Adjusted Mean Change (SE)	11.81 (1.13)	10.76 (1.16)	1.06 [-2.13; 4.24]	0.515

	Treatment Groups		Comparison	
BCVA by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 52: Adjusted Mean Change (SE)	10.24 (1.26)	10.87 (1.30)	-0.63 [-4.18; 2.93]	0.730
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.244			
≤ 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 52: Adjusted Mean Change (SE)	11.00 (0.56)	10.06 (0.56)	0.93 [-0.62; 2.49]	0.240
> 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 52: Adjusted Mean Change (SE)	10.85 (0.89)	10.69 (0.85)	0.16 [-2.25; 2.58]	0.896
≥ 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 52: Adjusted Mean Change (SE)	8.22 (0.90)	9.61 (0.91)	-1.39 [-3.90; 1.11]	0.276

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.

Table 3.9 BCVA by DME type (FAS), continuous analysis, week 52

	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=0.014 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.282			
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 52: Adjusted Mean Change (SE)	9.26 (1.02)	8.69 (1.15)	0.57 [-2.43; 3.58]	0.708
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 52: Adjusted Mean Change (SE)	9.63 (0.71)	11.32 (0.68)	-1.69 [-3.62; 0.23]	0.084
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.713			
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 52: Adjusted Mean Change (SE)	10.94 (1.02)	9.52 (0.97)	1.41 [-1.35; 4.18]	0.316
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 52: Adjusted Mean Change (SE)	11.55 (0.74)	9.92 (0.76)	1.63 [-0.45; 3.71]	0.125
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.366			
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 52: Adjusted Mean Change (SE)	10.03 (0.73)	9.20 (0.75)	0.83 [-1.22; 2.87]	0.427

	Treatment Groups		Comparison	
BCVA by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 52: Adjusted Mean Change (SE)	10.56 (0.51)	10.61 (0.51)	-0.05 [-1.47; 1.37]	0.946

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.

Table 3.10 BCVA by CSFT (FAS), continuous analysis, week 52

	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=0.014 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.031 *			
< 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 52: Adjusted Mean Change (SE)	10.10 (0.76)	9.91 (0.80)	0.19 [-1.98; 2.36]	0.861
≥ 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 52: Adjusted Mean Change (SE)	8.81 (0.94)	10.49 (0.92)	-1.68 [-4.27; 0.90]	0.201
≥ 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 52: Adjusted Mean Change (SE)	8.70 (2.31)	15.04 (1.75)	-6.35 [-12.01; -0.69]	0.028 *
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.185			
< 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 52: Adjusted Mean Change (SE)	9.51 (0.90)	8.61 (0.92)	0.89 [-1.63; 3.42]	0.487
≥ 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 52: Adjusted Mean Change (SE)	12.92 (0.94)	10.01 (0.90)	2.92 [0.35; 5.48]	0.026 *

	Treatment Groups		Comparison	
BCVA by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 52: Adjusted Mean Change (SE)	12.02 (1.83)	11.98 (1.88)	0.04 [-5.09; 5.17]	0.988
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.044 *			
< 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 52: Adjusted Mean Change (SE)	9.86 (0.59)	9.30 (0.61)	0.55 [-1.10; 2.20]	0.511
≥ 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 52: Adjusted Mean Change (SE)	10.93 (0.66)	10.22 (0.65)	0.71 [-1.11; 2.53]	0.443
≥ 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 52: Adjusted Mean Change (SE)	10.55 (1.43)	13.54 (1.29)	-2.99 [-6.74; 0.76]	0.118

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.

Table 3.11 BCVA by status of SRF (FAS), continuous analysis, week 52

	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=0.014 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.880			
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 52: Adjusted Mean Change (SE)	11.11 (1.00)	12.68 (1.00)	-1.57 [-4.33; 1.18]	0.263
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 52: Adjusted Mean Change (SE)	8.78 (0.70)	9.69 (0.70)	-0.91 [-2.85; 1.02]	0.354
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.658			
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 52: Adjusted Mean Change (SE)	13.25 (1.10)	11.36 (0.99)	1.89 [-1.01; 4.79]	0.200
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 52: Adjusted Mean Change (SE)	10.28 (0.74)	8.50 (0.76)	1.78 [-0.31; 3.86]	0.094
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.876			
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 52: Adjusted Mean Change (SE)	12.05 (0.74)	12.02 (0.70)	0.03 [-1.96; 2.01]	0.978

	Treatment Groups		Comparison	
BCVA by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 52: Adjusted Mean Change (SE)	9.53 (0.51)	9.11 (0.51)	0.42 [-0.99; 1.83]	0.556

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.

Table 3.12 BCVA by exposure (FAS), continuous analysis, week 52

	Treatment Groups		Comparison	
BCVA by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Best Corrected Visual Acuity - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.014 ***				
KESTREL: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.100			
Non-exposed				
N'/ N	71 / 71	75 / 75		
Baseline Mean (SD)	65.30 (11.30)	65.81 (13.02)		
Week 52 Mean (SD)	76.45 (10.33)	77.71 (10.23)		
Week 52: Adjusted Mean Change (SE)	9.14 (0.94)	11.61 (0.92)	-2.47 [-5.07; 0.13]	0.063
Exposed				
N'/ N	118 / 118	112 / 112		
Baseline Mean (SD)	67.40 (8.50)	64.74 (11.98)		
Week 52 Mean (SD)	77.99 (9.51)	74.90 (11.11)		
Week 52: Adjusted Mean Change (SE)	9.78 (0.72)	10.10 (0.73)	-0.32 [-2.34; 1.70]	0.756
KITE: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.360			
Non-exposed				
N'/ N	85 / 85	90 / 90		
Baseline Mean (SD)	66.56 (9.83)	63.38 (12.44)		
Week 52 Mean (SD)	78.31 (11.27)	74.12 (11.12)		
Week 52: Adjusted Mean Change (SE)	11.17 (0.90)	9.14 (0.87)	2.03 [-0.44; 4.50]	0.107
Exposed				
N'/ N	94 / 94	91 / 91		
Baseline Mean (SD)	65.50 (11.58)	64.03 (10.98)		
Week 52 Mean (SD)	76.83 (10.41)	73.43 (12.76)		
Week 52: Adjusted Mean Change (SE)	11.27 (0.84)	9.92 (0.85)	1.36 [-1.01; 3.72]	0.261
Pooled Analysis: Best Corrected Visual Acuity - Study Eye				
Interaction test	p=0.069			
Non-exposed				
N'/ N	156 / 156	165 / 165		
Baseline Mean (SD)	65.99 (10.51)	64.48 (12.72)		
Week 52 Mean (SD)	77.47 (10.86)	75.73 (10.84)		
Week 52: Adjusted Mean Change (SE)	10.19 (0.65)	10.33 (0.63)	-0.14 [-1.92; 1.65]	0.880

	Treatment Groups		Comparison	
BCVA by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Exposed				
N'/ N	212 / 212	203 / 203		
Baseline Mean (SD)	66.56 (10.00)	64.42 (11.52)		
Week 52 Mean (SD)	77.48 (9.91)	74.26 (11.83)		
Week 52: Adjusted Mean Change (SE)	10.45 (0.55)	9.95 (0.56)	0.50 [-1.04; 2.04]	0.525

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 + exposure + treatment * exposure + visit * exposure + treatment * exposure * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + exposure + treatment * exposure + visit * exposure + treatment * exposure * visit.

4 BCVA: Binary analysis (Gain)

Table 4.1 BCVA - Gain of 10 respectively 15 letters (FAS), binary analysis, week 52

	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 (%)	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
p_H=0.085					
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 *					

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.
RR and RD calculated directly (with Wald 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 52

	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 ≥ 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

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 + 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 52

	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 ≥ 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

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 52

	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 ≥ 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

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 52

	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 ≥ 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 = 0.673				
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

	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 ≥ 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
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 *

	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	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

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 + 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 52

	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 ≥ 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

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 + 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 52

	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 ≥ 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

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 52

	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 ≥ 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 = 0.452				
≤ 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

	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 ≥ 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
> 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

	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	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

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 52

	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 ≥ 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

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 52

	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 ≥ 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 = 0.133				
< 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

	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 ≥ 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
≥ 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

	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	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

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 + 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 52

	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 ≥ 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

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 + 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 (FAS), binary analysis, week 52

	Treatment Groups		Comparison		
BCVA - Gain of 10 respectively 15 letters by exposure (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 (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 (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
*: $p < 0.05$
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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 + treatment * exposure.
RR and RD calculated directly (with Wald 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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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 52

	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 (%) p_H=0.774	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
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 (%) p_H=N.E.	2 (0.5)	4 (1.1)	N.E.	0.56 [0.12; 2.60] 0.452	-0.01 [-0.02; 0.01] 0.416

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: 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 52

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

Table 5.3 BCVA - Loss of 10 respectively 15 letters by gender (FAS), binary analysis, week 52

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

Table 5.4 BCVA - Loss of 10 respectively 15 letters by BCVA (FAS), binary analysis, week 52

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

Table 5.5 BCVA - Loss of 10 respectively 15 letters by region (FAS), binary analysis, week 52

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

Table 5.6 BCVA - Loss of 10 respectively 15 letters by diabetes type (FAS), binary analysis, week 52

	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.

	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	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

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: 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, Loss in BCVA of ≥ 10 Letters / KITE: logit(proportion) = treatment [by diabetes type].
Loss in BCVA of ≥ 10 Letters / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 5.7 BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS), binary analysis, week 52

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

Table 5.8 BCVA - Loss of 10 respectively 15 letters by duration of DME (FAS), binary analysis, week 52

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

Table 5.9 BCVA - Loss of 10 respectively 15 letters by DME type (FAS), binary analysis, week 52

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

Table 5.10 BCVA - Loss of 10 respectively 15 letters by CSFT (FAS), binary analysis, week 52

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

Table 5.11 BCVA - Loss of 10 respectively 15 letters by status of SRF (FAS), binary analysis, week 52

	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

	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	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

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: 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: logit(proportion) = treatment [by status of SRF].

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

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

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

Table 6.1 BCVA - Gain of 10 respectively 15 letters (FAS), time-to-event analysis, week 52

	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 ≥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

	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 (%)	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

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 52

	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 ≥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=0.115			
< 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

	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 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
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

	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 (%)	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

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 52

	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 ≥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			
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

	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 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
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

	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 (%)	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

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 52

	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 ≥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=0.111			
≤ 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

	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 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
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

	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 (%)	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

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 52

	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 ≥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
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

	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 ≥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
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

	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 (%)	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

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 + 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 52

	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 ≥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=0.215			
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

	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 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
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

	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 (%)	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

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 52

	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 ≥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=0.637			
< 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

	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 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
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

	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 (%)	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

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 52

	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 ≥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

	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 (%)	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

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 52

	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 ≥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=0.127			
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

	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 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
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

	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 (%)	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

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 52

	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 ≥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

	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 (%)	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 *

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 52

	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 ≥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=0.193			
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

	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 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
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

	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 (%)	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

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 (FAS), time-to-event analysis, week 52

	Treatment Groups		Comparison	
BCVA - Gain of 10 respectively 15 letters by exposure (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 (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 (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

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

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 + treatment * exposure.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + exposure + treatment * exposure.

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

Table 7.1 BCVA - Loss of 10 respectively 15 letters (FAS), time-to-event analysis, week 52

	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 ≥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

	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 (%)	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

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.
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 52

	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 ≥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=0.995			
< 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 *

	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 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
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

	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 (%)	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

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 52

	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 ≥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=0.995			
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

	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 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 *
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

	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 (%)	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

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 52

	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 ≥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=0.995			
≤ 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

	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 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
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

	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 (%)	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

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 52

	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 ≥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
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

	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 ≥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
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

	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 (%)	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

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 52

	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 ≥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			
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

	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 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
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

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 7.7 BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS), time-to-event analysis, week 52

	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 ≥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			
< 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

	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 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
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

	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 (%)	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

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 52

	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 ≥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

	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 (%)	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

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 52

	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 ≥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			
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

	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 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
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

	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 (%)	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

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 + 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 52

	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 ≥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 CSFT (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			
< 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 ≥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

	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 (%)	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

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 52

	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 ≥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=0.995			
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

	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 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
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

	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 (%)	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

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

	Treatment Groups		Comparison	
BCVA - Loss of 10 respectively 15 letters by exposure (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 (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 (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

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

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 + treatment * exposure.
Pooled analysis: log(hazard ratio) = treatment + age category + baseline category + study + treatment * study + exposure + treatment * exposure.

8 VFQ: Continuous analysis

Table 8.0 VFQ (FAS), return rates, Week 52

	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)
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)
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)

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 52

	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)	85.02 (13.90)	85.15 (12.27)		
Week 28: Adjusted Mean Change (SE)	5.81 (0.80)	7.71 (0.80)		
Week 52: Adjusted Mean Change (SE)	7.17 (0.84)	8.34 (0.82)	-1.17 [-3.48; 1.13]	0.318
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 28: Adjusted Mean Change (SE)	5.86 (0.76)	6.05 (0.76)		
Week 52: Adjusted Mean Change (SE)	8.90 (0.83)	6.53 (0.82)	2.38 [0.09; 4.67]	0.042 *
Pooled Analysis: Composite Score p_H=0.071				
N'/ N	366 / 368	368 / 368		
Baseline Mean (SD)	77.21 (16.29)	76.64 (16.16)		
Week 52 Mean (SD)	85.74 (13.41)	84.37 (14.02)		
Week 28: Adjusted Mean Change (SE)	5.89 (0.56)	6.87 (0.56)		
Week 52: Adjusted Mean Change (SE)	8.05 (0.59)	7.44 (0.58)	0.61 [-1.02; 2.24]	0.462
KESTREL: General Vision				
N'/ N	188 / 189	187 / 187		
Baseline Mean (SD)	61.28 (17.26)	60.21 (14.66)		
Week 52 Mean (SD)	72.89 (14.16)	71.14 (12.87)		
Week 28: Adjusted Mean Change (SE)	11.33 (0.97)	10.64 (0.98)		
Week 52: Adjusted Mean Change (SE)	11.64 (1.03)	10.66 (1.00)	0.98 [-1.84; 3.81]	0.495
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 28: Adjusted Mean Change (SE)	9.43 (1.03)	9.66 (1.02)		
Week 52: Adjusted Mean Change (SE)	11.70 (1.14)	10.29 (1.12)	1.41 [-1.75; 4.56]	0.382

	Treatment Groups		Comparison	
VFQ (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: General Vision p_H=0.986				
N'/ N	366 / 368	368 / 368		
Baseline Mean (SD)	61.53 (16.68)	60.05 (16.54)		
Week 52 Mean (SD)	72.83 (14.30)	70.84 (15.08)		
Week 28: Adjusted Mean Change (SE)	10.40 (0.71)	10.15 (0.71)		
Week 52: Adjusted Mean Change (SE)	11.66 (0.77)	10.49 (0.75)	1.18 [-0.94; 3.29]	0.276
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 28: Adjusted Mean Change (SE)	2.74 (1.31)	4.34 (1.33)		
Week 52: Adjusted Mean Change (SE)	5.19 (1.21)	4.37 (1.18)	0.82 [-2.51; 4.15]	0.629
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 28: Adjusted Mean Change (SE)	4.66 (1.18)	4.02 (1.17)		
Week 52: Adjusted Mean Change (SE)	5.05 (1.23)	4.04 (1.21)	1.01 [-2.38; 4.40]	0.558
Pooled Analysis: Ocular Pain p_H=0.492				
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 28: Adjusted Mean Change (SE)	3.71 (0.89)	4.15 (0.89)		
Week 52: Adjusted Mean Change (SE)	5.15 (0.87)	4.20 (0.85)	0.95 [-1.43; 3.34]	0.433
KESTREL: Near Activities				
N'/ N	188 / 189	187 / 187		
Baseline Mean (SD)	63.50 (26.15)	65.64 (21.82)		
Week 52 Mean (SD)	79.17 (21.28)	78.69 (20.11)		
Week 28: Adjusted Mean Change (SE)	12.41 (1.35)	14.51 (1.37)		
Week 52: Adjusted Mean Change (SE)	13.45 (1.50)	13.76 (1.47)	-0.30 [-4.43; 3.82]	0.885

	Treatment Groups		Comparison	
VFQ (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 28: Adjusted Mean Change (SE)	6.50 (1.38)	6.09 (1.37)		
Week 52: Adjusted Mean Change (SE)	10.36 (1.39)	9.22 (1.37)	1.14 [-2.71; 4.99]	0.560
Pooled Analysis: Near Activities p_H=0.456				
N'/ N	365 / 368	368 / 368		
Baseline Mean (SD)	66.72 (24.59)	67.49 (22.91)		
Week 52 Mean (SD)	79.62 (20.94)	78.67 (21.06)		
Week 28: Adjusted Mean Change (SE)	9.66 (0.98)	10.25 (0.98)		
Week 52: Adjusted Mean Change (SE)	11.99 (1.04)	11.47 (1.02)	0.52 [-2.33; 3.37]	0.721
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 28: Adjusted Mean Change (SE)	7.45 (1.20)	8.97 (1.21)		
Week 52: Adjusted Mean Change (SE)	9.11 (1.14)	9.63 (1.12)	-0.52 [-3.67; 2.62]	0.744
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 28: Adjusted Mean Change (SE)	6.32 (1.19)	5.51 (1.19)		
Week 52: Adjusted Mean Change (SE)	11.39 (1.14)	8.20 (1.12)	3.19 [0.04; 6.33]	0.047 *
Pooled Analysis: Distance Activities p_H=0.136				
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 28: Adjusted Mean Change (SE)	6.95 (0.85)	7.24 (0.85)		
Week 52: Adjusted Mean Change (SE)	10.26 (0.81)	8.92 (0.80)	1.34 [-0.89; 3.57]	0.238

	Treatment Groups		Comparison	
VFQ (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 28: Adjusted Mean Change (SE)	1.64 (0.91)	4.04 (0.92)		
Week 52: Adjusted Mean Change (SE)	2.67 (1.03)	4.16 (1.01)	-1.49 [-4.32; 1.34]	0.302
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 28: Adjusted Mean Change (SE)	3.82 (1.06)	3.98 (1.05)		
Week 52: Adjusted Mean Change (SE)	7.45 (0.91)	4.46 (0.90)	2.99 [0.47; 5.51]	0.020 *
Pooled Analysis: Social Functioning p_H=0.037 *				
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 28: Adjusted Mean Change (SE)	2.76 (0.70)	3.96 (0.70)		
Week 52: Adjusted Mean Change (SE)	5.08 (0.69)	4.26 (0.68)	0.82 [-1.09; 2.72]	0.401
KESTREL: Mental Health				
N'/ N	188 / 189	187 / 187		
Baseline Mean (SD)	65.53 (24.93)	68.25 (23.03)		
Week 52 Mean (SD)	78.44 (20.04)	78.68 (17.88)		
Week 28: Adjusted Mean Change (SE)	7.37 (1.28)	9.08 (1.30)		
Week 52: Adjusted Mean Change (SE)	10.44 (1.33)	11.19 (1.29)	-0.75 [-4.40; 2.89]	0.685
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 28: Adjusted Mean Change (SE)	8.73 (1.29)	9.33 (1.28)		
Week 52: Adjusted Mean Change (SE)	13.00 (1.56)	9.59 (1.53)	3.41 [-0.89; 7.72]	0.120

	Treatment Groups		Comparison	
VFQ (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Mental Health p_H=0.300				
N'/ N	366 / 368	368 / 368		
Baseline Mean (SD)	67.18 (23.38)	67.03 (24.54)		
Week 52 Mean (SD)	79.88 (20.39)	77.72 (20.84)		
Week 28: Adjusted Mean Change (SE)	8.11 (0.91)	9.16 (0.91)		
Week 52: Adjusted Mean Change (SE)	11.74 (1.02)	10.36 (1.00)	1.38 [-1.42; 4.19]	0.334
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 28: Adjusted Mean Change (SE)	5.96 (1.60)	9.13 (1.62)		
Week 52: Adjusted Mean Change (SE)	6.99 (1.76)	11.15 (1.72)	-4.15 [-8.99; 0.68]	0.092
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 28: Adjusted Mean Change (SE)	7.56 (1.58)	8.39 (1.57)		
Week 52: Adjusted Mean Change (SE)	12.30 (1.70)	8.51 (1.67)	3.79 [-0.89; 8.48]	0.112
Pooled Analysis: Role Difficulties p_H=0.072				
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 28: Adjusted Mean Change (SE)	6.80 (1.13)	8.75 (1.13)		
Week 52: Adjusted Mean Change (SE)	9.60 (1.22)	9.85 (1.20)	-0.25 [-3.61; 3.11]	0.883
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 28: Adjusted Mean Change (SE)	5.62 (1.37)	6.81 (1.39)		
Week 52: Adjusted Mean Change (SE)	5.68 (1.44)	8.74 (1.41)	-3.05 [-7.02; 0.91]	0.131

	Treatment Groups		Comparison	
VFQ (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 28: Adjusted Mean Change (SE)	5.66 (1.29)	3.36 (1.28)		
Week 52: Adjusted Mean Change (SE)	7.53 (1.40)	3.45 (1.38)	4.09 [0.22; 7.96]	0.039 *
Pooled Analysis: Dependency p_H=0.029 *				
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 28: Adjusted Mean Change (SE)	5.72 (0.95)	5.11 (0.95)		
Week 52: Adjusted Mean Change (SE)	6.64 (1.01)	6.13 (0.99)	0.51 [-2.27; 3.29]	0.719
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 28: Adjusted Mean Change (SE)	2.06 (1.38)	5.74 (1.42)		
Week 52: Adjusted Mean Change (SE)	3.62 (1.59)	6.11 (1.64)	-2.49 [-6.99; 2.01]	0.277
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 28: Adjusted Mean Change (SE)	0.73 (1.44)	5.44 (1.50)		
Week 52: Adjusted Mean Change (SE)	5.85 (1.25)	5.24 (1.31)	0.62 [-2.96; 4.19]	0.734
Pooled Analysis: Driving p_H=0.778				
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 28: Adjusted Mean Change (SE)	1.43 (1.00)	5.63 (1.03)		
Week 52: Adjusted Mean Change (SE)	4.72 (1.03)	5.75 (1.07)	-1.03 [-3.94; 1.88]	0.488

	Treatment Groups		Comparison	
VFQ (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 28: Adjusted Mean Change (SE)	2.10 (0.84)	1.82 (0.85)		
Week 52: Adjusted Mean Change (SE)	2.20 (0.87)	1.78 (0.86)	0.43 [-1.97; 2.82]	0.727
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 28: Adjusted Mean Change (SE)	3.60 (0.82)	4.20 (0.82)		
Week 52: Adjusted Mean Change (SE)	5.75 (0.75)	3.43 (0.74)	2.32 [0.25; 4.40]	0.028 *
Pooled Analysis: Color Vision p_H=0.691				
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 28: Adjusted Mean Change (SE)	2.89 (0.60)	2.97 (0.60)		
Week 52: Adjusted Mean Change (SE)	3.97 (0.57)	2.57 (0.56)	1.40 [-0.18; 2.98]	0.082
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 28: Adjusted Mean Change (SE)	2.82 (1.35)	7.82 (1.36)		
Week 52: Adjusted Mean Change (SE)	5.79 (1.39)	7.36 (1.35)	-1.57 [-5.38; 2.25]	0.420
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 28: Adjusted Mean Change (SE)	4.77 (1.20)	4.60 (1.19)		
Week 52: Adjusted Mean Change (SE)	6.48 (1.28)	3.60 (1.27)	2.88 [-0.67; 6.43]	0.111

	Treatment Groups		Comparison	
VFQ (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Peripheral Vision p_H=0.021 *				
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 28: Adjusted Mean Change (SE)	3.69 (0.91)	6.33 (0.91)		
Week 52: Adjusted Mean Change (SE)	6.02 (0.95)	5.64 (0.93)	0.38 [-2.23; 2.99]	0.776
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 28: Adjusted Mean Change (SE)	4.35 (1.38)	4.71 (1.40)		
Week 52: Adjusted Mean Change (SE)	8.37 (1.69)	5.15 (1.65)	3.22 [-1.44; 7.88]	0.175
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 28: Adjusted Mean Change (SE)	3.61 (1.39)	4.40 (1.38)		
Week 52: Adjusted Mean Change (SE)	5.47 (1.65)	4.96 (1.62)	0.51 [-4.04; 5.06]	0.825
Pooled Analysis: General Health p_H=0.700				
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 28: Adjusted Mean Change (SE)	3.88 (0.98)	4.66 (0.98)		
Week 52: Adjusted Mean Change (SE)	6.84 (1.18)	5.16 (1.15)	1.68 [-1.56; 4.93]	0.308

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 52

	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=0.071**				
KESTREL: Composite Score				
Interaction test	p=0.627			
< 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 28: Adjusted Mean Change (SE)	7.27 (1.07)	8.97 (1.13)		
Week 52: Adjusted Mean Change (SE)	8.32 (1.12)	10.59 (1.14)	-2.27 [-5.42; 0.88]	0.157
≥ 65 years				
N'/ N	85 / 85	94 / 94		
Baseline Mean (SD)	76.63 (17.43)	78.85 (12.99)		
Week 52 Mean (SD)	83.46 (13.17)	83.01 (12.30)		
Week 28: Adjusted Mean Change (SE)	4.13 (1.20)	6.22 (1.15)		
Week 52: Adjusted Mean Change (SE)	5.88 (1.25)	5.78 (1.19)	0.10 [-3.29; 3.49]	0.954
KITE: Composite Score				
Interaction test	p=0.795			
< 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 28: Adjusted Mean Change (SE)	6.84 (1.02)	6.66 (1.01)		
Week 52: Adjusted Mean Change (SE)	8.92 (1.12)	6.48 (1.09)	2.44 [-0.64; 5.53]	0.120
≥ 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 28: Adjusted Mean Change (SE)	4.59 (1.16)	5.26 (1.15)		
Week 52: Adjusted Mean Change (SE)	8.83 (1.23)	6.57 (1.23)	2.26 [-1.16; 5.68]	0.195

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Composite Score				
Interaction test	p=0.784			
< 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 28: Adjusted Mean Change (SE)	7.12 (0.75)	7.91 (0.77)		
Week 52: Adjusted Mean Change (SE)	8.66 (0.80)	8.61 (0.80)	0.05 [-2.17; 2.26]	0.967
≥ 65 years				
N'/ N	163 / 164	173 / 173		
Baseline Mean (SD)	76.52 (16.96)	77.50 (15.53)		
Week 52 Mean (SD)	84.47 (13.63)	83.32 (13.83)		
Week 28: Adjusted Mean Change (SE)	4.39 (0.84)	5.62 (0.82)		
Week 52: Adjusted Mean Change (SE)	7.31 (0.88)	6.03 (0.86)	1.28 [-1.14; 3.70]	0.300
General Vision				
Test of heterogeneity in main analysis: **p_H=0.986**				
KESTREL: General Vision				
Interaction test	p=0.863			
< 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 28: Adjusted Mean Change (SE)	12.28 (1.30)	11.53 (1.38)		
Week 52: Adjusted Mean Change (SE)	13.10 (1.38)	12.52 (1.39)	0.58 [-3.27; 4.43]	0.767
≥ 65 years				
N'/ N	85 / 85	94 / 94		
Baseline Mean (SD)	61.65 (15.19)	60.21 (15.38)		
Week 52 Mean (SD)	71.34 (13.58)	68.53 (13.63)		
Week 28: Adjusted Mean Change (SE)	10.27 (1.46)	9.55 (1.40)		
Week 52: Adjusted Mean Change (SE)	9.94 (1.54)	8.52 (1.45)	1.42 [-2.74; 5.58]	0.502

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Vision				
Interaction test	p=0.768			
< 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 28: Adjusted Mean Change (SE)	11.10 (1.37)	11.42 (1.36)		
Week 52: Adjusted Mean Change (SE)	12.39 (1.55)	10.21 (1.51)	2.18 [-2.07; 6.42]	0.315
≥ 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 28: Adjusted Mean Change (SE)	7.31 (1.56)	7.42 (1.55)		
Week 52: Adjusted Mean Change (SE)	10.78 (1.69)	10.35 (1.69)	0.43 [-4.27; 5.13]	0.857
Pooled Analysis: General Vision				
Interaction test	p=0.917			
< 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 28: Adjusted Mean Change (SE)	11.74 (0.95)	11.54 (0.97)		
Week 52: Adjusted Mean Change (SE)	12.78 (1.04)	11.38 (1.03)	1.40 [-1.48; 4.27]	0.340
≥ 65 years				
N'/ N	163 / 164	173 / 173		
Baseline Mean (SD)	61.47 (15.16)	59.42 (15.91)		
Week 52 Mean (SD)	71.58 (14.19)	69.44 (14.23)		
Week 28: Adjusted Mean Change (SE)	8.79 (1.07)	8.48 (1.05)		
Week 52: Adjusted Mean Change (SE)	10.32 (1.15)	9.40 (1.11)	0.92 [-2.22; 4.06]	0.566

	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=0.492**				
KESTREL: Ocular Pain				
Interaction test	p=0.830			
< 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 28: Adjusted Mean Change (SE)	4.15 (1.76)	4.02 (1.86)		
Week 52: Adjusted Mean Change (SE)	5.61 (1.63)	5.87 (1.64)	-0.26 [-4.81; 4.29]	0.910
≥ 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 28: Adjusted Mean Change (SE)	1.06 (1.97)	4.58 (1.90)		
Week 52: Adjusted Mean Change (SE)	4.72 (1.81)	2.64 (1.71)	2.08 [-2.82; 6.98]	0.404
KITE: Ocular Pain				
Interaction test	p=0.629			
< 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 28: Adjusted Mean Change (SE)	4.68 (1.57)	4.11 (1.56)		
Week 52: Adjusted Mean Change (SE)	4.04 (1.67)	4.17 (1.62)	-0.13 [-4.72; 4.45]	0.954
≥ 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 28: Adjusted Mean Change (SE)	4.61 (1.79)	3.89 (1.78)		
Week 52: Adjusted Mean Change (SE)	6.25 (1.82)	3.87 (1.82)	2.39 [-2.67; 7.45]	0.354

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Ocular Pain				
Interaction test	p=0.789			
< 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 28: Adjusted Mean Change (SE)	4.40 (1.18)	4.13 (1.21)		
Week 52: Adjusted Mean Change (SE)	4.86 (1.17)	5.12 (1.16)	-0.27 [-3.51; 2.97]	0.871
≥ 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 28: Adjusted Mean Change (SE)	2.85 (1.34)	4.15 (1.31)		
Week 52: Adjusted Mean Change (SE)	5.51 (1.29)	3.11 (1.25)	2.40 [-1.13; 5.93]	0.183
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.456**				
KESTREL: Near Activities				
Interaction test	p=0.538			
< 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 28: Adjusted Mean Change (SE)	14.19 (1.81)	15.51 (1.92)		
Week 52: Adjusted Mean Change (SE)	14.86 (2.02)	17.84 (2.02)	-2.98 [-8.60; 2.64]	0.298
≥ 65 years				
N'/ N	85 / 85	94 / 94		
Baseline Mean (SD)	63.33 (26.23)	67.07 (22.75)		
Week 52 Mean (SD)	76.68 (21.18)	73.94 (21.02)		
Week 28: Adjusted Mean Change (SE)	10.39 (2.04)	13.23 (1.96)		
Week 52: Adjusted Mean Change (SE)	11.87 (2.24)	9.12 (2.12)	2.74 [-3.32; 8.80]	0.374

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Near Activities				
Interaction test	p=0.923			
< 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 28: Adjusted Mean Change (SE)	8.22 (1.84)	6.67 (1.82)		
Week 52: Adjusted Mean Change (SE)	9.22 (1.89)	9.01 (1.84)	0.21 [-4.97; 5.40]	0.936
≥ 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 28: Adjusted Mean Change (SE)	4.25 (2.08)	5.33 (2.07)		
Week 52: Adjusted Mean Change (SE)	11.64 (2.07)	9.46 (2.06)	2.18 [-3.56; 7.92]	0.455
Pooled Analysis: Near Activities				
Interaction test	p=0.711			
< 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 28: Adjusted Mean Change (SE)	11.42 (1.31)	11.08 (1.34)		
Week 52: Adjusted Mean Change (SE)	12.16 (1.40)	13.43 (1.39)	-1.27 [-5.14; 2.60]	0.519
≥ 65 years				
N'/ N	163 / 164	173 / 173		
Baseline Mean (SD)	65.95 (24.68)	68.09 (23.64)		
Week 52 Mean (SD)	78.35 (21.04)	76.56 (21.23)		
Week 28: Adjusted Mean Change (SE)	7.50 (1.47)	9.24 (1.44)		
Week 52: Adjusted Mean Change (SE)	11.76 (1.54)	9.14 (1.50)	2.63 [-1.59; 6.85]	0.222

	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=0.136**				
KESTREL: Distance Activities				
Interaction test	p=0.925			
< 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 28: Adjusted Mean Change (SE)	9.54 (1.60)	10.50 (1.70)		
Week 52: Adjusted Mean Change (SE)	11.61 (1.54)	12.88 (1.55)	-1.27 [-5.57; 3.02]	0.560
≥ 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 28: Adjusted Mean Change (SE)	5.07 (1.80)	7.09 (1.73)		
Week 52: Adjusted Mean Change (SE)	6.23 (1.71)	5.90 (1.62)	0.33 [-4.29; 4.96]	0.887
KITE: Distance Activities				
Interaction test	p=0.749			
< 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 28: Adjusted Mean Change (SE)	8.35 (1.59)	6.59 (1.58)		
Week 52: Adjusted Mean Change (SE)	12.05 (1.55)	9.07 (1.50)	2.98 [-1.26; 7.22]	0.168
≥ 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 28: Adjusted Mean Change (SE)	3.70 (1.81)	4.15 (1.80)		
Week 52: Adjusted Mean Change (SE)	10.49 (1.69)	7.10 (1.68)	3.39 [-1.30; 8.08]	0.156

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Distance Activities				
Interaction test	p=0.848			
< 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 28: Adjusted Mean Change (SE)	9.06 (1.14)	8.58 (1.17)		
Week 52: Adjusted Mean Change (SE)	11.94 (1.10)	11.01 (1.09)	0.93 [-2.10; 3.95]	0.548
≥ 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 28: Adjusted Mean Change (SE)	4.40 (1.29)	5.60 (1.26)		
Week 52: Adjusted Mean Change (SE)	8.23 (1.21)	6.41 (1.17)	1.83 [-1.48; 5.13]	0.278
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.037 ***				
KESTREL: Social Functioning				
Interaction test	p=0.263			
< 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 28: Adjusted Mean Change (SE)	2.11 (1.22)	6.47 (1.29)		
Week 52: Adjusted Mean Change (SE)	4.19 (1.39)	6.04 (1.40)	-1.85 [-5.72; 2.02]	0.347
≥ 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 28: Adjusted Mean Change (SE)	1.21 (1.37)	1.35 (1.31)		
Week 52: Adjusted Mean Change (SE)	0.94 (1.54)	2.02 (1.46)	-1.09 [-5.25; 3.08]	0.608

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Social Functioning				
Interaction test	p=0.661			
< 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 28: Adjusted Mean Change (SE)	4.25 (1.40)	3.27 (1.40)		
Week 52: Adjusted Mean Change (SE)	6.43 (1.24)	3.74 (1.21)	2.68 [-0.72; 6.09]	0.122
≥ 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 28: Adjusted Mean Change (SE)	3.23 (1.60)	4.88 (1.59)		
Week 52: Adjusted Mean Change (SE)	8.69 (1.35)	5.37 (1.35)	3.32 [-0.44; 7.07]	0.083
Pooled Analysis: Social Functioning				
Interaction test	p=0.585			
< 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 28: Adjusted Mean Change (SE)	3.21 (0.93)	4.82 (0.96)		
Week 52: Adjusted Mean Change (SE)	5.34 (0.94)	4.90 (0.93)	0.44 [-2.15; 3.03]	0.738
≥ 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 28: Adjusted Mean Change (SE)	2.23 (1.05)	2.93 (1.03)		
Week 52: Adjusted Mean Change (SE)	4.76 (1.03)	3.50 (1.00)	1.26 [-1.55; 4.08]	0.379

	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=0.300**				
KESTREL: Mental Health				
Interaction test	p=0.605			
< 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 28: Adjusted Mean Change (SE)	8.20 (1.72)	10.11 (1.83)		
Week 52: Adjusted Mean Change (SE)	11.18 (1.79)	13.21 (1.80)	-2.02 [-7.01; 2.96]	0.425
≥ 65 years				
N'/ N	85 / 85	94 / 94		
Baseline Mean (SD)	67.06 (24.63)	74.20 (17.94)		
Week 52 Mean (SD)	78.17 (19.92)	78.75 (17.04)		
Week 28: Adjusted Mean Change (SE)	6.44 (1.93)	7.88 (1.87)		
Week 52: Adjusted Mean Change (SE)	9.61 (1.98)	8.90 (1.89)	0.71 [-4.67; 6.09]	0.796
KITE: Mental Health				
Interaction test	p=0.822			
< 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 28: Adjusted Mean Change (SE)	9.68 (1.72)	10.18 (1.71)		
Week 52: Adjusted Mean Change (SE)	11.95 (2.11)	9.40 (2.06)	2.55 [-3.26; 8.36]	0.389
≥ 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 28: Adjusted Mean Change (SE)	7.46 (1.95)	8.23 (1.94)		
Week 52: Adjusted Mean Change (SE)	14.19 (2.31)	9.80 (2.30)	4.39 [-2.02; 10.81]	0.179

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Mental Health				
Interaction test	p=0.593			
< 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 28: Adjusted Mean Change (SE)	9.02 (1.21)	10.19 (1.25)		
Week 52: Adjusted Mean Change (SE)	11.63 (1.38)	11.28 (1.37)	0.35 [-3.47; 4.17]	0.857
≥ 65 years				
N'/ N	163 / 164	173 / 173		
Baseline Mean (SD)	67.29 (24.23)	71.32 (21.49)		
Week 52 Mean (SD)	80.03 (21.03)	78.79 (19.04)		
Week 28: Adjusted Mean Change (SE)	6.99 (1.37)	7.93 (1.34)		
Week 52: Adjusted Mean Change (SE)	11.87 (1.52)	9.26 (1.48)	2.62 [-1.55; 6.78]	0.218
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.072**				
KESTREL: Role Difficulties				
Interaction test	p=0.442			
< 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 28: Adjusted Mean Change (SE)	7.25 (2.14)	11.54 (2.28)		
Week 52: Adjusted Mean Change (SE)	7.78 (2.37)	13.69 (2.38)	-5.91 [-12.53; 0.71]	0.080
≥ 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 28: Adjusted Mean Change (SE)	4.52 (2.41)	6.43 (2.32)		
Week 52: Adjusted Mean Change (SE)	6.16 (2.63)	8.27 (2.49)	-2.11 [-9.24; 5.01]	0.560

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Role Difficulties				
Interaction test	p=0.744			
< 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 28: Adjusted Mean Change (SE)	9.48 (2.11)	10.80 (2.10)		
Week 52: Adjusted Mean Change (SE)	14.79 (2.30)	9.32 (2.24)	5.46 [-0.86; 11.79]	0.090
≥ 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 28: Adjusted Mean Change (SE)	5.17 (2.40)	5.33 (2.39)		
Week 52: Adjusted Mean Change (SE)	9.22 (2.52)	7.45 (2.50)	1.77 [-5.22; 8.75]	0.619
Pooled Analysis: Role Difficulties				
Interaction test	p=0.691			
< 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 28: Adjusted Mean Change (SE)	8.36 (1.51)	11.22 (1.55)		
Week 52: Adjusted Mean Change (SE)	11.21 (1.65)	11.56 (1.63)	-0.36 [-4.92; 4.21]	0.878
≥ 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 28: Adjusted Mean Change (SE)	4.93 (1.70)	5.80 (1.67)		
Week 52: Adjusted Mean Change (SE)	7.68 (1.82)	7.80 (1.77)	-0.12 [-5.10; 4.86]	0.962

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Dependency				
Test of heterogeneity in main analysis: **p_H=0.029 ***				
KESTREL: Dependency				
Interaction test	p=0.828			
< 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 28: Adjusted Mean Change (SE)	6.52 (1.84)	8.56 (1.96)		
Week 52: Adjusted Mean Change (SE)	6.33 (1.94)	9.24 (1.95)	-2.91 [-8.34; 2.52]	0.292
≥ 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 28: Adjusted Mean Change (SE)	4.60 (2.07)	4.89 (1.99)		
Week 52: Adjusted Mean Change (SE)	4.96 (2.16)	8.16 (2.04)	-3.20 [-9.04; 2.65]	0.283
KITE: Dependency				
Interaction test	p=0.140			
< 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 28: Adjusted Mean Change (SE)	7.07 (1.72)	2.59 (1.71)		
Week 52: Adjusted Mean Change (SE)	8.32 (1.90)	2.13 (1.85)	6.19 [0.97; 11.40]	0.020 *
≥ 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 28: Adjusted Mean Change (SE)	3.85 (1.95)	4.36 (1.95)		
Week 52: Adjusted Mean Change (SE)	6.55 (2.08)	5.10 (2.07)	1.45 [-4.32; 7.22]	0.620

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Dependency				
Interaction test	p=0.471			
< 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 28: Adjusted Mean Change (SE)	6.85 (1.27)	5.72 (1.30)		
Week 52: Adjusted Mean Change (SE)	7.36 (1.37)	5.82 (1.35)	1.54 [-2.24; 5.32]	0.425
≥ 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 28: Adjusted Mean Change (SE)	4.31 (1.43)	4.37 (1.40)		
Week 52: Adjusted Mean Change (SE)	5.76 (1.51)	6.47 (1.46)	-0.71 [-4.84; 3.41]	0.735
Driving				
Test of heterogeneity in main analysis: **p_H=0.778**				
KESTREL: Driving				
Interaction test	p=0.949			
< 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 28: Adjusted Mean Change (SE)	5.21 (1.79)	7.78 (1.85)		
Week 52: Adjusted Mean Change (SE)	6.39 (2.07)	9.70 (2.10)	-3.31 [-9.12; 2.50]	0.263
≥ 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 28: Adjusted Mean Change (SE)	-2.17 (2.16)	3.12 (2.23)		
Week 52: Adjusted Mean Change (SE)	-0.09 (2.47)	1.00 (2.64)	-1.09 [-8.22; 6.04]	0.764

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Driving				
Interaction test	p=0.708			
< 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 28: Adjusted Mean Change (SE)	0.77 (1.77)	5.94 (1.91)		
Week 52: Adjusted Mean Change (SE)	8.72 (1.54)	6.54 (1.72)	2.18 [-2.37; 6.74]	0.346
≥ 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 28: Adjusted Mean Change (SE)	1.30 (2.49)	4.60 (2.42)		
Week 52: Adjusted Mean Change (SE)	0.88 (2.07)	3.14 (1.99)	-2.26 [-7.93; 3.41]	0.433
Pooled Analysis: Driving				
Interaction test	p=0.808			
< 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 28: Adjusted Mean Change (SE)	2.99 (1.26)	6.94 (1.33)		
Week 52: Adjusted Mean Change (SE)	7.58 (1.31)	8.35 (1.38)	-0.78 [-4.52; 2.96]	0.683
≥ 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 28: Adjusted Mean Change (SE)	-0.73 (1.63)	3.77 (1.64)		
Week 52: Adjusted Mean Change (SE)	0.44 (1.65)	1.93 (1.68)	-1.49 [-6.12; 3.14]	0.527

	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=0.691**				
KESTREL: Color Vision				
Interaction test	p=1.000			
< 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 28: Adjusted Mean Change (SE)	2.18 (1.12)	1.77 (1.19)		
Week 52: Adjusted Mean Change (SE)	2.92 (1.16)	2.61 (1.18)	0.32 [-2.95; 3.58]	0.849
≥ 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 28: Adjusted Mean Change (SE)	2.04 (1.27)	1.82 (1.22)		
Week 52: Adjusted Mean Change (SE)	1.34 (1.30)	0.83 (1.24)	0.51 [-3.01; 4.04]	0.775
KITE: Color Vision				
Interaction test	p=0.521			
< 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 28: Adjusted Mean Change (SE)	2.79 (1.10)	4.08 (1.09)		
Week 52: Adjusted Mean Change (SE)	5.10 (1.02)	3.11 (0.99)	1.99 [-0.80; 4.79]	0.162
≥ 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 28: Adjusted Mean Change (SE)	4.65 (1.26)	4.33 (1.26)		
Week 52: Adjusted Mean Change (SE)	6.58 (1.12)	3.84 (1.12)	2.75 [-0.37; 5.86]	0.083

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Color Vision				
Interaction test	p=0.623			
< 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 28: Adjusted Mean Change (SE)	2.51 (0.79)	2.94 (0.82)		
Week 52: Adjusted Mean Change (SE)	4.02 (0.77)	2.87 (0.77)	1.16 [-0.98; 3.29]	0.288
≥ 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 28: Adjusted Mean Change (SE)	3.38 (0.90)	3.01 (0.89)		
Week 52: Adjusted Mean Change (SE)	3.92 (0.85)	2.23 (0.83)	1.69 [-0.65; 4.04]	0.156
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.021 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.640			
< 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 28: Adjusted Mean Change (SE)	6.68 (1.79)	8.47 (1.89)		
Week 52: Adjusted Mean Change (SE)	7.46 (1.86)	10.85 (1.86)	-3.38 [-8.57; 1.80]	0.200
≥ 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 28: Adjusted Mean Change (SE)	-1.79 (2.02)	6.84 (1.93)		
Week 52: Adjusted Mean Change (SE)	3.89 (2.07)	3.32 (1.96)	0.56 [-5.04; 6.17]	0.843

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Peripheral Vision				
Interaction test	p=0.752			
< 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 28: Adjusted Mean Change (SE)	6.12 (1.59)	5.98 (1.59)		
Week 52: Adjusted Mean Change (SE)	5.80 (1.74)	3.76 (1.70)	2.04 [-2.75; 6.83]	0.403
≥ 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 28: Adjusted Mean Change (SE)	3.02 (1.82)	2.84 (1.80)		
Week 52: Adjusted Mean Change (SE)	7.22 (1.90)	3.37 (1.89)	3.85 [-1.43; 9.13]	0.152
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.864			
< 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 28: Adjusted Mean Change (SE)	6.37 (1.21)	7.47 (1.24)		
Week 52: Adjusted Mean Change (SE)	6.64 (1.28)	7.51 (1.27)	-0.87 [-4.42; 2.67]	0.629
≥ 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 28: Adjusted Mean Change (SE)	0.37 (1.37)	4.94 (1.33)		
Week 52: Adjusted Mean Change (SE)	5.26 (1.41)	3.41 (1.37)	1.86 [-2.01; 5.72]	0.346

	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=0.700**				
KESTREL: General Health				
Interaction test	p=0.385			
< 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 28: Adjusted Mean Change (SE)	6.41 (1.84)	3.81 (1.94)		
Week 52: Adjusted Mean Change (SE)	9.34 (2.28)	6.18 (2.28)	3.16 [-3.19; 9.50]	0.328
≥ 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 28: Adjusted Mean Change (SE)	1.84 (2.06)	5.56 (1.99)		
Week 52: Adjusted Mean Change (SE)	7.22 (2.52)	3.93 (2.40)	3.29 [-3.57; 10.14]	0.346
KITE: General Health				
Interaction test	p=0.202			
< 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 28: Adjusted Mean Change (SE)	2.85 (1.84)	5.84 (1.83)		
Week 52: Adjusted Mean Change (SE)	4.17 (2.24)	5.30 (2.18)	-1.13 [-7.28; 5.02]	0.717
≥ 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 28: Adjusted Mean Change (SE)	4.60 (2.10)	2.52 (2.09)		
Week 52: Adjusted Mean Change (SE)	7.02 (2.45)	4.50 (2.43)	2.51 [-4.26; 9.29]	0.466

	Treatment Groups		Comparison	
VFQ by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: General Health				
Interaction test	p=0.851			
< 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 28: Adjusted Mean Change (SE)	4.55 (1.31)	4.95 (1.34)		
Week 52: Adjusted Mean Change (SE)	6.67 (1.60)	5.81 (1.57)	0.87 [-3.53; 5.27]	0.699
≥ 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 28: Adjusted Mean Change (SE)	3.04 (1.48)	4.30 (1.45)		
Week 52: Adjusted Mean Change (SE)	7.04 (1.75)	4.38 (1.70)	2.66 [-2.14; 7.45]	0.278

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 52

	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=0.071**				
KESTREL: Composite Score				
Interaction test	p=0.558			
Male				
N'/ N	110 / 110	126 / 126		
Baseline Mean (SD)	78.32 (16.74)	78.50 (13.72)		
Week 52 Mean (SD)	86.44 (13.06)	85.45 (12.18)		
Week 28: Adjusted Mean Change (SE)	6.76 (1.05)	8.49 (0.98)		
Week 52: Adjusted Mean Change (SE)	7.97 (1.10)	8.08 (1.02)	-0.11 [-3.05; 2.83]	0.942
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 28: Adjusted Mean Change (SE)	4.50 (1.23)	6.14 (1.40)		
Week 52: Adjusted Mean Change (SE)	6.07 (1.29)	8.74 (1.39)	-2.66 [-6.40; 1.07]	0.161
KITE: Composite Score				
Interaction test	p=0.267			
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 28: Adjusted Mean Change (SE)	5.69 (0.93)	6.16 (0.96)		
Week 52: Adjusted Mean Change (SE)	8.70 (1.01)	7.72 (1.03)	0.98 [-1.86; 3.81]	0.497
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 28: Adjusted Mean Change (SE)	6.23 (1.38)	5.86 (1.26)		
Week 52: Adjusted Mean Change (SE)	9.33 (1.48)	4.51 (1.34)	4.82 [0.90; 8.74]	0.016 *

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Composite Score				
Interaction test	p=0.747			
Male				
N'/ N	229 / 230	241 / 241		
Baseline Mean (SD)	79.07 (15.02)	78.74 (14.92)		
Week 52 Mean (SD)	87.36 (12.53)	85.58 (12.97)		
Week 28: Adjusted Mean Change (SE)	6.23 (0.71)	7.36 (0.70)		
Week 52: Adjusted Mean Change (SE)	8.38 (0.75)	7.92 (0.73)	0.46 [-1.59; 2.51]	0.661
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 28: Adjusted Mean Change (SE)	5.32 (0.93)	5.95 (0.95)		
Week 52: Adjusted Mean Change (SE)	7.50 (0.98)	6.57 (0.98)	0.93 [-1.77; 3.64]	0.499
General Vision				
Test of heterogeneity in main analysis: **p_H=0.986**				
KESTREL: General Vision				
Interaction test	p=0.420			
Male				
N'/ N	110 / 110	126 / 126		
Baseline Mean (SD)	60.55 (16.80)	60.16 (15.49)		
Week 52 Mean (SD)	73.33 (14.20)	71.57 (12.72)		
Week 28: Adjusted Mean Change (SE)	11.58 (1.27)	11.78 (1.20)		
Week 52: Adjusted Mean Change (SE)	12.04 (1.35)	11.34 (1.25)	0.70 [-2.91; 4.31]	0.703
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 28: Adjusted Mean Change (SE)	10.98 (1.49)	8.34 (1.70)		
Week 52: Adjusted Mean Change (SE)	11.07 (1.59)	9.34 (1.69)	1.74 [-2.84; 6.31]	0.456

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Vision				
Interaction test	p=0.276			
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 28: Adjusted Mean Change (SE)	9.27 (1.25)	10.62 (1.29)		
Week 52: Adjusted Mean Change (SE)	11.94 (1.39)	11.63 (1.42)	0.31 [-3.59; 4.21]	0.875
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 28: Adjusted Mean Change (SE)	9.81 (1.84)	8.02 (1.69)		
Week 52: Adjusted Mean Change (SE)	11.19 (2.03)	8.02 (1.84)	3.16 [-2.23; 8.56]	0.250
Pooled Analysis: General Vision				
Interaction test	p=0.182			
Male				
N'/ N	229 / 230	241 / 241		
Baseline Mean (SD)	61.66 (16.72)	60.75 (16.47)		
Week 52 Mean (SD)	73.62 (14.61)	71.94 (14.12)		
Week 28: Adjusted Mean Change (SE)	10.48 (0.89)	11.28 (0.88)		
Week 52: Adjusted Mean Change (SE)	12.10 (0.97)	11.56 (0.94)	0.54 [-2.12; 3.20]	0.690
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 28: Adjusted Mean Change (SE)	10.29 (1.17)	8.05 (1.20)		
Week 52: Adjusted Mean Change (SE)	10.92 (1.27)	8.56 (1.25)	2.37 [-1.14; 5.87]	0.185

	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=0.492**				
KESTREL: Ocular Pain				
Interaction test	p=0.472			
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 28: Adjusted Mean Change (SE)	4.15 (1.73)	5.30 (1.63)		
Week 52: Adjusted Mean Change (SE)	6.41 (1.60)	3.92 (1.47)	2.49 [-1.77; 6.75]	0.251
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 28: Adjusted Mean Change (SE)	0.82 (2.03)	2.39 (2.32)		
Week 52: Adjusted Mean Change (SE)	3.51 (1.88)	5.10 (2.02)	-1.59 [-6.99; 3.81]	0.563
KITE: Ocular Pain				
Interaction test	p=0.207			
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 28: Adjusted Mean Change (SE)	4.18 (1.43)	5.63 (1.47)		
Week 52: Adjusted Mean Change (SE)	5.13 (1.51)	4.67 (1.53)	0.47 [-3.75; 4.69]	0.828
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 28: Adjusted Mean Change (SE)	5.73 (2.11)	1.25 (1.93)		
Week 52: Adjusted Mean Change (SE)	4.89 (2.21)	2.96 (1.99)	1.92 [-3.91; 7.75]	0.517

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Ocular Pain				
Interaction test	p=0.815			
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 28: Adjusted Mean Change (SE)	4.16 (1.12)	5.39 (1.10)		
Week 52: Adjusted Mean Change (SE)	5.72 (1.10)	4.24 (1.07)	1.48 [-1.53; 4.48]	0.334
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 28: Adjusted Mean Change (SE)	2.96 (1.47)	1.83 (1.51)		
Week 52: Adjusted Mean Change (SE)	4.21 (1.44)	4.07 (1.42)	0.13 [-3.82; 4.09]	0.947
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.456**				
KESTREL: Near Activities				
Interaction test	p=0.880			
Male				
N'/ N	110 / 110	126 / 126		
Baseline Mean (SD)	63.94 (25.19)	66.40 (21.84)		
Week 52 Mean (SD)	79.84 (21.24)	78.76 (20.97)		
Week 28: Adjusted Mean Change (SE)	12.82 (1.78)	15.48 (1.68)		
Week 52: Adjusted Mean Change (SE)	14.17 (1.97)	14.02 (1.82)	0.15 [-5.14; 5.43]	0.957
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 28: Adjusted Mean Change (SE)	11.86 (2.09)	12.56 (2.38)		
Week 52: Adjusted Mean Change (SE)	12.45 (2.33)	13.20 (2.48)	-0.75 [-7.45; 5.94]	0.825

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Near Activities				
Interaction test	p=0.908			
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 28: Adjusted Mean Change (SE)	6.78 (1.68)	6.20 (1.73)		
Week 52: Adjusted Mean Change (SE)	10.89 (1.70)	10.36 (1.74)	0.53 [-4.24; 5.30]	0.826
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 28: Adjusted Mean Change (SE)	5.92 (2.47)	5.90 (2.27)		
Week 52: Adjusted Mean Change (SE)	9.22 (2.49)	7.29 (2.26)	1.93 [-4.67; 8.53]	0.565
Pooled Analysis: Near Activities				
Interaction test	p=0.722			
Male				
N'/ N	228 / 230	241 / 241		
Baseline Mean (SD)	68.00 (23.82)	69.48 (22.14)		
Week 52 Mean (SD)	81.06 (21.07)	79.87 (20.97)		
Week 28: Adjusted Mean Change (SE)	9.95 (1.24)	11.02 (1.22)		
Week 52: Adjusted Mean Change (SE)	12.71 (1.31)	12.31 (1.27)	0.39 [-3.19; 3.98]	0.830
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 28: Adjusted Mean Change (SE)	9.18 (1.61)	8.85 (1.66)		
Week 52: Adjusted Mean Change (SE)	10.76 (1.71)	9.96 (1.69)	0.80 [-3.92; 5.53]	0.739

	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=0.136**				
KESTREL: Distance Activities				
Interaction test	p=0.591			
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 28: Adjusted Mean Change (SE)	9.91 (1.56)	9.97 (1.47)		
Week 52: Adjusted Mean Change (SE)	10.31 (1.50)	10.47 (1.39)	-0.17 [-4.18; 3.85]	0.935
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 28: Adjusted Mean Change (SE)	4.04 (1.84)	6.95 (2.09)		
Week 52: Adjusted Mean Change (SE)	7.49 (1.77)	8.01 (1.90)	-0.52 [-5.61; 4.58]	0.842
KITE: Distance Activities				
Interaction test	p=0.339			
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 28: Adjusted Mean Change (SE)	6.47 (1.45)	6.06 (1.50)		
Week 52: Adjusted Mean Change (SE)	11.39 (1.38)	9.93 (1.41)	1.46 [-2.43; 5.34]	0.461
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 28: Adjusted Mean Change (SE)	5.99 (2.14)	4.56 (1.97)		
Week 52: Adjusted Mean Change (SE)	11.39 (2.03)	5.28 (1.84)	6.11 [0.74; 11.48]	0.026 *

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Distance Activities				
Interaction test	p=0.689			
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 28: Adjusted Mean Change (SE)	8.03 (1.08)	8.07 (1.06)		
Week 52: Adjusted Mean Change (SE)	10.78 (1.02)	10.22 (0.99)	0.55 [-2.24; 3.35]	0.697
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 28: Adjusted Mean Change (SE)	5.11 (1.41)	5.70 (1.45)		
Week 52: Adjusted Mean Change (SE)	9.40 (1.34)	6.60 (1.33)	2.80 [-0.89; 6.49]	0.136
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.037 ***				
KESTREL: Social Functioning				
Interaction test	p=0.324			
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 28: Adjusted Mean Change (SE)	4.00 (1.18)	4.92 (1.11)		
Week 52: Adjusted Mean Change (SE)	3.10 (1.35)	3.96 (1.25)	-0.85 [-4.47; 2.76]	0.642
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 28: Adjusted Mean Change (SE)	-1.63 (1.39)	2.26 (1.58)		
Week 52: Adjusted Mean Change (SE)	2.09 (1.60)	4.47 (1.71)	-2.38 [-6.98; 2.21]	0.309

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Social Functioning				
Interaction test	p=0.891			
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 28: Adjusted Mean Change (SE)	4.39 (1.28)	3.80 (1.32)		
Week 52: Adjusted Mean Change (SE)	7.56 (1.11)	5.69 (1.13)	1.88 [-1.24; 5.00]	0.238
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 28: Adjusted Mean Change (SE)	2.59 (1.90)	4.29 (1.73)		
Week 52: Adjusted Mean Change (SE)	7.23 (1.63)	2.40 (1.47)	4.82 [0.51; 9.14]	0.029 *
Pooled Analysis: Social Functioning				
Interaction test	p=0.620			
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 28: Adjusted Mean Change (SE)	4.08 (0.88)	4.34 (0.87)		
Week 52: Adjusted Mean Change (SE)	5.33 (0.88)	4.80 (0.85)	0.53 [-1.87; 2.92]	0.665
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 28: Adjusted Mean Change (SE)	0.50 (1.15)	3.23 (1.18)		
Week 52: Adjusted Mean Change (SE)	4.67 (1.15)	3.30 (1.13)	1.37 [-1.79; 4.53]	0.396

	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=0.300**				
KESTREL: Mental Health				
Interaction test	p=0.264			
Male				
N'/ N	110 / 110	126 / 126		
Baseline Mean (SD)	67.44 (22.78)	71.28 (21.30)		
Week 52 Mean (SD)	81.11 (17.08)	79.17 (17.53)		
Week 28: Adjusted Mean Change (SE)	8.22 (1.68)	9.76 (1.59)		
Week 52: Adjusted Mean Change (SE)	12.34 (1.73)	10.26 (1.60)	2.08 [-2.56; 6.72]	0.379
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 28: Adjusted Mean Change (SE)	6.20 (1.98)	7.69 (2.26)		
Week 52: Adjusted Mean Change (SE)	7.78 (2.05)	12.83 (2.18)	-5.05 [-10.93; 0.83]	0.092
KITE: Mental Health				
Interaction test	p=0.297			
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 28: Adjusted Mean Change (SE)	8.64 (1.57)	10.43 (1.61)		
Week 52: Adjusted Mean Change (SE)	13.75 (1.89)	12.03 (1.93)	1.72 [-3.58; 7.03]	0.523
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 28: Adjusted Mean Change (SE)	8.99 (2.31)	7.42 (2.13)		
Week 52: Adjusted Mean Change (SE)	11.45 (2.77)	5.46 (2.51)	5.99 [-1.34; 13.32]	0.109

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Mental Health				
Interaction test	p=0.986			
Male				
N'/ N	229 / 230	241 / 241		
Baseline Mean (SD)	69.76 (21.36)	70.31 (22.26)		
Week 52 Mean (SD)	82.77 (18.19)	79.69 (18.99)		
Week 28: Adjusted Mean Change (SE)	8.47 (1.15)	10.04 (1.13)		
Week 52: Adjusted Mean Change (SE)	13.10 (1.29)	11.06 (1.25)	2.04 [-1.48; 5.56]	0.256
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 28: Adjusted Mean Change (SE)	7.52 (1.50)	7.50 (1.55)		
Week 52: Adjusted Mean Change (SE)	9.44 (1.69)	9.08 (1.67)	0.35 [-4.29; 5.00]	0.881
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.072**				
KESTREL: Role Difficulties				
Interaction test	p=0.217			
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 28: Adjusted Mean Change (SE)	6.91 (2.11)	9.92 (1.99)		
Week 52: Adjusted Mean Change (SE)	8.62 (2.30)	8.85 (2.12)	-0.23 [-6.37; 5.92]	0.942
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 28: Adjusted Mean Change (SE)	4.65 (2.48)	7.50 (2.82)		
Week 52: Adjusted Mean Change (SE)	4.72 (2.71)	15.28 (2.89)	-10.55 [-18.33; -2.77]	0.008 *

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Role Difficulties				
Interaction test	p=0.798			
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 28: Adjusted Mean Change (SE)	8.00 (1.92)	8.77 (1.99)		
Week 52: Adjusted Mean Change (SE)	13.08 (2.07)	10.29 (2.11)	2.79 [-3.01; 8.59]	0.345
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 28: Adjusted Mean Change (SE)	6.67 (2.84)	7.71 (2.62)		
Week 52: Adjusted Mean Change (SE)	10.65 (3.03)	5.50 (2.74)	5.15 [-2.87; 13.18]	0.207
Pooled Analysis: Role Difficulties				
Interaction test	p=0.500			
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 28: Adjusted Mean Change (SE)	7.40 (1.43)	9.40 (1.41)		
Week 52: Adjusted Mean Change (SE)	10.88 (1.54)	9.57 (1.50)	1.30 [-2.92; 5.52]	0.545
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 28: Adjusted Mean Change (SE)	5.79 (1.87)	7.52 (1.92)		
Week 52: Adjusted Mean Change (SE)	7.44 (2.02)	10.31 (1.99)	-2.87 [-8.44; 2.69]	0.311

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Dependency				
Test of heterogeneity in main analysis: **p_H=0.029 ***				
KESTREL: Dependency				
Interaction test	p=0.746			
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 28: Adjusted Mean Change (SE)	5.77 (1.81)	7.33 (1.71)		
Week 52: Adjusted Mean Change (SE)	6.68 (1.89)	8.34 (1.75)	-1.66 [-6.73; 3.41]	0.520
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 28: Adjusted Mean Change (SE)	5.42 (2.13)	5.76 (2.43)		
Week 52: Adjusted Mean Change (SE)	4.29 (2.23)	9.42 (2.39)	-5.14 [-11.56; 1.29]	0.117
KITE: Dependency				
Interaction test	p=0.163			
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 28: Adjusted Mean Change (SE)	5.12 (1.57)	3.81 (1.62)		
Week 52: Adjusted Mean Change (SE)	7.36 (1.70)	5.77 (1.74)	1.59 [-3.19; 6.37]	0.513
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 28: Adjusted Mean Change (SE)	6.85 (2.33)	2.60 (2.13)		
Week 52: Adjusted Mean Change (SE)	7.90 (2.50)	-0.46 (2.26)	8.37 [1.76; 14.97]	0.013 *

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Dependency				
Interaction test	p=0.536			
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 28: Adjusted Mean Change (SE)	5.54 (1.20)	5.60 (1.19)		
Week 52: Adjusted Mean Change (SE)	7.16 (1.28)	7.06 (1.24)	0.10 [-3.40; 3.60]	0.956
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 28: Adjusted Mean Change (SE)	6.02 (1.58)	4.19 (1.62)		
Week 52: Adjusted Mean Change (SE)	5.75 (1.68)	4.48 (1.66)	1.27 [-3.34; 5.89]	0.589
Driving				
Test of heterogeneity in main analysis: **p_H=0.778**				
KESTREL: Driving				
Interaction test	p=0.284			
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 28: Adjusted Mean Change (SE)	4.46 (1.57)	6.52 (1.54)		
Week 52: Adjusted Mean Change (SE)	6.10 (1.82)	6.88 (1.80)	-0.78 [-5.83; 4.27]	0.762
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 28: Adjusted Mean Change (SE)	-4.86 (2.69)	1.95 (3.31)		
Week 52: Adjusted Mean Change (SE)	-3.26 (3.05)	2.50 (3.71)	-5.76 [-15.21; 3.70]	0.231

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Driving				
Interaction test	p=0.839			
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 28: Adjusted Mean Change (SE)	1.39 (1.52)	5.66 (1.58)		
Week 52: Adjusted Mean Change (SE)	6.09 (1.28)	6.14 (1.36)	-0.06 [-3.76; 3.64]	0.976
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 28: Adjusted Mean Change (SE)	-5.65 (4.69)	3.28 (4.98)		
Week 52: Adjusted Mean Change (SE)	3.41 (4.51)	-3.55 (4.28)	6.96 [-5.33; 19.26]	0.265
Pooled Analysis: Driving				
Interaction test	p=0.314			
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 28: Adjusted Mean Change (SE)	2.91 (1.09)	6.16 (1.10)		
Week 52: Adjusted Mean Change (SE)	6.20 (1.12)	6.56 (1.14)	-0.36 [-3.51; 2.80]	0.825
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 28: Adjusted Mean Change (SE)	-5.29 (2.36)	2.36 (2.76)		
Week 52: Adjusted Mean Change (SE)	-2.06 (2.45)	0.94 (2.79)	-3.00 [-10.29; 4.30]	0.420

	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=0.691**				
KESTREL: Color Vision				
Interaction test	p=0.641			
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 28: Adjusted Mean Change (SE)	2.63 (1.10)	2.38 (1.04)		
Week 52: Adjusted Mean Change (SE)	1.54 (1.13)	1.73 (1.07)	-0.19 [-3.25; 2.87]	0.902
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 28: Adjusted Mean Change (SE)	1.35 (1.30)	0.69 (1.48)		
Week 52: Adjusted Mean Change (SE)	3.15 (1.35)	1.82 (1.43)	1.33 [-2.54; 5.20]	0.499
KITE: Color Vision				
Interaction test	p=0.401			
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 28: Adjusted Mean Change (SE)	4.44 (1.00)	3.94 (1.03)		
Week 52: Adjusted Mean Change (SE)	5.90 (0.92)	3.65 (0.94)	2.25 [-0.33; 4.83]	0.088
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 28: Adjusted Mean Change (SE)	1.77 (1.47)	4.65 (1.36)		
Week 52: Adjusted Mean Change (SE)	5.44 (1.34)	3.06 (1.22)	2.38 [-1.18; 5.94]	0.190

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Color Vision				
Interaction test	p=0.920			
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 28: Adjusted Mean Change (SE)	3.54 (0.75)	3.15 (0.74)		
Week 52: Adjusted Mean Change (SE)	3.74 (0.72)	2.70 (0.71)	1.05 [-0.94; 3.04]	0.300
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 28: Adjusted Mean Change (SE)	1.76 (0.99)	2.64 (1.01)		
Week 52: Adjusted Mean Change (SE)	4.38 (0.95)	2.36 (0.94)	2.02 [-0.59; 4.63]	0.130
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.021 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.810			
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 28: Adjusted Mean Change (SE)	4.68 (1.75)	9.78 (1.65)		
Week 52: Adjusted Mean Change (SE)	6.57 (1.82)	7.95 (1.68)	-1.38 [-6.25; 3.50]	0.579
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 28: Adjusted Mean Change (SE)	0.22 (2.08)	3.79 (2.35)		
Week 52: Adjusted Mean Change (SE)	4.75 (2.15)	6.12 (2.28)	-1.37 [-7.53; 4.79]	0.663

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Peripheral Vision				
Interaction test	p=0.655			
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 28: Adjusted Mean Change (SE)	5.16 (1.45)	4.55 (1.50)		
Week 52: Adjusted Mean Change (SE)	6.41 (1.56)	5.05 (1.59)	1.36 [-3.03; 5.75]	0.542
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 28: Adjusted Mean Change (SE)	3.93 (2.15)	4.69 (1.98)		
Week 52: Adjusted Mean Change (SE)	6.62 (2.29)	1.13 (2.09)	5.49 [-0.61; 11.60]	0.078
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.699			
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 28: Adjusted Mean Change (SE)	4.76 (1.14)	7.29 (1.12)		
Week 52: Adjusted Mean Change (SE)	6.32 (1.20)	6.60 (1.17)	-0.29 [-3.57; 3.00]	0.864
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 28: Adjusted Mean Change (SE)	1.83 (1.50)	4.54 (1.54)		
Week 52: Adjusted Mean Change (SE)	5.54 (1.57)	3.92 (1.55)	1.62 [-2.71; 5.95]	0.462

	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=0.700**				
KESTREL: General Health				
Interaction test	p=0.490			
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 28: Adjusted Mean Change (SE)	4.77 (1.81)	5.63 (1.70)		
Week 52: Adjusted Mean Change (SE)	8.04 (2.22)	5.97 (2.05)	2.08 [-3.87; 8.02]	0.493
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 28: Adjusted Mean Change (SE)	3.79 (2.12)	2.83 (2.43)		
Week 52: Adjusted Mean Change (SE)	8.88 (2.62)	3.56 (2.79)	5.31 [-2.22; 12.85]	0.166
KITE: General Health				
Interaction test	p=0.326			
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 28: Adjusted Mean Change (SE)	5.33 (1.67)	5.86 (1.73)		
Week 52: Adjusted Mean Change (SE)	5.46 (1.99)	8.16 (2.03)	-2.70 [-8.29; 2.89]	0.343
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 28: Adjusted Mean Change (SE)	-0.16 (2.48)	1.92 (2.26)		
Week 52: Adjusted Mean Change (SE)	5.47 (2.91)	-0.41 (2.63)	5.88 [-1.84; 13.61]	0.135

	Treatment Groups		Comparison	
VFQ by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: General Health				
Interaction test	p=0.204			
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 28: Adjusted Mean Change (SE)	5.00 (1.23)	5.81 (1.22)		
Week 52: Adjusted Mean Change (SE)	6.57 (1.48)	7.12 (1.44)	-0.55 [-4.61; 3.51]	0.790
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 28: Adjusted Mean Change (SE)	1.97 (1.61)	2.50 (1.66)		
Week 52: Adjusted Mean Change (SE)	7.34 (1.94)	1.67 (1.91)	5.67 [0.32; 11.02]	0.038 *

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 52

	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=0.071**				
KESTREL: Composite Score				
Interaction test	p=0.473			
≤ 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 28: Adjusted Mean Change (SE)	3.40 (1.28)	7.10 (1.38)		
Week 52: Adjusted Mean Change (SE)	5.37 (1.39)	6.36 (1.43)	-0.99 [-4.89; 2.91]	0.617
> 65 letters				
N'/ N	114 / 115	123 / 123		
Baseline Mean (SD)	80.97 (15.49)	79.51 (12.74)		
Week 52 Mean (SD)	87.52 (11.16)	87.06 (10.86)		
Week 28: Adjusted Mean Change (SE)	7.37 (1.03)	7.99 (0.99)		
Week 52: Adjusted Mean Change (SE)	8.33 (1.06)	9.33 (1.01)	-1.01 [-3.88; 1.86]	0.490
KITE: Composite Score				
Interaction test	p=0.354			
≤ 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 28: Adjusted Mean Change (SE)	5.40 (1.27)	4.80 (1.08)		
Week 52: Adjusted Mean Change (SE)	8.74 (1.39)	5.43 (1.17)	3.31 [-0.22; 6.85]	0.066
> 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 28: Adjusted Mean Change (SE)	6.15 (0.97)	7.36 (1.11)		
Week 52: Adjusted Mean Change (SE)	9.01 (1.05)	7.65 (1.17)	1.36 [-1.70; 4.43]	0.383

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Composite Score				
Interaction test	p=0.560			
≤ 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 28: Adjusted Mean Change (SE)	4.65 (0.91)	5.66 (0.87)		
Week 52: Adjusted Mean Change (SE)	7.26 (0.98)	5.71 (0.92)	1.55 [-1.06; 4.16]	0.245
> 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 28: Adjusted Mean Change (SE)	6.67 (0.72)	7.74 (0.75)		
Week 52: Adjusted Mean Change (SE)	8.55 (0.75)	8.67 (0.77)	-0.12 [-2.21; 1.97]	0.910
General Vision				
Test of heterogeneity in main analysis: **p_H=0.986**				
KESTREL: General Vision				
Interaction test	p=0.646			
≤ 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 28: Adjusted Mean Change (SE)	8.82 (1.54)	9.32 (1.67)		
Week 52: Adjusted Mean Change (SE)	9.37 (1.70)	8.24 (1.73)	1.14 [-3.63; 5.91]	0.639
> 65 letters				
N'/ N	114 / 115	123 / 123		
Baseline Mean (SD)	63.68 (17.76)	61.79 (14.26)		
Week 52 Mean (SD)	74.74 (14.05)	72.76 (12.75)		
Week 28: Adjusted Mean Change (SE)	12.99 (1.25)	11.29 (1.21)		
Week 52: Adjusted Mean Change (SE)	13.03 (1.29)	11.86 (1.22)	1.18 [-2.32; 4.67]	0.508

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Vision				
Interaction test	p=0.855			
≤ 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 28: Adjusted Mean Change (SE)	8.09 (1.69)	7.97 (1.43)		
Week 52: Adjusted Mean Change (SE)	9.56 (1.90)	8.77 (1.59)	0.79 [-4.07; 5.65]	0.750
> 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 28: Adjusted Mean Change (SE)	10.25 (1.30)	11.42 (1.47)		
Week 52: Adjusted Mean Change (SE)	12.93 (1.43)	11.82 (1.59)	1.12 [-3.08; 5.31]	0.601
Pooled Analysis: General Vision				
Interaction test	p=0.974			
≤ 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 28: Adjusted Mean Change (SE)	8.57 (1.14)	8.42 (1.10)		
Week 52: Adjusted Mean Change (SE)	9.53 (1.27)	8.42 (1.17)	1.11 [-2.27; 4.49]	0.520
> 65 letters				
N'/ N	227 / 229	213 / 213		
Baseline Mean (SD)	63.52 (17.09)	62.91 (15.81)		
Week 52 Mean (SD)	75.08 (14.27)	73.33 (14.18)		
Week 28: Adjusted Mean Change (SE)	11.57 (0.90)	11.41 (0.95)		
Week 52: Adjusted Mean Change (SE)	12.94 (0.96)	11.94 (0.99)	1.00 [-1.71; 3.70]	0.469

	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=0.492**				
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 28: Adjusted Mean Change (SE)	2.26 (2.10)	3.24 (2.27)		
Week 52: Adjusted Mean Change (SE)	4.52 (2.01)	5.70 (2.06)	-1.18 [-6.85; 4.49]	0.682
> 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 28: Adjusted Mean Change (SE)	3.05 (1.70)	4.97 (1.65)		
Week 52: Adjusted Mean Change (SE)	5.59 (1.53)	3.70 (1.45)	1.89 [-2.26; 6.04]	0.372
KITE: Ocular Pain				
Interaction test	p=0.056			
≤ 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 28: Adjusted Mean Change (SE)	6.26 (1.94)	3.04 (1.64)		
Week 52: Adjusted Mean Change (SE)	5.67 (2.05)	1.40 (1.70)	4.27 [-0.97; 9.51]	0.110
> 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 28: Adjusted Mean Change (SE)	3.71 (1.49)	5.03 (1.69)		
Week 52: Adjusted Mean Change (SE)	4.70 (1.54)	6.68 (1.70)	-1.98 [-6.49; 2.53]	0.388

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Ocular Pain				
Interaction test	p=0.221			
≤ 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 28: Adjusted Mean Change (SE)	4.40 (1.43)	3.04 (1.37)		
Week 52: Adjusted Mean Change (SE)	5.35 (1.44)	3.14 (1.33)	2.21 [-1.64; 6.06]	0.260
> 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 28: Adjusted Mean Change (SE)	3.28 (1.13)	4.97 (1.19)		
Week 52: Adjusted Mean Change (SE)	5.03 (1.09)	4.96 (1.12)	0.07 [-2.99; 3.14]	0.962
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.456**				
KESTREL: Near Activities				
Interaction test	p=0.309			
≤ 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 28: Adjusted Mean Change (SE)	8.90 (2.19)	13.24 (2.34)		
Week 52: Adjusted Mean Change (SE)	10.58 (2.51)	13.01 (2.55)	-2.43 [-9.43; 4.58]	0.496
> 65 letters				
N'/ N	114 / 115	123 / 123		
Baseline Mean (SD)	70.25 (24.52)	70.09 (19.82)		
Week 52 Mean (SD)	82.32 (19.18)	80.60 (19.00)		
Week 28: Adjusted Mean Change (SE)	14.65 (1.75)	15.22 (1.70)		
Week 52: Adjusted Mean Change (SE)	15.21 (1.90)	14.16 (1.81)	1.05 [-4.08; 6.18]	0.687

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Near Activities				
Interaction test	p=0.440			
≤ 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 28: Adjusted Mean Change (SE)	3.27 (2.29)	2.73 (1.91)		
Week 52: Adjusted Mean Change (SE)	9.06 (2.34)	6.44 (1.94)	2.62 [-3.30; 8.54]	0.385
> 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 28: Adjusted Mean Change (SE)	8.42 (1.74)	9.64 (1.97)		
Week 52: Adjusted Mean Change (SE)	11.12 (1.75)	12.07 (1.96)	-0.95 [-6.07; 4.16]	0.714
Pooled Analysis: Near Activities				
Interaction test	p=0.865			
≤ 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 28: Adjusted Mean Change (SE)	6.62 (1.59)	7.33 (1.51)		
Week 52: Adjusted Mean Change (SE)	10.14 (1.73)	9.38 (1.59)	0.76 [-3.81; 5.32]	0.746
> 65 letters				
N'/ N	227 / 229	213 / 213		
Baseline Mean (SD)	72.67 (22.60)	73.20 (19.68)		
Week 52 Mean (SD)	83.18 (19.08)	82.78 (18.07)		
Week 28: Adjusted Mean Change (SE)	11.53 (1.25)	12.46 (1.31)		
Week 52: Adjusted Mean Change (SE)	13.10 (1.31)	12.98 (1.34)	0.12 [-3.53; 3.77]	0.948

	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=0.136**				
KESTREL: Distance Activities				
Interaction test	p=0.778			
≤ 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 28: Adjusted Mean Change (SE)	4.93 (1.93)	7.22 (2.07)		
Week 52: Adjusted Mean Change (SE)	6.67 (1.89)	7.15 (1.94)	-0.48 [-5.80; 4.84]	0.860
> 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 28: Adjusted Mean Change (SE)	9.07 (1.54)	9.85 (1.50)		
Week 52: Adjusted Mean Change (SE)	10.60 (1.44)	10.88 (1.37)	-0.27 [-4.18; 3.63]	0.890
KITE: Distance Activities				
Interaction test	p=0.175			
≤ 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 28: Adjusted Mean Change (SE)	3.96 (1.97)	3.14 (1.66)		
Week 52: Adjusted Mean Change (SE)	11.46 (1.89)	4.96 (1.58)	6.50 [1.69; 11.30]	0.008 *
> 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 28: Adjusted Mean Change (SE)	7.74 (1.51)	8.01 (1.71)		
Week 52: Adjusted Mean Change (SE)	11.37 (1.42)	11.47 (1.58)	-0.10 [-4.25; 4.05]	0.962

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Distance Activities				
Interaction test	p=0.290			
≤ 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 28: Adjusted Mean Change (SE)	4.72 (1.38)	4.75 (1.32)		
Week 52: Adjusted Mean Change (SE)	9.25 (1.34)	5.81 (1.24)	3.43 [-0.12; 6.99]	0.058
> 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 28: Adjusted Mean Change (SE)	8.34 (1.09)	9.07 (1.14)		
Week 52: Adjusted Mean Change (SE)	10.90 (1.02)	11.15 (1.04)	-0.25 [-3.09; 2.60]	0.865
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.037 ***				
KESTREL: Social Functioning				
Interaction test	p=0.477			
≤ 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 28: Adjusted Mean Change (SE)	-0.81 (1.45)	2.60 (1.56)		
Week 52: Adjusted Mean Change (SE)	-0.47 (1.70)	1.81 (1.72)	-2.28 [-7.04; 2.48]	0.346
> 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 28: Adjusted Mean Change (SE)	3.22 (1.17)	4.80 (1.14)		
Week 52: Adjusted Mean Change (SE)	4.53 (1.28)	5.36 (1.23)	-0.83 [-4.31; 2.66]	0.641

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Social Functioning				
Interaction test	p=0.095			
≤ 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 28: Adjusted Mean Change (SE)	2.26 (1.72)	1.10 (1.46)		
Week 52: Adjusted Mean Change (SE)	6.87 (1.51)	1.89 (1.26)	4.98 [1.12; 8.84]	0.012 *
> 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 28: Adjusted Mean Change (SE)	4.78 (1.33)	7.02 (1.51)		
Week 52: Adjusted Mean Change (SE)	7.81 (1.13)	7.05 (1.26)	0.76 [-2.56; 4.08]	0.654
Pooled Analysis: Social Functioning				
Interaction test	p=0.257			
≤ 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 28: Adjusted Mean Change (SE)	1.04 (1.12)	1.46 (1.07)		
Week 52: Adjusted Mean Change (SE)	3.53 (1.14)	1.60 (1.05)	1.93 [-1.10; 4.97]	0.211
> 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 28: Adjusted Mean Change (SE)	3.84 (0.89)	5.82 (0.93)		
Week 52: Adjusted Mean Change (SE)	6.00 (0.86)	6.18 (0.89)	-0.18 [-2.60; 2.24]	0.882

	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=0.300**				
KESTREL: Mental Health				
Interaction test	p=0.322			
≤ 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 28: Adjusted Mean Change (SE)	3.13 (2.06)	9.65 (2.21)		
Week 52: Adjusted Mean Change (SE)	9.30 (2.21)	8.92 (2.25)	0.38 [-5.82; 6.58]	0.905
> 65 letters				
N'/ N	114 / 115	123 / 123		
Baseline Mean (SD)	71.60 (22.41)	71.39 (20.91)		
Week 52 Mean (SD)	81.12 (18.35)	80.60 (16.26)		
Week 28: Adjusted Mean Change (SE)	10.10 (1.64)	8.75 (1.60)		
Week 52: Adjusted Mean Change (SE)	11.23 (1.68)	12.33 (1.59)	-1.10 [-5.64; 3.43]	0.632
KITE: Mental Health				
Interaction test	p=0.347			
≤ 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 28: Adjusted Mean Change (SE)	8.20 (2.12)	7.14 (1.81)		
Week 52: Adjusted Mean Change (SE)	12.81 (2.60)	7.91 (2.19)	4.90 [-1.76; 11.56]	0.149
> 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 28: Adjusted Mean Change (SE)	9.08 (1.64)	11.61 (1.85)		
Week 52: Adjusted Mean Change (SE)	13.15 (1.96)	11.30 (2.19)	1.85 [-3.90; 7.61]	0.527

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Mental Health				
Interaction test	p=0.794			
≤ 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 28: Adjusted Mean Change (SE)	5.81 (1.47)	8.00 (1.41)		
Week 52: Adjusted Mean Change (SE)	11.17 (1.69)	8.05 (1.57)	3.13 [-1.38; 7.64]	0.173
> 65 letters				
N'/ N	227 / 229	213 / 213		
Baseline Mean (SD)	71.92 (21.89)	72.42 (20.55)		
Week 52 Mean (SD)	82.12 (19.17)	81.42 (18.23)		
Week 28: Adjusted Mean Change (SE)	9.55 (1.16)	9.98 (1.22)		
Week 52: Adjusted Mean Change (SE)	12.14 (1.29)	12.00 (1.32)	0.13 [-3.47; 3.74]	0.942
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.072**				
KESTREL: Role Difficulties				
Interaction test	p=0.572			
≤ 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 28: Adjusted Mean Change (SE)	0.65 (2.54)	5.41 (2.75)		
Week 52: Adjusted Mean Change (SE)	2.08 (2.90)	6.86 (2.97)	-4.78 [-12.93; 3.37]	0.250
> 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 28: Adjusted Mean Change (SE)	9.40 (2.04)	11.06 (1.98)		
Week 52: Adjusted Mean Change (SE)	10.04 (2.21)	13.27 (2.10)	-3.23 [-9.20; 2.75]	0.289

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Role Difficulties				
Interaction test	p=0.376			
≤ 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 28: Adjusted Mean Change (SE)	6.62 (2.62)	5.16 (2.21)		
Week 52: Adjusted Mean Change (SE)	8.90 (2.82)	4.88 (2.35)	4.02 [-3.16; 11.19]	0.272
> 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 28: Adjusted Mean Change (SE)	8.15 (2.02)	11.74 (2.27)		
Week 52: Adjusted Mean Change (SE)	14.28 (2.12)	12.16 (2.35)	2.12 [-4.08; 8.31]	0.502
Pooled Analysis: Role Difficulties				
Interaction test	p=0.825			
≤ 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 28: Adjusted Mean Change (SE)	3.59 (1.82)	5.23 (1.74)		
Week 52: Adjusted Mean Change (SE)	5.39 (2.01)	5.69 (1.86)	-0.30 [-5.64; 5.05]	0.913
> 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 28: Adjusted Mean Change (SE)	8.82 (1.44)	11.31 (1.50)		
Week 52: Adjusted Mean Change (SE)	12.12 (1.53)	12.81 (1.56)	-0.69 [-4.96; 3.58]	0.752

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Dependency				
Test of heterogeneity in main analysis: **p_H=0.029 ***				
KESTREL: Dependency				
Interaction test	p=0.925			
≤ 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 28: Adjusted Mean Change (SE)	2.57 (2.22)	4.25 (2.39)		
Week 52: Adjusted Mean Change (SE)	2.89 (2.38)	4.52 (2.44)	-1.63 [-8.32; 5.05]	0.631
> 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 28: Adjusted Mean Change (SE)	7.58 (1.78)	8.10 (1.72)		
Week 52: Adjusted Mean Change (SE)	7.40 (1.81)	10.85 (1.72)	-3.45 [-8.35; 1.45]	0.167
KITE: Dependency				
Interaction test	p=0.877			
≤ 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 28: Adjusted Mean Change (SE)	5.01 (2.14)	1.75 (1.82)		
Week 52: Adjusted Mean Change (SE)	6.00 (2.35)	2.88 (1.98)	3.12 [-2.88; 9.12]	0.307
> 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 28: Adjusted Mean Change (SE)	6.05 (1.64)	5.07 (1.88)		
Week 52: Adjusted Mean Change (SE)	8.41 (1.76)	4.05 (1.99)	4.36 [-0.83; 9.56]	0.100

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Dependency				
Interaction test	p=0.559			
≤ 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 28: Adjusted Mean Change (SE)	4.14 (1.54)	2.83 (1.48)		
Week 52: Adjusted Mean Change (SE)	4.73 (1.68)	3.52 (1.56)	1.21 [-3.25; 5.67]	0.594
> 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 28: Adjusted Mean Change (SE)	6.69 (1.21)	6.78 (1.28)		
Week 52: Adjusted Mean Change (SE)	7.77 (1.27)	8.00 (1.31)	-0.23 [-3.80; 3.33]	0.898
Driving				
Test of heterogeneity in main analysis: **p_H=0.778**				
KESTREL: Driving				
Interaction test	p=0.987			
≤ 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 28: Adjusted Mean Change (SE)	-2.67 (2.55)	5.96 (2.82)		
Week 52: Adjusted Mean Change (SE)	4.50 (3.09)	1.48 (3.23)	3.03 [-5.78; 11.84]	0.499
> 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 28: Adjusted Mean Change (SE)	4.14 (1.67)	5.56 (1.64)		
Week 52: Adjusted Mean Change (SE)	3.66 (1.87)	7.71 (1.90)	-4.05 [-9.32; 1.22]	0.131

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Driving				
Interaction test	p=0.048 *			
≤ 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 28: Adjusted Mean Change (SE)	-5.54 (2.71)	5.02 (2.56)		
Week 52: Adjusted Mean Change (SE)	1.81 (2.30)	5.47 (2.27)	-3.66 [-10.01; 2.69]	0.257
> 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 28: Adjusted Mean Change (SE)	3.15 (1.68)	5.65 (1.82)		
Week 52: Adjusted Mean Change (SE)	7.47 (1.48)	5.10 (1.60)	2.37 [-1.94; 6.68]	0.279
Pooled Analysis: Driving				
Interaction test	p=0.392			
≤ 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 28: Adjusted Mean Change (SE)	-3.62 (1.84)	5.38 (1.91)		
Week 52: Adjusted Mean Change (SE)	3.93 (1.96)	3.52 (1.99)	0.41 [-5.06; 5.88]	0.883
> 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 28: Adjusted Mean Change (SE)	3.51 (1.18)	5.73 (1.22)		
Week 52: Adjusted Mean Change (SE)	5.11 (1.21)	6.67 (1.27)	-1.56 [-5.01; 1.89]	0.375

	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=0.691**				
KESTREL: Color Vision				
Interaction test	p=0.843			
≤ 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 28: Adjusted Mean Change (SE)	-0.27 (1.32)	-0.59 (1.44)		
Week 52: Adjusted Mean Change (SE)	-0.65 (1.42)	-1.99 (1.47)	1.34 [-2.70; 5.38]	0.515
> 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 28: Adjusted Mean Change (SE)	3.63 (1.06)	3.05 (1.04)		
Week 52: Adjusted Mean Change (SE)	3.88 (1.07)	3.62 (1.02)	0.27 [-2.64; 3.18]	0.857
KITE: Color Vision				
Interaction test	p=0.683			
≤ 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 28: Adjusted Mean Change (SE)	3.83 (1.36)	3.27 (1.16)		
Week 52: Adjusted Mean Change (SE)	5.35 (1.26)	3.50 (1.07)	1.86 [-1.40; 5.11]	0.264
> 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 28: Adjusted Mean Change (SE)	3.46 (1.04)	5.18 (1.19)		
Week 52: Adjusted Mean Change (SE)	5.98 (0.94)	3.38 (1.05)	2.59 [-0.18; 5.36]	0.067

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Color Vision				
Interaction test	p=0.431			
≤ 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 28: Adjusted Mean Change (SE)	1.95 (0.96)	1.27 (0.92)		
Week 52: Adjusted Mean Change (SE)	2.53 (0.95)	0.79 (0.89)	1.74 [-0.81; 4.29]	0.180
> 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 28: Adjusted Mean Change (SE)	3.47 (0.75)	4.22 (0.79)		
Week 52: Adjusted Mean Change (SE)	4.80 (0.71)	3.81 (0.73)	0.99 [-1.02; 2.99]	0.333
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.021 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.085			
≤ 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 28: Adjusted Mean Change (SE)	0.36 (2.13)	10.18 (2.31)		
Week 52: Adjusted Mean Change (SE)	3.00 (2.29)	6.65 (2.36)	-3.65 [-10.12; 2.83]	0.269
> 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 28: Adjusted Mean Change (SE)	4.48 (1.75)	6.53 (1.67)		
Week 52: Adjusted Mean Change (SE)	7.47 (1.75)	7.68 (1.65)	-0.21 [-4.94; 4.52]	0.931

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Peripheral Vision				
Interaction test	p=0.080			
≤ 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 28: Adjusted Mean Change (SE)	4.31 (1.97)	2.26 (1.65)		
Week 52: Adjusted Mean Change (SE)	7.73 (2.15)	1.53 (1.78)	6.20 [0.73; 11.67]	0.026 *
> 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 28: Adjusted Mean Change (SE)	5.04 (1.51)	7.15 (1.73)		
Week 52: Adjusted Mean Change (SE)	5.76 (1.61)	5.77 (1.81)	-0.01 [-4.76; 4.74]	0.997
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.782			
≤ 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 28: Adjusted Mean Change (SE)	2.43 (1.46)	5.70 (1.40)		
Week 52: Adjusted Mean Change (SE)	5.42 (1.58)	3.78 (1.46)	1.64 [-2.56; 5.84]	0.444
> 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 28: Adjusted Mean Change (SE)	4.49 (1.16)	6.78 (1.21)		
Week 52: Adjusted Mean Change (SE)	6.40 (1.19)	6.96 (1.23)	-0.56 [-3.91; 2.79]	0.742

	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=0.700**				
KESTREL: General Health				
Interaction test	p=0.995			
≤ 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 28: Adjusted Mean Change (SE)	4.56 (2.19)	4.61 (2.38)		
Week 52: Adjusted Mean Change (SE)	4.68 (2.78)	1.57 (2.83)	3.11 [-4.72; 10.94]	0.436
> 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 28: Adjusted Mean Change (SE)	4.21 (1.78)	4.72 (1.73)		
Week 52: Adjusted Mean Change (SE)	10.47 (2.12)	6.95 (2.01)	3.51 [-2.25; 9.28]	0.231
KITE: General Health				
Interaction test	p=0.196			
≤ 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 28: Adjusted Mean Change (SE)	3.52 (2.29)	3.37 (1.92)		
Week 52: Adjusted Mean Change (SE)	6.51 (2.75)	2.30 (2.28)	4.21 [-2.81; 11.24]	0.239
> 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 28: Adjusted Mean Change (SE)	3.67 (1.76)	5.49 (1.99)		
Week 52: Adjusted Mean Change (SE)	4.87 (2.06)	7.65 (2.29)	-2.77 [-8.84; 3.29]	0.369

	Treatment Groups		Comparison	
VFQ by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: General Health				
Interaction test	p=0.316			
≤ 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 28: Adjusted Mean Change (SE)	4.00 (1.58)	3.82 (1.51)		
Week 52: Adjusted Mean Change (SE)	5.52 (1.95)	1.93 (1.79)	3.60 [-1.60; 8.79]	0.175
> 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 28: Adjusted Mean Change (SE)	3.81 (1.25)	5.25 (1.31)		
Week 52: Adjusted Mean Change (SE)	7.59 (1.47)	7.45 (1.51)	0.14 [-4.00; 4.28]	0.947

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 52

	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=0.071**				
KESTREL: Composite Score				
Interaction test	p=0.712			
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 28: Adjusted Mean Change (SE)	6.05 (1.17)	7.57 (1.24)		
Week 52: Adjusted Mean Change (SE)	6.66 (1.22)	9.88 (1.24)	-3.21 [-6.60; 0.17]	0.063
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 28: Adjusted Mean Change (SE)	5.23 (1.34)	7.68 (1.29)		
Week 52: Adjusted Mean Change (SE)	8.51 (1.40)	7.10 (1.33)	1.42 [-2.33; 5.17]	0.457
Western Pacific Region				
N'/ N	30 / 30	29 / 29		
Baseline Mean (SD)	72.37 (15.07)	76.27 (12.20)		
Week 52 Mean (SD)	79.41 (15.73)	82.12 (10.24)		
Week 28: Adjusted Mean Change (SE)	6.52 (2.01)	8.05 (2.09)		
Week 52: Adjusted Mean Change (SE)	5.57 (2.09)	6.97 (2.09)	-1.40 [-7.20; 4.40]	0.636
KITE: Composite Score				
Interaction test	p=0.731			
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 28: Adjusted Mean Change (SE)	6.03 (2.04)	5.29 (2.29)		
Week 52: Adjusted Mean Change (SE)	11.69 (2.37)	7.07 (2.63)	4.63 [-2.30; 11.56]	0.190

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 28: Adjusted Mean Change (SE)	5.94 (0.89)	5.86 (0.89)		
Week 52: Adjusted Mean Change (SE)	8.76 (0.95)	6.76 (0.95)	2.00 [-0.65; 4.64]	0.138
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 28: Adjusted Mean Change (SE)	5.07 (2.41)	7.66 (2.03)		
Week 52: Adjusted Mean Change (SE)	6.76 (2.60)	5.23 (2.10)	1.53 [-5.02; 8.07]	0.647
Pooled Analysis: Composite Score				
Interaction test	p=0.699			
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 28: Adjusted Mean Change (SE)	6.91 (1.31)	7.88 (1.36)		
Week 52: Adjusted Mean Change (SE)	7.46 (1.37)	10.22 (1.37)	-2.76 [-6.53; 1.02]	0.152
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 28: Adjusted Mean Change (SE)	5.05 (2.22)	4.98 (2.46)		
Week 52: Adjusted Mean Change (SE)	10.77 (2.48)	6.67 (2.72)	4.10 [-3.12; 11.32]	0.265
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 28: Adjusted Mean Change (SE)	5.49 (0.79)	6.43 (0.77)		
Week 52: Adjusted Mean Change (SE)	8.42 (0.82)	6.81 (0.80)	1.61 [-0.63; 3.86]	0.159

	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)	74.38 (14.80)	76.02 (16.13)		
Week 52 Mean (SD)	81.08 (16.44)	83.06 (14.04)		
Week 28: Adjusted Mean Change (SE)	6.23 (1.56)	7.65 (1.46)		
Week 52: Adjusted Mean Change (SE)	6.31 (1.63)	5.95 (1.47)	0.36 [-3.96; 4.68]	0.870
General Vision				
Test of heterogeneity in main analysis: **p_H=0.986**				
KESTREL: General Vision				
Interaction test	p=0.755			
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 28: Adjusted Mean Change (SE)	11.67 (1.41)	9.79 (1.50)		
Week 52: Adjusted Mean Change (SE)	11.50 (1.45)	12.65 (1.46)	-1.15 [-5.18; 2.88]	0.574
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 28: Adjusted Mean Change (SE)	11.56 (1.62)	12.56 (1.55)		
Week 52: Adjusted Mean Change (SE)	15.45 (1.66)	10.25 (1.57)	5.19 [0.73; 9.66]	0.023 *
Western Pacific Region				
N'/ N	30 / 30	29 / 29		
Baseline Mean (SD)	51.33 (16.34)	57.24 (14.86)		
Week 52 Mean (SD)	60.83 (11.00)	64.00 (10.00)		
Week 28: Adjusted Mean Change (SE)	10.02 (2.44)	7.55 (2.54)		
Week 52: Adjusted Mean Change (SE)	3.54 (2.51)	5.58 (2.48)	-2.05 [-8.93; 4.84]	0.559
KITE: General Vision				
Interaction test	p=0.554			
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 28: Adjusted Mean Change (SE)	8.68 (2.73)	8.02 (3.07)		
Week 52: Adjusted Mean Change (SE)	9.82 (3.27)	5.70 (3.61)	4.12 [-5.44; 13.68]	0.397

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 28: Adjusted Mean Change (SE)	9.60 (1.19)	9.75 (1.20)		
Week 52: Adjusted Mean Change (SE)	12.73 (1.30)	10.75 (1.30)	1.98 [-1.63; 5.59]	0.281
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 28: Adjusted Mean Change (SE)	9.19 (3.24)	10.42 (2.74)		
Week 52: Adjusted Mean Change (SE)	6.25 (3.55)	10.90 (2.85)	-4.66 [-13.56; 4.25]	0.304
Pooled Analysis: General Vision				
Interaction test	p=0.665			
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 28: Adjusted Mean Change (SE)	11.16 (1.64)	10.05 (1.70)		
Week 52: Adjusted Mean Change (SE)	10.94 (1.73)	12.94 (1.73)	-2.00 [-6.79; 2.79]	0.413
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 28: Adjusted Mean Change (SE)	9.13 (2.81)	7.68 (3.12)		
Week 52: Adjusted Mean Change (SE)	9.97 (3.21)	5.06 (3.52)	4.91 [-4.45; 14.26]	0.303
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 28: Adjusted Mean Change (SE)	10.25 (1.00)	10.55 (0.98)		
Week 52: Adjusted Mean Change (SE)	13.61 (1.05)	10.38 (1.02)	3.24 [0.36; 6.11]	0.027 *

	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)	64.10 (13.90)	69.39 (17.84)		
Week 28: Adjusted Mean Change (SE)	10.36 (1.97)	9.52 (1.85)		
Week 52: Adjusted Mean Change (SE)	5.44 (2.10)	8.85 (1.88)	-3.41 [-8.94; 2.12]	0.226
Ocular Pain				
Test of heterogeneity in main analysis: **p_H=0.492**				
KESTREL: Ocular Pain				
Interaction test	p=0.557			
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 28: Adjusted Mean Change (SE)	2.64 (1.91)	5.98 (2.02)		
Week 52: Adjusted Mean Change (SE)	4.90 (1.77)	6.08 (1.79)	-1.19 [-6.10; 3.73]	0.636
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 28: Adjusted Mean Change (SE)	1.31 (2.17)	1.03 (2.09)		
Week 52: Adjusted Mean Change (SE)	4.31 (2.01)	2.24 (1.91)	2.07 [-3.37; 7.51]	0.455
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 28: Adjusted Mean Change (SE)	6.33 (3.27)	8.32 (3.41)		
Week 52: Adjusted Mean Change (SE)	8.06 (3.03)	4.82 (3.03)	3.24 [-5.16; 11.64]	0.449
KITE: Ocular Pain				
Interaction test	p=0.974			
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 28: Adjusted Mean Change (SE)	6.40 (3.14)	3.21 (3.53)		
Week 52: Adjusted Mean Change (SE)	3.87 (3.58)	3.67 (3.96)	0.20 [-10.24; 10.64]	0.970

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 28: Adjusted Mean Change (SE)	4.50 (1.37)	3.87 (1.37)		
Week 52: Adjusted Mean Change (SE)	4.75 (1.41)	3.83 (1.41)	0.92 [-2.99; 4.82]	0.645
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 28: Adjusted Mean Change (SE)	3.37 (3.72)	5.45 (3.14)		
Week 52: Adjusted Mean Change (SE)	8.45 (3.84)	5.28 (3.07)	3.17 [-6.47; 12.80]	0.518
Pooled Analysis: Ocular Pain				
Interaction test	p=0.657			
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 28: Adjusted Mean Change (SE)	3.71 (2.02)	7.35 (2.10)		
Week 52: Adjusted Mean Change (SE)	6.03 (2.00)	7.51 (1.99)	-1.48 [-6.98; 4.02]	0.598
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 28: Adjusted Mean Change (SE)	4.88 (3.48)	1.45 (3.87)		
Week 52: Adjusted Mean Change (SE)	2.46 (3.69)	1.76 (4.04)	0.70 [-10.02; 11.43]	0.898
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 28: Adjusted Mean Change (SE)	3.20 (1.23)	2.53 (1.21)		
Week 52: Adjusted Mean Change (SE)	4.33 (1.20)	2.93 (1.17)	1.40 [-1.88; 4.69]	0.402

	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)	85.42 (16.97)	81.80 (20.74)		
Week 52 Mean (SD)	91.67 (13.85)	88.27 (16.42)		
Week 28: Adjusted Mean Change (SE)	5.24 (2.45)	6.51 (2.31)		
Week 52: Adjusted Mean Change (SE)	8.23 (2.39)	4.74 (2.14)	3.49 [-2.81; 9.79]	0.278
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.456**				
KESTREL: Near Activities				
Interaction test	p=0.760			
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 28: Adjusted Mean Change (SE)	11.38 (1.99)	12.97 (2.08)		
Week 52: Adjusted Mean Change (SE)	12.83 (2.20)	16.10 (2.20)	-3.28 [-9.36; 2.81]	0.290
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 28: Adjusted Mean Change (SE)	13.92 (2.26)	17.13 (2.17)		
Week 52: Adjusted Mean Change (SE)	15.11 (2.51)	12.40 (2.37)	2.71 [-4.03; 9.44]	0.430
Western Pacific Region				
N'/ N	30 / 30	29 / 29		
Baseline Mean (SD)	54.86 (23.82)	62.07 (18.84)		
Week 52 Mean (SD)	72.57 (23.11)	71.67 (15.77)		
Week 28: Adjusted Mean Change (SE)	11.97 (3.40)	11.84 (3.54)		
Week 52: Adjusted Mean Change (SE)	11.51 (3.77)	10.18 (3.74)	1.32 [-9.08; 11.73]	0.803
KITE: Near Activities				
Interaction test	p=0.190			
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 28: Adjusted Mean Change (SE)	6.46 (3.72)	5.96 (4.09)		
Week 52: Adjusted Mean Change (SE)	6.23 (4.00)	10.65 (4.41)	-4.42 [-16.10; 7.27]	0.458

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 28: Adjusted Mean Change (SE)	7.45 (1.59)	5.52 (1.59)		
Week 52: Adjusted Mean Change (SE)	11.40 (1.59)	8.63 (1.60)	2.77 [-1.66; 7.20]	0.219
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 28: Adjusted Mean Change (SE)	-0.54 (4.32)	9.07 (3.64)		
Week 52: Adjusted Mean Change (SE)	7.22 (4.36)	11.25 (3.52)	-4.02 [-14.99; 6.95]	0.471
Pooled Analysis: Near Activities				
Interaction test	p=0.672			
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 28: Adjusted Mean Change (SE)	9.71 (2.28)	10.55 (2.35)		
Week 52: Adjusted Mean Change (SE)	10.95 (2.38)	13.84 (2.37)	-2.88 [-9.46; 3.69]	0.390
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 28: Adjusted Mean Change (SE)	8.50 (3.94)	8.26 (4.29)		
Week 52: Adjusted Mean Change (SE)	8.44 (4.39)	12.77 (4.79)	-4.32 [-17.09; 8.44]	0.506
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 28: Adjusted Mean Change (SE)	10.36 (1.37)	10.28 (1.35)		
Week 52: Adjusted Mean Change (SE)	13.29 (1.44)	10.62 (1.40)	2.67 [-1.26; 6.60]	0.183

	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)	73.72 (25.55)	77.64 (18.33)		
Week 28: Adjusted Mean Change (SE)	7.18 (2.71)	10.34 (2.55)		
Week 52: Adjusted Mean Change (SE)	9.84 (2.87)	10.69 (2.57)	-0.85 [-8.41; 6.71]	0.826
Distance Activities				
Test of heterogeneity in main analysis: **p_H=0.136**				
KESTREL: Distance Activities				
Interaction test	p=0.629			
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 28: Adjusted Mean Change (SE)	8.83 (1.76)	7.21 (1.85)		
Week 52: Adjusted Mean Change (SE)	9.58 (1.67)	10.83 (1.68)	-1.25 [-5.86; 3.35]	0.593
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 28: Adjusted Mean Change (SE)	6.61 (2.02)	10.32 (1.93)		
Week 52: Adjusted Mean Change (SE)	10.91 (1.92)	9.52 (1.81)	1.39 [-3.71; 6.49]	0.592
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 28: Adjusted Mean Change (SE)	5.31 (3.01)	10.26 (3.14)		
Week 52: Adjusted Mean Change (SE)	3.52 (2.85)	6.36 (2.85)	-2.85 [-10.73; 5.04]	0.478
KITE: Distance Activities				
Interaction test	p=0.921			
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 28: Adjusted Mean Change (SE)	5.02 (3.16)	2.06 (3.54)		
Week 52: Adjusted Mean Change (SE)	13.09 (3.29)	8.88 (3.63)	4.21 [-5.41; 13.83]	0.390

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 28: Adjusted Mean Change (SE)	6.03 (1.38)	5.40 (1.38)		
Week 52: Adjusted Mean Change (SE)	11.38 (1.31)	8.33 (1.31)	3.05 [-0.58; 6.68]	0.099
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 28: Adjusted Mean Change (SE)	10.25 (3.75)	8.82 (3.16)		
Week 52: Adjusted Mean Change (SE)	9.64 (3.58)	7.49 (2.87)	2.15 [-6.83; 11.13]	0.638
Pooled Analysis: Distance Activities				
Interaction test	p=0.807			
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 28: Adjusted Mean Change (SE)	10.36 (1.97)	7.04 (2.03)		
Week 52: Adjusted Mean Change (SE)	11.09 (1.89)	10.69 (1.89)	0.39 [-4.81; 5.59]	0.882
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 28: Adjusted Mean Change (SE)	3.81 (3.35)	2.58 (3.72)		
Week 52: Adjusted Mean Change (SE)	12.11 (3.42)	9.45 (3.75)	2.66 [-7.30; 12.62]	0.600
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 28: Adjusted Mean Change (SE)	5.77 (1.19)	7.21 (1.17)		
Week 52: Adjusted Mean Change (SE)	10.69 (1.13)	8.80 (1.10)	1.89 [-1.19; 4.97]	0.229

	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)	71.96 (23.04)	71.49 (20.73)		
Week 52 Mean (SD)	78.53 (22.71)	81.21 (18.54)		
Week 28: Adjusted Mean Change (SE)	7.38 (2.36)	9.35 (2.22)		
Week 52: Adjusted Mean Change (SE)	6.10 (2.24)	6.79 (2.01)	-0.68 [-6.58; 5.21]	0.820
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.037 ***				
KESTREL: Social Functioning				
Interaction test	p=0.454			
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 28: Adjusted Mean Change (SE)	1.55 (1.33)	3.75 (1.41)		
Week 52: Adjusted Mean Change (SE)	1.80 (1.50)	4.73 (1.51)	-2.94 [-7.11; 1.24]	0.167
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 28: Adjusted Mean Change (SE)	0.77 (1.51)	5.16 (1.46)		
Week 52: Adjusted Mean Change (SE)	4.29 (1.71)	4.81 (1.63)	-0.52 [-5.13; 4.08]	0.824
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 28: Adjusted Mean Change (SE)	3.91 (2.29)	1.90 (2.39)		
Week 52: Adjusted Mean Change (SE)	1.51 (2.59)	0.87 (2.55)	0.65 [-6.46; 7.76]	0.858
KITE: Social Functioning				
Interaction test	p=0.912			
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 28: Adjusted Mean Change (SE)	6.52 (2.80)	3.14 (3.14)		
Week 52: Adjusted Mean Change (SE)	7.40 (2.65)	5.92 (2.93)	1.48 [-6.29; 9.25]	0.708

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 28: Adjusted Mean Change (SE)	3.50 (1.22)	4.31 (1.22)		
Week 52: Adjusted Mean Change (SE)	7.59 (1.04)	4.75 (1.05)	2.83 [-0.07; 5.73]	0.056
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 28: Adjusted Mean Change (SE)	2.34 (3.32)	2.95 (2.80)		
Week 52: Adjusted Mean Change (SE)	6.31 (2.86)	2.28 (2.29)	4.02 [-3.14; 11.18]	0.270
Pooled Analysis: Social Functioning				
Interaction test	p=0.554			
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 28: Adjusted Mean Change (SE)	3.20 (1.59)	4.35 (1.65)		
Week 52: Adjusted Mean Change (SE)	3.47 (1.58)	5.36 (1.58)	-1.88 [-6.26; 2.49]	0.398
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 28: Adjusted Mean Change (SE)	4.59 (2.74)	2.47 (3.04)		
Week 52: Adjusted Mean Change (SE)	5.77 (2.95)	5.52 (3.22)	0.24 [-8.33; 8.82]	0.955
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 28: Adjusted Mean Change (SE)	2.11 (0.97)	4.47 (0.95)		
Week 52: Adjusted Mean Change (SE)	5.96 (0.96)	4.61 (0.93)	1.35 [-1.26; 3.97]	0.310

	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 28: Adjusted Mean Change (SE)	3.73 (1.93)	1.95 (1.82)		
Week 52: Adjusted Mean Change (SE)	3.81 (1.91)	1.10 (1.70)	2.71 [-2.31; 7.74]	0.290
Mental Health				
Test of heterogeneity in main analysis: **p_H=0.300**				
KESTREL: Mental Health				
Interaction test	p=0.103			
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 28: Adjusted Mean Change (SE)	6.06 (1.87)	9.89 (1.99)		
Week 52: Adjusted Mean Change (SE)	9.04 (1.93)	12.84 (1.95)	-3.81 [-9.16; 1.54]	0.162
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 28: Adjusted Mean Change (SE)	8.31 (2.12)	7.41 (2.06)		
Week 52: Adjusted Mean Change (SE)	13.76 (2.19)	8.78 (2.09)	4.98 [-0.93; 10.90]	0.098
Western Pacific Region				
N'/ N	30 / 30	29 / 29		
Baseline Mean (SD)	62.29 (24.54)	75.43 (20.72)		
Week 52 Mean (SD)	71.61 (25.74)	82.75 (13.54)		
Week 28: Adjusted Mean Change (SE)	9.11 (3.21)	11.06 (3.35)		
Week 52: Adjusted Mean Change (SE)	6.98 (3.30)	12.38 (3.29)	-5.40 [-14.55; 3.76]	0.247
KITE: Mental Health				
Interaction test	p=0.384			
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 28: Adjusted Mean Change (SE)	4.37 (3.41)	4.45 (3.83)		
Week 52: Adjusted Mean Change (SE)	17.55 (4.47)	6.71 (4.95)	10.84 [-2.24; 23.92]	0.104

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 28: Adjusted Mean Change (SE)	9.51 (1.49)	9.36 (1.49)		
Week 52: Adjusted Mean Change (SE)	13.18 (1.79)	9.57 (1.79)	3.61 [-1.35; 8.56]	0.153
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 28: Adjusted Mean Change (SE)	9.15 (4.04)	12.92 (3.41)		
Week 52: Adjusted Mean Change (SE)	7.32 (4.88)	11.84 (3.92)	-4.52 [-16.77; 7.74]	0.469
Pooled Analysis: Mental Health				
Interaction test	p=0.097			
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 28: Adjusted Mean Change (SE)	6.61 (2.10)	11.16 (2.20)		
Week 52: Adjusted Mean Change (SE)	9.55 (2.31)	14.08 (2.32)	-4.52 [-10.93; 1.88]	0.166
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 28: Adjusted Mean Change (SE)	3.74 (3.58)	3.26 (3.97)		
Week 52: Adjusted Mean Change (SE)	16.66 (4.30)	4.88 (4.71)	11.78 [-0.73; 24.29]	0.065
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 28: Adjusted Mean Change (SE)	9.04 (1.27)	8.29 (1.25)		
Week 52: Adjusted Mean Change (SE)	13.26 (1.41)	8.95 (1.37)	4.30 [0.46; 8.14]	0.028 *

	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)	63.80 (25.03)	68.31 (27.87)		
Week 52 Mean (SD)	72.44 (27.08)	80.48 (21.75)		
Week 28: Adjusted Mean Change (SE)	9.25 (2.51)	11.57 (2.36)		
Week 52: Adjusted Mean Change (SE)	7.33 (2.81)	11.73 (2.52)	-4.40 [-11.81; 3.01]	0.244
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.072**				
KESTREL: Role Difficulties				
Interaction test	p=0.836			
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 28: Adjusted Mean Change (SE)	4.61 (2.34)	7.34 (2.48)		
Week 52: Adjusted Mean Change (SE)	4.70 (2.58)	11.75 (2.60)	-7.06 [-14.21; 0.09]	0.053
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 28: Adjusted Mean Change (SE)	6.43 (2.67)	10.53 (2.57)		
Week 52: Adjusted Mean Change (SE)	9.58 (2.94)	10.49 (2.78)	-0.92 [-8.84; 7.01]	0.820
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 28: Adjusted Mean Change (SE)	8.85 (4.02)	10.50 (4.19)		
Week 52: Adjusted Mean Change (SE)	7.82 (4.42)	10.95 (4.40)	-3.13 [-15.38; 9.12]	0.616
KITE: Role Difficulties				
Interaction test	p=0.640			
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 28: Adjusted Mean Change (SE)	0.09 (4.18)	8.29 (4.69)		
Week 52: Adjusted Mean Change (SE)	16.39 (4.89)	8.16 (5.41)	8.23 [-6.08; 22.54]	0.259

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 28: Adjusted Mean Change (SE)	9.37 (1.83)	7.54 (1.82)		
Week 52: Adjusted Mean Change (SE)	12.42 (1.94)	9.23 (1.94)	3.19 [-2.20; 8.57]	0.245
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 28: Adjusted Mean Change (SE)	4.90 (4.96)	12.87 (4.18)		
Week 52: Adjusted Mean Change (SE)	7.64 (5.30)	5.46 (4.25)	2.18 [-11.12; 15.49]	0.747
Pooled Analysis: Role Difficulties				
Interaction test	p=0.868			
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 28: Adjusted Mean Change (SE)	6.05 (2.61)	6.79 (2.71)		
Week 52: Adjusted Mean Change (SE)	6.03 (2.79)	11.24 (2.78)	-5.22 [-12.91; 2.47]	0.183
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 28: Adjusted Mean Change (SE)	-1.44 (4.45)	8.81 (4.94)		
Week 52: Adjusted Mean Change (SE)	14.87 (5.17)	8.62 (5.67)	6.25 [-8.80; 21.30]	0.415
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 28: Adjusted Mean Change (SE)	7.94 (1.58)	8.77 (1.55)		
Week 52: Adjusted Mean Change (SE)	10.98 (1.69)	9.89 (1.65)	1.09 [-3.53; 5.71]	0.642

	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 28: Adjusted Mean Change (SE)	7.77 (3.13)	11.48 (2.94)		
Week 52: Adjusted Mean Change (SE)	8.18 (3.37)	8.08 (3.02)	0.10 [-8.79; 9.00]	0.982
Dependency				
Test of heterogeneity in main analysis: **p_H=0.029 ***				
KESTREL: Dependency				
Interaction test	p=0.471			
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 28: Adjusted Mean Change (SE)	4.86 (2.02)	7.52 (2.14)		
Week 52: Adjusted Mean Change (SE)	4.58 (2.10)	8.20 (2.12)	-3.63 [-9.46; 2.21]	0.222
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 28: Adjusted Mean Change (SE)	6.69 (2.29)	5.28 (2.21)		
Week 52: Adjusted Mean Change (SE)	8.92 (2.39)	9.58 (2.28)	-0.66 [-7.12; 5.79]	0.841
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 28: Adjusted Mean Change (SE)	5.43 (3.45)	8.89 (3.60)		
Week 52: Adjusted Mean Change (SE)	1.55 (3.60)	8.30 (3.59)	-6.75 [-16.72; 3.23]	0.184
KITE: Dependency				
Interaction test	p=0.588			
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 28: Adjusted Mean Change (SE)	5.56 (3.44)	0.71 (3.86)		
Week 52: Adjusted Mean Change (SE)	13.03 (4.02)	2.55 (4.45)	10.49 [-1.28; 22.25]	0.080

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 28: Adjusted Mean Change (SE)	5.95 (1.50)	3.74 (1.50)		
Week 52: Adjusted Mean Change (SE)	6.81 (1.60)	4.25 (1.61)	2.56 [-1.90; 7.01]	0.260
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 28: Adjusted Mean Change (SE)	3.78 (4.09)	3.51 (3.44)		
Week 52: Adjusted Mean Change (SE)	6.71 (4.40)	0.36 (3.53)	6.35 [-4.68; 17.39]	0.258
Pooled Analysis: Dependency				
Interaction test	p=0.543			
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 28: Adjusted Mean Change (SE)	5.26 (2.21)	6.75 (2.30)		
Week 52: Adjusted Mean Change (SE)	4.93 (2.32)	7.35 (2.32)	-2.42 [-8.83; 3.99]	0.458
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 28: Adjusted Mean Change (SE)	5.18 (3.76)	1.62 (4.17)		
Week 52: Adjusted Mean Change (SE)	12.88 (4.27)	3.36 (4.68)	9.53 [-2.92; 21.97]	0.133
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 28: Adjusted Mean Change (SE)	6.26 (1.33)	4.63 (1.31)		
Week 52: Adjusted Mean Change (SE)	7.51 (1.40)	6.49 (1.37)	1.02 [-2.82; 4.85]	0.603

	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)	78.12 (25.59)	83.48 (23.54)		
Week 52 Mean (SD)	83.33 (27.64)	87.76 (22.19)		
Week 28: Adjusted Mean Change (SE)	4.57 (2.64)	5.80 (2.48)		
Week 52: Adjusted Mean Change (SE)	3.31 (2.80)	4.02 (2.51)	-0.71 [-8.08; 6.67]	0.851
Driving				
Test of heterogeneity in main analysis: **p_H=0.778**				
KESTREL: Driving				
Interaction test	p=0.970			
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 28: Adjusted Mean Change (SE)	0.86 (1.99)	3.98 (2.07)		
Week 52: Adjusted Mean Change (SE)	2.78 (2.31)	5.59 (2.38)	-2.81 [-9.29; 3.67]	0.393
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 28: Adjusted Mean Change (SE)	3.97 (2.33)	9.15 (2.40)		
Week 52: Adjusted Mean Change (SE)	5.92 (2.66)	7.73 (2.80)	-1.81 [-9.35; 5.72]	0.636
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 28: Adjusted Mean Change (SE)	1.53 (3.50)	3.09 (3.63)		
Week 52: Adjusted Mean Change (SE)	0.99 (4.10)	3.60 (4.25)	-2.62 [-14.20; 8.96]	0.656
KITE: Driving				
Interaction test	p=0.261			
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 28: Adjusted Mean Change (SE)	2.08 (4.70)	7.39 (4.10)		
Week 52: Adjusted Mean Change (SE)	15.30 (3.98)	3.63 (3.90)	11.67 [0.72; 22.62]	0.037 *

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 28: Adjusted Mean Change (SE)	0.26 (1.64)	5.31 (1.78)		
Week 52: Adjusted Mean Change (SE)	4.18 (1.39)	6.04 (1.52)	-1.86 [-5.92; 2.21]	0.368
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 28: Adjusted Mean Change (SE)	2.52 (4.28)	4.07 (4.11)		
Week 52: Adjusted Mean Change (SE)	9.40 (3.60)	2.33 (3.33)	7.07 [-2.57; 16.71]	0.150
Pooled Analysis: Driving				
Interaction test	p=0.582			
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 28: Adjusted Mean Change (SE)	0.48 (2.23)	3.49 (2.31)		
Week 52: Adjusted Mean Change (SE)	2.74 (2.28)	5.17 (2.34)	-2.44 [-8.81; 3.94]	0.453
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 28: Adjusted Mean Change (SE)	2.32 (4.84)	8.11 (4.31)		
Week 52: Adjusted Mean Change (SE)	16.39 (5.01)	4.42 (4.91)	11.97 [-1.82; 25.75]	0.089
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 28: Adjusted Mean Change (SE)	1.68 (1.41)	7.04 (1.49)		
Week 52: Adjusted Mean Change (SE)	4.88 (1.44)	6.95 (1.54)	-2.07 [-6.21; 2.06]	0.324

	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 28: Adjusted Mean Change (SE)	1.75 (2.70)	3.32 (2.70)		
Week 52: Adjusted Mean Change (SE)	4.04 (2.80)	2.78 (2.75)	1.27 [-6.45; 8.98]	0.747
Color Vision				
Test of heterogeneity in main analysis: **p_H=0.691**				
KESTREL: Color Vision				
Interaction test	p=0.603			
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 28: Adjusted Mean Change (SE)	2.23 (1.22)	-0.03 (1.29)		
Week 52: Adjusted Mean Change (SE)	1.24 (1.26)	1.80 (1.29)	-0.55 [-4.09; 2.98]	0.759
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 28: Adjusted Mean Change (SE)	2.14 (1.38)	4.57 (1.32)		
Week 52: Adjusted Mean Change (SE)	3.83 (1.44)	2.76 (1.37)	1.07 [-2.84; 4.97]	0.592
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 28: Adjusted Mean Change (SE)	1.64 (2.07)	-0.40 (2.20)		
Week 52: Adjusted Mean Change (SE)	1.29 (2.16)	-0.89 (2.19)	2.18 [-3.85; 8.22]	0.477
KITE: Color Vision				
Interaction test	p=0.054			
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 28: Adjusted Mean Change (SE)	5.41 (2.18)	1.49 (2.44)		
Week 52: Adjusted Mean Change (SE)	7.74 (2.13)	-1.76 (2.35)	9.50 [3.27; 15.72]	0.003 *

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 28: Adjusted Mean Change (SE)	3.35 (0.95)	4.36 (0.96)		
Week 52: Adjusted Mean Change (SE)	5.87 (0.84)	4.66 (0.85)	1.21 [-1.14; 3.56]	0.312
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 28: Adjusted Mean Change (SE)	2.80 (2.59)	5.53 (2.18)		
Week 52: Adjusted Mean Change (SE)	2.56 (2.30)	0.99 (1.84)	1.58 [-4.19; 7.34]	0.591
Pooled Analysis: Color Vision				
Interaction test	p=0.139			
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 28: Adjusted Mean Change (SE)	3.36 (1.35)	1.03 (1.42)		
Week 52: Adjusted Mean Change (SE)	2.40 (1.30)	2.93 (1.31)	-0.53 [-4.15; 3.09]	0.773
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 28: Adjusted Mean Change (SE)	3.98 (2.32)	0.29 (2.58)		
Week 52: Adjusted Mean Change (SE)	6.41 (2.41)	-2.91 (2.63)	9.32 [2.33; 16.32]	0.009 *
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 28: Adjusted Mean Change (SE)	2.62 (0.83)	4.15 (0.81)		
Week 52: Adjusted Mean Change (SE)	4.79 (0.79)	3.68 (0.77)	1.11 [-1.05; 3.26]	0.313

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 28: Adjusted Mean Change (SE)	2.55 (1.64)	2.31 (1.56)		
Week 52: Adjusted Mean Change (SE)	2.25 (1.56)	-0.22 (1.41)	2.48 [-1.64; 6.60]	0.238
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.021 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.577			
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 28: Adjusted Mean Change (SE)	4.03 (1.97)	7.53 (2.08)		
Week 52: Adjusted Mean Change (SE)	4.66 (2.02)	9.99 (2.04)	-5.33 [-10.94; 0.29]	0.063
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 28: Adjusted Mean Change (SE)	2.64 (2.23)	8.11 (2.15)		
Week 52: Adjusted Mean Change (SE)	8.00 (2.30)	4.97 (2.18)	3.03 [-3.14; 9.21]	0.335
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 28: Adjusted Mean Change (SE)	-0.34 (3.41)	7.74 (3.53)		
Week 52: Adjusted Mean Change (SE)	3.92 (3.45)	5.72 (3.45)	-1.80 [-11.38; 7.77]	0.711
KITE: Peripheral Vision				
Interaction test	p=0.964			
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 28: Adjusted Mean Change (SE)	3.68 (3.18)	3.34 (3.57)		
Week 52: Adjusted Mean Change (SE)	8.82 (3.71)	4.30 (4.11)	4.51 [-6.37; 15.40]	0.415

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 28: Adjusted Mean Change (SE)	4.88 (1.39)	4.51 (1.40)		
Week 52: Adjusted Mean Change (SE)	6.45 (1.47)	4.31 (1.48)	2.14 [-1.95; 6.24]	0.304
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 28: Adjusted Mean Change (SE)	5.51 (3.77)	6.09 (3.19)		
Week 52: Adjusted Mean Change (SE)	4.19 (4.02)	0.03 (3.23)	4.17 [-5.92; 14.25]	0.417
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.775			
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 28: Adjusted Mean Change (SE)	5.07 (2.09)	7.30 (2.16)		
Week 52: Adjusted Mean Change (SE)	5.60 (2.16)	9.89 (2.16)	-4.29 [-10.27; 1.69]	0.160
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 28: Adjusted Mean Change (SE)	2.38 (3.55)	3.49 (3.95)		
Week 52: Adjusted Mean Change (SE)	7.54 (4.03)	4.23 (4.42)	3.31 [-8.44; 15.05]	0.581
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 28: Adjusted Mean Change (SE)	3.68 (1.26)	5.99 (1.24)		
Week 52: Adjusted Mean Change (SE)	6.49 (1.31)	4.74 (1.28)	1.75 [-1.84; 5.33]	0.339

	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 28: Adjusted Mean Change (SE)	1.91 (2.53)	7.18 (2.36)		
Week 52: Adjusted Mean Change (SE)	4.12 (2.62)	3.22 (2.34)	0.90 [-5.99; 7.80]	0.797
General Health				
Test of heterogeneity in main analysis: **p_H=0.700**				
KESTREL: General Health				
Interaction test	p=0.321			
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 28: Adjusted Mean Change (SE)	2.02 (2.00)	4.13 (2.12)		
Week 52: Adjusted Mean Change (SE)	11.05 (2.46)	7.59 (2.45)	3.46 [-3.35; 10.28]	0.318
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 28: Adjusted Mean Change (SE)	8.34 (2.27)	4.38 (2.18)		
Week 52: Adjusted Mean Change (SE)	8.43 (2.77)	3.38 (2.63)	5.05 [-2.46; 12.55]	0.187
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 28: Adjusted Mean Change (SE)	2.15 (3.43)	6.92 (3.60)		
Week 52: Adjusted Mean Change (SE)	0.79 (4.19)	2.27 (4.17)	-1.47 [-13.04; 10.09]	0.802
KITE: General Health				
Interaction test	p=0.436			
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 28: Adjusted Mean Change (SE)	2.75 (3.67)	4.92 (4.12)		
Week 52: Adjusted Mean Change (SE)	6.22 (4.76)	-0.71 (5.25)	6.93 [-7.01; 20.87]	0.329

	Treatment Groups		Comparison	
VFQ by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 28: Adjusted Mean Change (SE)	3.13 (1.60)	3.28 (1.61)		
Week 52: Adjusted Mean Change (SE)	6.43 (1.87)	5.20 (1.87)	1.23 [-3.96; 6.42]	0.642
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 28: Adjusted Mean Change (SE)	8.29 (4.36)	9.80 (3.71)		
Week 52: Adjusted Mean Change (SE)	-2.52 (5.12)	7.28 (4.11)	-9.80 [-22.62; 3.01]	0.133
Pooled Analysis: General Health				
Interaction test	p=0.212			
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 28: Adjusted Mean Change (SE)	0.49 (2.26)	4.87 (2.34)		
Week 52: Adjusted Mean Change (SE)	9.47 (2.63)	8.37 (2.60)	1.10 [-6.15; 8.35]	0.766
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 28: Adjusted Mean Change (SE)	3.92 (3.85)	4.28 (4.27)		
Week 52: Adjusted Mean Change (SE)	7.50 (4.96)	-0.92 (5.44)	8.42 [-6.03; 22.87]	0.253
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 28: Adjusted Mean Change (SE)	5.19 (1.36)	3.50 (1.34)		
Week 52: Adjusted Mean Change (SE)	7.42 (1.60)	4.32 (1.57)	3.09 [-1.31; 7.49]	0.168

	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)	40.63 (26.61)	43.42 (28.55)		
Week 52 Mean (SD)	41.03 (23.98)	48.98 (27.46)		
Week 28: Adjusted Mean Change (SE)	4.45 (2.70)	8.79 (2.55)		
Week 52: Adjusted Mean Change (SE)	-0.47 (3.23)	5.21 (2.88)	-5.68 [-14.18; 2.82]	0.190

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 52

	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=0.071**				
KESTREL: Composite Score				
Interaction test	p=0.491			
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 28: Adjusted Mean Change (SE)	7.78 (3.18)	1.98 (4.57)		
Week 52: Adjusted Mean Change (SE)	4.87 (3.54)	7.08 (4.29)	-2.21 [-13.16; 8.73]	0.691
Type 2				
N'/ N	176 / 177	181 / 181		
Baseline Mean (SD)	76.41 (17.89)	76.77 (14.76)		
Week 52 Mean (SD)	85.19 (13.85)	85.18 (12.26)		
Week 28: Adjusted Mean Change (SE)	5.67 (0.82)	7.89 (0.82)		
Week 52: Adjusted Mean Change (SE)	7.29 (0.86)	8.38 (0.84)	-1.09 [-3.45; 1.27]	0.365
KITE: Composite Score				
Interaction test	p=0.098			
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 28: Adjusted Mean Change (SE)	5.85 (2.29)	11.44 (3.73)		
Week 52: Adjusted Mean Change (SE)	6.96 (2.41)	12.01 (3.86)	-5.05 [-13.99; 3.89]	0.267
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 28: Adjusted Mean Change (SE)	5.86 (0.81)	5.81 (0.78)		
Week 52: Adjusted Mean Change (SE)	9.18 (0.89)	6.28 (0.84)	2.91 [0.51; 5.30]	0.018 *

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Composite Score				
Interaction test	p=0.460			
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 28: Adjusted Mean Change (SE)	6.52 (1.91)	7.73 (2.95)		
Week 52: Adjusted Mean Change (SE)	6.38 (2.02)	10.03 (2.89)	-3.65 [-10.57; 3.27]	0.300
Type 2				
N'/ N	335 / 337	355 / 355		
Baseline Mean (SD)	76.78 (16.68)	76.49 (16.31)		
Week 52 Mean (SD)	85.61 (13.65)	84.16 (14.13)		
Week 28: Adjusted Mean Change (SE)	5.83 (0.59)	6.83 (0.57)		
Week 52: Adjusted Mean Change (SE)	8.22 (0.62)	7.33 (0.59)	0.89 [-0.80; 2.57]	0.303
General Vision				
Test of heterogeneity in main analysis: **p_H=0.986**				
KESTREL: General Vision				
Interaction test	p=0.335			
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 28: Adjusted Mean Change (SE)	10.53 (3.87)	11.20 (5.66)		
Week 52: Adjusted Mean Change (SE)	6.97 (4.39)	15.20 (5.18)	-8.23 [-21.59; 5.13]	0.226
Type 2				
N'/ N	176 / 177	181 / 181		
Baseline Mean (SD)	61.14 (17.59)	60.11 (14.68)		
Week 52 Mean (SD)	73.19 (14.31)	70.92 (12.99)		
Week 28: Adjusted Mean Change (SE)	11.38 (1.00)	10.61 (1.00)		
Week 52: Adjusted Mean Change (SE)	11.91 (1.06)	10.48 (1.02)	1.43 [-1.46; 4.32]	0.332

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Vision				
Interaction test	p=0.535			
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 28: Adjusted Mean Change (SE)	10.03 (3.06)	17.11 (5.02)		
Week 52: Adjusted Mean Change (SE)	13.07 (3.30)	11.39 (5.30)	1.67 [-10.60; 13.95]	0.789
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 28: Adjusted Mean Change (SE)	9.36 (1.09)	9.33 (1.04)		
Week 52: Adjusted Mean Change (SE)	11.51 (1.23)	10.26 (1.15)	1.25 [-2.06; 4.57]	0.458
Pooled Analysis: General Vision				
Interaction test	p=0.250			
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 28: Adjusted Mean Change (SE)	10.25 (2.41)	15.29 (3.76)		
Week 52: Adjusted Mean Change (SE)	11.41 (2.61)	13.58 (3.72)	-2.17 [-11.09; 6.76]	0.633
Type 2				
N'/ N	335 / 337	355 / 355		
Baseline Mean (SD)	61.49 (16.78)	59.77 (16.60)		
Week 52 Mean (SD)	72.81 (14.69)	70.58 (15.19)		
Week 28: Adjusted Mean Change (SE)	10.42 (0.74)	9.96 (0.73)		
Week 52: Adjusted Mean Change (SE)	11.69 (0.81)	10.36 (0.77)	1.33 [-0.86; 3.53]	0.234

	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=0.492**				
KESTREL: Ocular Pain				
Interaction test	p=0.289			
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 28: Adjusted Mean Change (SE)	7.89 (5.25)	-0.09 (7.62)		
Week 52: Adjusted Mean Change (SE)	7.20 (5.18)	0.87 (6.16)	6.32 [-9.50; 22.15]	0.432
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 28: Adjusted Mean Change (SE)	2.40 (1.36)	4.49 (1.35)		
Week 52: Adjusted Mean Change (SE)	5.06 (1.25)	4.50 (1.21)	0.56 [-2.86; 3.98]	0.747
KITE: Ocular Pain				
Interaction test	p=0.911			
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 28: Adjusted Mean Change (SE)	5.42 (3.52)	9.20 (5.76)		
Week 52: Adjusted Mean Change (SE)	4.45 (3.54)	0.27 (5.64)	4.18 [-8.92; 17.27]	0.531
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 28: Adjusted Mean Change (SE)	4.56 (1.26)	3.79 (1.20)		
Week 52: Adjusted Mean Change (SE)	5.14 (1.32)	4.23 (1.24)	0.91 [-2.66; 4.47]	0.617

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Ocular Pain				
Interaction test	p=0.566			
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 28: Adjusted Mean Change (SE)	5.85 (3.01)	5.00 (4.70)		
Week 52: Adjusted Mean Change (SE)	4.94 (2.95)	0.32 (4.18)	4.62 [-5.43; 14.66]	0.367
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 28: Adjusted Mean Change (SE)	3.50 (0.93)	4.12 (0.91)		
Week 52: Adjusted Mean Change (SE)	5.18 (0.91)	4.37 (0.87)	0.80 [-1.67; 3.28]	0.524
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.456**				
KESTREL: Near Activities				
Interaction test	p=0.673			
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 28: Adjusted Mean Change (SE)	12.84 (5.41)	15.75 (7.88)		
Week 52: Adjusted Mean Change (SE)	12.38 (6.42)	18.67 (7.61)	-6.29 [-25.88; 13.30]	0.528
Type 2				
N'/ N	176 / 177	181 / 181		
Baseline Mean (SD)	63.49 (26.59)	65.79 (21.87)		
Week 52 Mean (SD)	79.34 (21.28)	78.56 (20.17)		
Week 28: Adjusted Mean Change (SE)	12.38 (1.40)	14.46 (1.40)		
Week 52: Adjusted Mean Change (SE)	13.51 (1.55)	13.57 (1.50)	-0.05 [-4.29; 4.18]	0.981

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Near Activities				
Interaction test	p=0.163			
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 28: Adjusted Mean Change (SE)	7.24 (4.10)	19.13 (6.70)		
Week 52: Adjusted Mean Change (SE)	11.16 (4.05)	16.75 (6.48)	-5.60 [-20.60; 9.41]	0.464
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 28: Adjusted Mean Change (SE)	6.41 (1.46)	5.52 (1.39)		
Week 52: Adjusted Mean Change (SE)	10.25 (1.49)	8.89 (1.41)	1.36 [-2.67; 5.39]	0.507
Pooled Analysis: Near Activities				
Interaction test	p=0.176			
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 28: Adjusted Mean Change (SE)	10.28 (3.32)	18.92 (5.15)		
Week 52: Adjusted Mean Change (SE)	12.89 (3.52)	18.60 (5.02)	-5.71 [-17.75; 6.32]	0.352
Type 2				
N'/ N	334 / 337	355 / 355		
Baseline Mean (SD)	66.19 (24.94)	67.38 (22.99)		
Week 52 Mean (SD)	79.26 (21.01)	78.29 (21.21)		
Week 28: Adjusted Mean Change (SE)	9.60 (1.02)	9.93 (1.00)		
Week 52: Adjusted Mean Change (SE)	11.90 (1.09)	11.17 (1.04)	0.73 [-2.22; 3.68]	0.629

	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=0.136**				
KESTREL: Distance Activities				
Interaction test	p=0.841			
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 28: Adjusted Mean Change (SE)	6.67 (4.80)	8.06 (6.91)		
Week 52: Adjusted Mean Change (SE)	4.15 (4.85)	7.45 (5.84)	-3.30 [-18.23; 11.62]	0.664
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 28: Adjusted Mean Change (SE)	7.50 (1.24)	9.00 (1.23)		
Week 52: Adjusted Mean Change (SE)	9.39 (1.18)	9.72 (1.14)	-0.32 [-3.54; 2.90]	0.844
KITE: Distance Activities				
Interaction test	p=0.038 *			
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 28: Adjusted Mean Change (SE)	3.26 (3.56)	14.13 (5.81)		
Week 52: Adjusted Mean Change (SE)	7.79 (3.30)	15.32 (5.26)	-7.53 [-19.70; 4.65]	0.225
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 28: Adjusted Mean Change (SE)	6.70 (1.27)	5.13 (1.21)		
Week 52: Adjusted Mean Change (SE)	11.88 (1.22)	7.87 (1.15)	4.01 [0.72; 7.30]	0.017 *

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Distance Activities				
Interaction test	p=0.101			
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 28: Adjusted Mean Change (SE)	4.46 (2.90)	11.86 (4.50)		
Week 52: Adjusted Mean Change (SE)	6.66 (2.76)	12.19 (3.93)	-5.52 [-14.95; 3.90]	0.250
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 28: Adjusted Mean Change (SE)	7.19 (0.89)	7.07 (0.87)		
Week 52: Adjusted Mean Change (SE)	10.61 (0.85)	8.79 (0.81)	1.82 [-0.49; 4.13]	0.122
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.037 ***				
KESTREL: Social Functioning				
Interaction test	p=0.552			
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 28: Adjusted Mean Change (SE)	2.32 (3.63)	-3.31 (5.33)		
Week 52: Adjusted Mean Change (SE)	-1.70 (4.42)	1.44 (5.17)	-3.15 [-16.53; 10.23]	0.644
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 28: Adjusted Mean Change (SE)	1.59 (0.94)	4.27 (0.94)		
Week 52: Adjusted Mean Change (SE)	2.92 (1.06)	4.25 (1.03)	-1.34 [-4.24; 1.56]	0.364

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Social Functioning				
Interaction test	p=0.407			
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 28: Adjusted Mean Change (SE)	6.29 (3.14)	10.16 (5.15)		
Week 52: Adjusted Mean Change (SE)	9.16 (2.62)	10.16 (4.17)	-0.99 [-10.68; 8.69]	0.840
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 28: Adjusted Mean Change (SE)	3.51 (1.12)	3.71 (1.07)		
Week 52: Adjusted Mean Change (SE)	7.22 (0.98)	4.19 (0.92)	3.02 [0.39; 5.66]	0.025 *
Pooled Analysis: Social Functioning				
Interaction test	p=0.831			
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 28: Adjusted Mean Change (SE)	4.04 (2.37)	4.49 (3.71)		
Week 52: Adjusted Mean Change (SE)	4.70 (2.35)	6.12 (3.32)	-1.43 [-9.42; 6.57]	0.726
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 28: Adjusted Mean Change (SE)	2.64 (0.73)	3.94 (0.71)		
Week 52: Adjusted Mean Change (SE)	5.12 (0.73)	4.18 (0.69)	0.94 [-1.04; 2.91]	0.352

	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=0.300**				
KESTREL: Mental Health				
Interaction test	p=0.057			
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 28: Adjusted Mean Change (SE)	17.01 (5.05)	-7.53 (7.38)		
Week 52: Adjusted Mean Change (SE)	7.82 (5.69)	7.26 (6.72)	0.55 [-16.76; 17.86]	0.950
Type 2				
N'/ N	176 / 177	181 / 181		
Baseline Mean (SD)	65.66 (25.37)	68.47 (23.07)		
Week 52 Mean (SD)	78.72 (19.78)	78.95 (17.93)		
Week 28: Adjusted Mean Change (SE)	6.71 (1.31)	9.59 (1.30)		
Week 52: Adjusted Mean Change (SE)	10.55 (1.37)	11.31 (1.32)	-0.76 [-4.51; 2.98]	0.688
KITE: Mental Health				
Interaction test	p=0.339			
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 28: Adjusted Mean Change (SE)	9.91 (3.86)	11.80 (6.30)		
Week 52: Adjusted Mean Change (SE)	10.71 (4.50)	18.94 (7.21)	-8.23 [-24.93; 8.47]	0.333
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 28: Adjusted Mean Change (SE)	8.57 (1.37)	9.22 (1.31)		
Week 52: Adjusted Mean Change (SE)	13.35 (1.66)	9.14 (1.57)	4.21 [-0.29; 8.71]	0.067

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Mental Health				
Interaction test	p=0.662			
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 28: Adjusted Mean Change (SE)	12.44 (3.08)	3.89 (4.79)		
Week 52: Adjusted Mean Change (SE)	9.89 (3.47)	13.87 (4.94)	-3.98 [-15.82; 7.86]	0.510
Type 2				
N'/ N	335 / 337	355 / 355		
Baseline Mean (SD)	66.92 (23.86)	66.92 (24.71)		
Week 52 Mean (SD)	79.92 (20.55)	77.50 (21.02)		
Week 28: Adjusted Mean Change (SE)	7.69 (0.95)	9.35 (0.93)		
Week 52: Adjusted Mean Change (SE)	11.93 (1.07)	10.19 (1.02)	1.74 [-1.17; 4.65]	0.240
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.072**				
KESTREL: Role Difficulties				
Interaction test	p=0.667			
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 28: Adjusted Mean Change (SE)	13.80 (6.38)	8.89 (9.30)		
Week 52: Adjusted Mean Change (SE)	7.78 (7.54)	12.15 (8.92)	-4.37 [-27.35; 18.61]	0.709
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 28: Adjusted Mean Change (SE)	5.43 (1.65)	9.13 (1.65)		
Week 52: Adjusted Mean Change (SE)	6.91 (1.81)	11.10 (1.76)	-4.19 [-9.16; 0.78]	0.098

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Role Difficulties				
Interaction test	p=0.134			
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 28: Adjusted Mean Change (SE)	5.93 (4.73)	14.20 (7.74)		
Week 52: Adjusted Mean Change (SE)	6.75 (4.89)	17.77 (7.81)	-11.02 [-29.11; 7.07]	0.231
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 28: Adjusted Mean Change (SE)	7.77 (1.68)	8.14 (1.61)		
Week 52: Adjusted Mean Change (SE)	13.09 (1.81)	8.07 (1.71)	5.02 [0.12; 9.92]	0.045 *
Pooled Analysis: Role Difficulties				
Interaction test	p=0.416			
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 28: Adjusted Mean Change (SE)	8.77 (3.84)	12.33 (5.98)		
Week 52: Adjusted Mean Change (SE)	7.21 (4.14)	15.51 (5.89)	-8.30 [-22.44; 5.83]	0.249
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 28: Adjusted Mean Change (SE)	6.61 (1.18)	8.61 (1.16)		
Week 52: Adjusted Mean Change (SE)	9.84 (1.28)	9.61 (1.22)	0.23 [-3.25; 3.70]	0.898

	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=0.029 ***				
KESTREL: Dependency				
Interaction test	p=0.126			
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 28: Adjusted Mean Change (SE)	8.51 (5.46)	-11.72 (7.95)		
Week 52: Adjusted Mean Change (SE)	2.69 (6.16)	2.67 (7.31)	0.02 [-18.80; 18.84]	0.998
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 28: Adjusted Mean Change (SE)	5.42 (1.41)	7.39 (1.41)		
Week 52: Adjusted Mean Change (SE)	5.85 (1.48)	8.94 (1.44)	-3.10 [-7.16; 0.97]	0.135
KITE: Dependency				
Interaction test	p=0.531			
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 28: Adjusted Mean Change (SE)	8.14 (3.87)	8.20 (6.32)		
Week 52: Adjusted Mean Change (SE)	8.61 (4.06)	10.58 (6.50)	-1.97 [-17.02; 13.09]	0.797
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 28: Adjusted Mean Change (SE)	5.35 (1.38)	3.15 (1.31)		
Week 52: Adjusted Mean Change (SE)	7.40 (1.50)	3.11 (1.41)	4.29 [0.23; 8.34]	0.038 *

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Dependency				
Interaction test	p=0.557			
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 28: Adjusted Mean Change (SE)	8.43 (3.23)	0.67 (5.02)		
Week 52: Adjusted Mean Change (SE)	6.94 (3.44)	7.74 (4.90)	-0.80 [-12.57; 10.97]	0.894
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 28: Adjusted Mean Change (SE)	5.45 (1.00)	5.27 (0.97)		
Week 52: Adjusted Mean Change (SE)	6.62 (1.06)	6.05 (1.02)	0.57 [-2.32; 3.45]	0.699
Driving				
Test of heterogeneity in main analysis: **p_H=0.778**				
KESTREL: Driving				
Interaction test	p=0.571			
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 28: Adjusted Mean Change (SE)	-0.50 (5.47)	6.75 (8.37)		
Week 52: Adjusted Mean Change (SE)	2.70 (6.84)	12.31 (9.37)	-9.61 [-32.44; 13.23]	0.408
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 28: Adjusted Mean Change (SE)	2.24 (1.43)	5.71 (1.45)		
Week 52: Adjusted Mean Change (SE)	3.69 (1.64)	5.90 (1.68)	-2.22 [-6.84; 2.40]	0.345

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Driving				
Interaction test	p=0.279			
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 28: Adjusted Mean Change (SE)	-0.24 (3.94)	6.46 (6.32)		
Week 52: Adjusted Mean Change (SE)	3.61 (3.22)	13.13 (5.17)	-9.52 [-21.58; 2.54]	0.121
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 28: Adjusted Mean Change (SE)	0.87 (1.57)	5.39 (1.56)		
Week 52: Adjusted Mean Change (SE)	6.25 (1.35)	4.69 (1.35)	1.55 [-2.21; 5.32]	0.416
Pooled Analysis: Driving				
Interaction test	p=0.217			
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 28: Adjusted Mean Change (SE)	-0.47 (3.22)	7.06 (5.05)		
Week 52: Adjusted Mean Change (SE)	2.96 (3.31)	13.31 (5.00)	-10.35 [-22.14; 1.45]	0.085
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 28: Adjusted Mean Change (SE)	1.63 (1.05)	5.58 (1.06)		
Week 52: Adjusted Mean Change (SE)	4.91 (1.08)	5.37 (1.09)	-0.47 [-3.49; 2.55]	0.761

	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=0.691**				
KESTREL: Color Vision				
Interaction test	p=0.827			
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 28: Adjusted Mean Change (SE)	0.85 (3.32)	-5.36 (4.86)		
Week 52: Adjusted Mean Change (SE)	-3.08 (3.69)	0.20 (4.35)	-3.28 [-14.50; 7.95]	0.566
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 28: Adjusted Mean Change (SE)	2.18 (0.87)	2.05 (0.86)		
Week 52: Adjusted Mean Change (SE)	2.51 (0.89)	1.83 (0.87)	0.68 [-1.77; 3.13]	0.587
KITE: Color Vision				
Interaction test	p=0.509			
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 28: Adjusted Mean Change (SE)	6.92 (2.45)	7.89 (4.00)		
Week 52: Adjusted Mean Change (SE)	5.63 (2.15)	7.89 (3.43)	-2.26 [-10.22; 5.69]	0.576
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 28: Adjusted Mean Change (SE)	3.17 (0.88)	4.04 (0.84)		
Week 52: Adjusted Mean Change (SE)	5.79 (0.80)	3.21 (0.76)	2.57 [0.40; 4.75]	0.020 *

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Color Vision				
Interaction test	p=0.901			
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 28: Adjusted Mean Change (SE)	4.30 (2.01)	1.93 (3.15)		
Week 52: Adjusted Mean Change (SE)	2.32 (1.93)	4.06 (2.74)	-1.74 [-8.32; 4.84]	0.603
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 28: Adjusted Mean Change (SE)	2.75 (0.62)	3.01 (0.61)		
Week 52: Adjusted Mean Change (SE)	4.14 (0.60)	2.50 (0.58)	1.63 [-0.00; 3.27]	0.050
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.021 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.968			
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 28: Adjusted Mean Change (SE)	4.47 (5.35)	6.80 (7.85)		
Week 52: Adjusted Mean Change (SE)	2.86 (5.96)	7.68 (6.96)	-4.82 [-22.83; 13.20]	0.599
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 28: Adjusted Mean Change (SE)	2.71 (1.39)	7.85 (1.38)		
Week 52: Adjusted Mean Change (SE)	5.95 (1.43)	7.34 (1.38)	-1.39 [-5.31; 2.53]	0.486

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Peripheral Vision				
Interaction test	p=0.023 *			
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 28: Adjusted Mean Change (SE)	4.10 (3.58)	11.80 (5.83)		
Week 52: Adjusted Mean Change (SE)	0.61 (3.68)	15.37 (5.86)	-14.76 [-28.38; -1.15]	0.034 *
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 28: Adjusted Mean Change (SE)	4.86 (1.27)	4.28 (1.22)		
Week 52: Adjusted Mean Change (SE)	7.33 (1.37)	3.03 (1.29)	4.30 [0.60; 8.00]	0.023 *
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.137			
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 28: Adjusted Mean Change (SE)	4.13 (3.07)	9.50 (4.79)		
Week 52: Adjusted Mean Change (SE)	1.24 (3.22)	11.52 (4.55)	-10.27 [-21.22; 0.67]	0.066
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 28: Adjusted Mean Change (SE)	3.64 (0.95)	6.21 (0.92)		
Week 52: Adjusted Mean Change (SE)	6.49 (0.99)	5.39 (0.95)	1.10 [-1.60; 3.80]	0.425

	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=0.700**				
KESTREL: General Health				
Interaction test	p=0.569			
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 28: Adjusted Mean Change (SE)	2.94 (5.50)	-6.49 (8.01)		
Week 52: Adjusted Mean Change (SE)	5.32 (7.26)	2.16 (8.51)	3.16 [-18.83; 25.15]	0.778
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 28: Adjusted Mean Change (SE)	4.43 (1.42)	5.07 (1.42)		
Week 52: Adjusted Mean Change (SE)	8.53 (1.74)	5.27 (1.68)	3.27 [-1.51; 8.05]	0.179
KITE: General Health				
Interaction test	p=0.852			
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 28: Adjusted Mean Change (SE)	4.16 (4.13)	11.57 (6.76)		
Week 52: Adjusted Mean Change (SE)	12.00 (4.71)	8.00 (7.52)	4.00 [-13.45; 21.45]	0.653
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 28: Adjusted Mean Change (SE)	3.55 (1.48)	4.09 (1.41)		
Week 52: Adjusted Mean Change (SE)	4.53 (1.76)	4.82 (1.66)	-0.29 [-5.05; 4.47]	0.905

	Treatment Groups		Comparison	
VFQ by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: General Health				
Interaction test	p=0.756			
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 28: Adjusted Mean Change (SE)	3.49 (3.33)	3.92 (5.20)		
Week 52: Adjusted Mean Change (SE)	9.73 (4.00)	5.25 (5.65)	4.48 [-9.11; 18.07]	0.518
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 28: Adjusted Mean Change (SE)	3.92 (1.03)	4.68 (1.00)		
Week 52: Adjusted Mean Change (SE)	6.56 (1.24)	5.15 (1.18)	1.41 [-1.95; 4.77]	0.410

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 52

	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=0.071**				
KESTREL: Composite Score				
Interaction test	p=0.031 *			
< 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 28: Adjusted Mean Change (SE)	7.12 (1.25)	7.20 (1.06)		
Week 52: Adjusted Mean Change (SE)	9.27 (1.29)	7.58 (1.07)	1.68 [-1.60; 4.97]	0.315
≥ 7.5 %				
N'/ N	111 / 112	80 / 80		
Baseline Mean (SD)	76.15 (17.28)	77.63 (14.72)		
Week 52 Mean (SD)	83.39 (15.21)	86.22 (12.44)		
Week 28: Adjusted Mean Change (SE)	4.80 (1.04)	8.35 (1.23)		
Week 52: Adjusted Mean Change (SE)	5.59 (1.09)	9.35 (1.27)	-3.76 [-7.05; -0.48]	0.025 *
KITE: Composite Score				
Interaction test	p=0.602			
< 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 28: Adjusted Mean Change (SE)	6.89 (1.14)	6.49 (1.05)		
Week 52: Adjusted Mean Change (SE)	8.54 (1.24)	7.64 (1.13)	0.90 [-2.41; 4.20]	0.594
≥ 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 28: Adjusted Mean Change (SE)	5.01 (1.03)	5.54 (1.11)		
Week 52: Adjusted Mean Change (SE)	9.18 (1.12)	5.28 (1.20)	3.91 [0.69; 7.12]	0.017 *

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Composite Score				
Interaction test	p=0.212			
< 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 28: Adjusted Mean Change (SE)	7.03 (0.85)	6.77 (0.75)		
Week 52: Adjusted Mean Change (SE)	8.91 (0.90)	7.51 (0.78)	1.40 [-0.95; 3.74]	0.242
≥ 7.5 %				
N'/ N	208 / 209	165 / 165		
Baseline Mean (SD)	76.94 (16.28)	78.38 (15.31)		
Week 52 Mean (SD)	84.95 (14.34)	85.22 (13.97)		
Week 28: Adjusted Mean Change (SE)	4.98 (0.74)	6.97 (0.84)		
Week 52: Adjusted Mean Change (SE)	7.36 (0.79)	7.33 (0.88)	0.03 [-2.28; 2.34]	0.981
General Vision				
Test of heterogeneity in main analysis: **p_H=0.986**				
KESTREL: General Vision				
Interaction test	p=0.716			
< 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 28: Adjusted Mean Change (SE)	12.38 (1.53)	10.26 (1.30)		
Week 52: Adjusted Mean Change (SE)	12.01 (1.59)	11.27 (1.31)	0.73 [-3.32; 4.79]	0.721
≥ 7.5 %				
N'/ N	111 / 112	80 / 80		
Baseline Mean (SD)	61.08 (16.59)	60.25 (15.42)		
Week 52 Mean (SD)	72.09 (15.42)	69.85 (13.29)		
Week 28: Adjusted Mean Change (SE)	10.53 (1.26)	11.04 (1.51)		
Week 52: Adjusted Mean Change (SE)	11.31 (1.35)	9.66 (1.56)	1.64 [-2.42; 5.71]	0.427

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Vision				
Interaction test	p=0.688			
< 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 28: Adjusted Mean Change (SE)	10.91 (1.53)	9.36 (1.41)		
Week 52: Adjusted Mean Change (SE)	11.36 (1.72)	10.60 (1.56)	0.76 [-3.80; 5.32]	0.742
≥ 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 28: Adjusted Mean Change (SE)	8.22 (1.39)	9.99 (1.50)		
Week 52: Adjusted Mean Change (SE)	11.95 (1.54)	9.96 (1.65)	1.99 [-2.44; 6.42]	0.378
Pooled Analysis: General Vision				
Interaction test	p=0.562			
< 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 28: Adjusted Mean Change (SE)	11.50 (1.09)	9.67 (0.96)		
Week 52: Adjusted Mean Change (SE)	11.52 (1.17)	10.79 (1.01)	0.73 [-2.31; 3.78]	0.637
≥ 7.5 %				
N'/ N	208 / 209	165 / 165		
Baseline Mean (SD)	62.21 (16.71)	62.18 (16.53)		
Week 52 Mean (SD)	72.89 (14.94)	71.18 (15.73)		
Week 28: Adjusted Mean Change (SE)	9.52 (0.94)	10.70 (1.07)		
Week 52: Adjusted Mean Change (SE)	11.73 (1.02)	10.06 (1.14)	1.67 [-1.34; 4.67]	0.276

	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=0.492**				
KESTREL: Ocular Pain				
Interaction test	p=0.004 *			
< 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 28: Adjusted Mean Change (SE)	6.50 (2.04)	2.15 (1.73)		
Week 52: Adjusted Mean Change (SE)	8.00 (1.86)	3.56 (1.54)	4.44 [-0.31; 9.19]	0.067
≥ 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 28: Adjusted Mean Change (SE)	0.29 (1.69)	7.19 (2.02)		
Week 52: Adjusted Mean Change (SE)	3.21 (1.59)	5.33 (1.83)	-2.13 [-6.90; 2.65]	0.382
KITE: Ocular Pain				
Interaction test	p=0.783			
< 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 28: Adjusted Mean Change (SE)	6.25 (1.76)	3.97 (1.61)		
Week 52: Adjusted Mean Change (SE)	3.93 (1.85)	5.23 (1.67)	-1.30 [-6.19; 3.59]	0.602
≥ 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 28: Adjusted Mean Change (SE)	3.35 (1.59)	4.07 (1.71)		
Week 52: Adjusted Mean Change (SE)	5.94 (1.65)	2.71 (1.76)	3.23 [-1.52; 7.98]	0.182

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Ocular Pain				
Interaction test	p=0.045 *			
< 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 28: Adjusted Mean Change (SE)	6.42 (1.35)	2.99 (1.19)		
Week 52: Adjusted Mean Change (SE)	5.98 (1.32)	4.31 (1.14)	1.66 [-1.76; 5.09]	0.340
≥ 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 28: Adjusted Mean Change (SE)	1.74 (1.17)	5.51 (1.32)		
Week 52: Adjusted Mean Change (SE)	4.54 (1.15)	4.00 (1.28)	0.54 [-2.84; 3.93]	0.752
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.456**				
KESTREL: Near Activities				
Interaction test	p=0.304			
< 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 28: Adjusted Mean Change (SE)	14.82 (2.13)	14.95 (1.81)		
Week 52: Adjusted Mean Change (SE)	15.40 (2.32)	13.50 (1.92)	1.90 [-4.01; 7.82]	0.527
≥ 7.5 %				
N'/ N	111 / 112	80 / 80		
Baseline Mean (SD)	62.20 (25.73)	66.46 (22.99)		
Week 52 Mean (SD)	77.47 (22.35)	78.78 (21.85)		
Week 28: Adjusted Mean Change (SE)	10.69 (1.76)	13.91 (2.10)		
Week 52: Adjusted Mean Change (SE)	12.03 (1.98)	14.13 (2.28)	-2.10 [-8.04; 3.84]	0.487

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Near Activities				
Interaction test	p=0.381			
< 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 28: Adjusted Mean Change (SE)	8.27 (2.05)	4.70 (1.88)		
Week 52: Adjusted Mean Change (SE)	10.30 (2.10)	9.28 (1.90)	1.02 [-4.54; 6.57]	0.719
≥ 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 28: Adjusted Mean Change (SE)	5.02 (1.87)	7.65 (2.00)		
Week 52: Adjusted Mean Change (SE)	10.38 (1.88)	9.18 (2.01)	1.20 [-4.21; 6.62]	0.663
Pooled Analysis: Near Activities				
Interaction test	p=0.214			
< 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 28: Adjusted Mean Change (SE)	11.50 (1.49)	9.83 (1.32)		
Week 52: Adjusted Mean Change (SE)	12.75 (1.58)	11.22 (1.36)	1.53 [-2.57; 5.62]	0.464
≥ 7.5 %				
N'/ N	207 / 209	165 / 165		
Baseline Mean (SD)	66.79 (24.36)	69.27 (23.20)		
Week 52 Mean (SD)	79.24 (21.39)	79.81 (21.06)		
Week 28: Adjusted Mean Change (SE)	8.22 (1.30)	10.76 (1.46)		
Week 52: Adjusted Mean Change (SE)	11.38 (1.38)	11.76 (1.53)	-0.38 [-4.42; 3.67]	0.854

	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=0.136**				
KESTREL: Distance Activities				
Interaction test	p=0.003 *			
< 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 28: Adjusted Mean Change (SE)	10.55 (1.87)	6.76 (1.58)		
Week 52: Adjusted Mean Change (SE)	10.50 (1.76)	7.67 (1.46)	2.83 [-1.66; 7.31]	0.216
≥ 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 28: Adjusted Mean Change (SE)	5.28 (1.55)	11.89 (1.84)		
Week 52: Adjusted Mean Change (SE)	8.11 (1.49)	12.28 (1.73)	-4.18 [-8.67; 0.32]	0.069
KITE: Distance Activities				
Interaction test	p=0.933			
< 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 28: Adjusted Mean Change (SE)	6.74 (1.78)	4.71 (1.63)		
Week 52: Adjusted Mean Change (SE)	11.29 (1.71)	9.51 (1.54)	1.78 [-2.75; 6.31]	0.440
≥ 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 28: Adjusted Mean Change (SE)	5.97 (1.61)	6.38 (1.74)		
Week 52: Adjusted Mean Change (SE)	11.46 (1.53)	6.76 (1.64)	4.70 [0.29; 9.11]	0.037 *

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Distance Activities				
Interaction test	p=0.039 *			
< 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 28: Adjusted Mean Change (SE)	8.61 (1.30)	5.74 (1.15)		
Week 52: Adjusted Mean Change (SE)	10.90 (1.24)	8.44 (1.07)	2.46 [-0.74; 5.67]	0.132
≥ 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 28: Adjusted Mean Change (SE)	5.68 (1.13)	9.06 (1.28)		
Week 52: Adjusted Mean Change (SE)	9.75 (1.08)	9.48 (1.20)	0.27 [-2.89; 3.44]	0.866
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.037 ***				
KESTREL: Social Functioning				
Interaction test	p=0.126			
< 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 28: Adjusted Mean Change (SE)	2.78 (1.44)	3.44 (1.22)		
Week 52: Adjusted Mean Change (SE)	5.32 (1.58)	4.55 (1.31)	0.77 [-3.27; 4.80]	0.709
≥ 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 28: Adjusted Mean Change (SE)	0.93 (1.19)	4.89 (1.42)		
Week 52: Adjusted Mean Change (SE)	0.79 (1.35)	3.61 (1.55)	-2.82 [-6.87; 1.22]	0.171

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Social Functioning				
Interaction test	p=0.758			
< 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 28: Adjusted Mean Change (SE)	4.17 (1.57)	3.52 (1.45)		
Week 52: Adjusted Mean Change (SE)	7.48 (1.37)	4.59 (1.24)	2.89 [-0.75; 6.53]	0.119
≥ 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 28: Adjusted Mean Change (SE)	3.54 (1.43)	4.49 (1.54)		
Week 52: Adjusted Mean Change (SE)	7.43 (1.23)	4.33 (1.31)	3.10 [-0.44; 6.63]	0.086
Pooled Analysis: Social Functioning				
Interaction test	p=0.237			
< 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 28: Adjusted Mean Change (SE)	3.47 (1.07)	3.51 (0.94)		
Week 52: Adjusted Mean Change (SE)	6.43 (1.05)	4.61 (0.91)	1.82 [-0.91; 4.55]	0.192
≥ 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 28: Adjusted Mean Change (SE)	2.28 (0.93)	4.52 (1.05)		
Week 52: Adjusted Mean Change (SE)	4.07 (0.92)	3.83 (1.02)	0.23 [-2.46; 2.93]	0.864

	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=0.300**				
KESTREL: Mental Health				
Interaction test	p=0.143			
< 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 28: Adjusted Mean Change (SE)	6.84 (2.02)	8.38 (1.72)		
Week 52: Adjusted Mean Change (SE)	12.88 (2.04)	9.45 (1.68)	3.43 [-1.76; 8.63]	0.194
≥ 7.5 %				
N'/ N	111 / 112	80 / 80		
Baseline Mean (SD)	63.74 (25.17)	70.00 (22.25)		
Week 52 Mean (SD)	75.87 (22.01)	81.54 (16.55)		
Week 28: Adjusted Mean Change (SE)	7.64 (1.67)	9.90 (2.00)		
Week 52: Adjusted Mean Change (SE)	8.56 (1.73)	13.54 (2.00)	-4.98 [-10.20; 0.23]	0.061
KITE: Mental Health				
Interaction test	p=0.173			
< 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 28: Adjusted Mean Change (SE)	9.39 (1.91)	11.67 (1.77)		
Week 52: Adjusted Mean Change (SE)	12.42 (2.34)	11.87 (2.13)	0.55 [-5.69; 6.79]	0.862
≥ 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 28: Adjusted Mean Change (SE)	8.13 (1.73)	6.70 (1.87)		
Week 52: Adjusted Mean Change (SE)	13.44 (2.10)	7.03 (2.24)	6.41 [0.36; 12.45]	0.038 *

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Mental Health				
Interaction test	p=0.949			
< 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 28: Adjusted Mean Change (SE)	8.21 (1.39)	9.81 (1.23)		
Week 52: Adjusted Mean Change (SE)	12.70 (1.56)	10.41 (1.35)	2.30 [-1.75; 6.34]	0.265
≥ 7.5 %				
N'/ N	208 / 209	165 / 165		
Baseline Mean (SD)	65.02 (24.22)	70.72 (22.67)		
Week 52 Mean (SD)	78.01 (22.13)	79.50 (19.69)		
Week 28: Adjusted Mean Change (SE)	7.99 (1.20)	8.30 (1.37)		
Week 52: Adjusted Mean Change (SE)	10.97 (1.36)	10.25 (1.51)	0.72 [-3.27; 4.70]	0.725
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.072**				
KESTREL: Role Difficulties				
Interaction test	p=0.407			
< 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 28: Adjusted Mean Change (SE)	6.69 (2.52)	10.02 (2.14)		
Week 52: Adjusted Mean Change (SE)	10.32 (2.71)	10.26 (2.24)	0.06 [-6.86; 6.99]	0.986
≥ 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 28: Adjusted Mean Change (SE)	5.57 (2.09)	7.82 (2.49)		
Week 52: Adjusted Mean Change (SE)	4.59 (2.31)	12.34 (2.67)	-7.74 [-14.69; -0.80]	0.029 *

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Role Difficulties				
Interaction test	p=0.731			
< 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 28: Adjusted Mean Change (SE)	9.26 (2.36)	8.14 (2.18)		
Week 52: Adjusted Mean Change (SE)	11.26 (2.55)	10.62 (2.31)	0.64 [-6.13; 7.40]	0.853
≥ 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 28: Adjusted Mean Change (SE)	6.16 (2.14)	8.65 (2.31)		
Week 52: Adjusted Mean Change (SE)	13.11 (2.28)	6.17 (2.44)	6.94 [0.38; 13.51]	0.038 *
Pooled Analysis: Role Difficulties				
Interaction test	p=0.650			
< 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 28: Adjusted Mean Change (SE)	7.96 (1.73)	8.93 (1.53)		
Week 52: Adjusted Mean Change (SE)	10.73 (1.86)	10.24 (1.61)	0.48 [-4.35; 5.32]	0.844
≥ 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 28: Adjusted Mean Change (SE)	5.99 (1.50)	8.47 (1.70)		
Week 52: Adjusted Mean Change (SE)	8.75 (1.62)	9.31 (1.80)	-0.56 [-5.32; 4.21]	0.818

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Dependency				
Test of heterogeneity in main analysis: **p_H=0.029 ***				
KESTREL: Dependency				
Interaction test	p=0.419			
< 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 28: Adjusted Mean Change (SE)	5.64 (2.17)	6.90 (1.84)		
Week 52: Adjusted Mean Change (SE)	7.30 (2.22)	7.61 (1.84)	-0.31 [-5.99; 5.36]	0.914
≥ 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 28: Adjusted Mean Change (SE)	5.47 (1.79)	6.66 (2.14)		
Week 52: Adjusted Mean Change (SE)	4.43 (1.89)	10.32 (2.19)	-5.89 [-11.59; -0.20]	0.043 *
KITE: Dependency				
Interaction test	p=0.191			
< 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 28: Adjusted Mean Change (SE)	5.56 (1.93)	4.65 (1.78)		
Week 52: Adjusted Mean Change (SE)	5.49 (2.11)	4.46 (1.91)	1.03 [-4.58; 6.64]	0.719
≥ 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 28: Adjusted Mean Change (SE)	5.74 (1.75)	1.91 (1.89)		
Week 52: Adjusted Mean Change (SE)	9.16 (1.89)	2.29 (2.02)	6.87 [1.42; 12.33]	0.014 *

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Dependency				
Interaction test	p=0.993			
< 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 28: Adjusted Mean Change (SE)	5.86 (1.46)	5.54 (1.29)		
Week 52: Adjusted Mean Change (SE)	6.67 (1.54)	5.86 (1.33)	0.81 [-3.20; 4.82]	0.692
≥ 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 28: Adjusted Mean Change (SE)	5.54 (1.26)	4.56 (1.43)		
Week 52: Adjusted Mean Change (SE)	6.58 (1.35)	6.46 (1.50)	0.12 [-3.83; 4.08]	0.951
Driving				
Test of heterogeneity in main analysis: **p_H=0.778**				
KESTREL: Driving				
Interaction test	p=0.280			
< 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 28: Adjusted Mean Change (SE)	4.66 (2.10)	6.39 (1.88)		
Week 52: Adjusted Mean Change (SE)	7.25 (2.44)	6.49 (2.14)	0.76 [-5.64; 7.16]	0.815
≥ 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 28: Adjusted Mean Change (SE)	0.14 (1.81)	4.85 (2.18)		
Week 52: Adjusted Mean Change (SE)	1.01 (2.07)	5.56 (2.53)	-4.55 [-10.99; 1.89]	0.165

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Driving				
Interaction test	p=0.180			
< 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 28: Adjusted Mean Change (SE)	2.84 (2.13)	5.95 (2.16)		
Week 52: Adjusted Mean Change (SE)	8.65 (1.81)	4.89 (1.86)	3.76 [-1.37; 8.89]	0.149
≥ 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 28: Adjusted Mean Change (SE)	-1.09 (1.96)	4.98 (2.10)		
Week 52: Adjusted Mean Change (SE)	3.41 (1.69)	5.59 (1.84)	-2.17 [-7.10; 2.76]	0.386
Pooled Analysis: Driving				
Interaction test	p=0.101			
< 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 28: Adjusted Mean Change (SE)	3.74 (1.50)	6.31 (1.41)		
Week 52: Adjusted Mean Change (SE)	8.07 (1.54)	5.91 (1.44)	2.17 [-1.97; 6.30]	0.304
≥ 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 28: Adjusted Mean Change (SE)	-0.41 (1.33)	4.86 (1.51)		
Week 52: Adjusted Mean Change (SE)	2.10 (1.36)	5.56 (1.57)	-3.46 [-7.55; 0.62]	0.097

	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=0.691**				
KESTREL: Color Vision				
Interaction test	p=0.392			
< 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 28: Adjusted Mean Change (SE)	2.50 (1.31)	2.58 (1.12)		
Week 52: Adjusted Mean Change (SE)	2.71 (1.33)	3.05 (1.10)	-0.34 [-3.74; 3.05]	0.842
≥ 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 28: Adjusted Mean Change (SE)	1.84 (1.09)	0.76 (1.32)		
Week 52: Adjusted Mean Change (SE)	1.84 (1.14)	-0.12 (1.35)	1.96 [-1.51; 5.44]	0.267
KITE: Color Vision				
Interaction test	p=0.812			
< 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 28: Adjusted Mean Change (SE)	3.66 (1.23)	4.33 (1.13)		
Week 52: Adjusted Mean Change (SE)	5.11 (1.12)	3.21 (1.01)	1.90 [-1.08; 4.87]	0.210
≥ 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 28: Adjusted Mean Change (SE)	3.55 (1.12)	4.05 (1.21)		
Week 52: Adjusted Mean Change (SE)	6.28 (1.01)	3.68 (1.09)	2.59 [-0.34; 5.52]	0.083

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Color Vision				
Interaction test	p=0.390			
< 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 28: Adjusted Mean Change (SE)	3.12 (0.91)	3.50 (0.80)		
Week 52: Adjusted Mean Change (SE)	3.95 (0.87)	3.22 (0.75)	0.73 [-1.52; 2.98]	0.525
≥ 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 28: Adjusted Mean Change (SE)	2.72 (0.79)	2.30 (0.90)		
Week 52: Adjusted Mean Change (SE)	3.99 (0.76)	1.72 (0.86)	2.27 [0.02; 4.53]	0.048 *
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.021 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.002 *			
< 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 28: Adjusted Mean Change (SE)	3.92 (2.11)	6.15 (1.79)		
Week 52: Adjusted Mean Change (SE)	9.36 (2.10)	4.34 (1.73)	5.02 [-0.34; 10.37]	0.066
≥ 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 28: Adjusted Mean Change (SE)	2.04 (1.75)	10.06 (2.08)		
Week 52: Adjusted Mean Change (SE)	3.19 (1.79)	11.66 (2.08)	-8.47 [-13.88; -3.07]	0.002 *

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Peripheral Vision				
Interaction test	p=0.110			
< 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 28: Adjusted Mean Change (SE)	6.56 (1.78)	3.97 (1.63)		
Week 52: Adjusted Mean Change (SE)	8.05 (1.93)	2.72 (1.74)	5.33 [0.22; 10.44]	0.041 *
≥ 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 28: Adjusted Mean Change (SE)	3.31 (1.61)	5.32 (1.75)		
Week 52: Adjusted Mean Change (SE)	5.22 (1.73)	4.60 (1.85)	0.62 [-4.35; 5.60]	0.806
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.001 *			
< 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 28: Adjusted Mean Change (SE)	5.10 (1.38)	5.26 (1.22)		
Week 52: Adjusted Mean Change (SE)	8.55 (1.43)	3.71 (1.24)	4.85 [1.13; 8.56]	0.011 *
≥ 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 28: Adjusted Mean Change (SE)	2.63 (1.20)	7.67 (1.36)		
Week 52: Adjusted Mean Change (SE)	4.10 (1.25)	8.12 (1.40)	-4.02 [-7.71; -0.33]	0.033 *

	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=0.700**				
KESTREL: General Health				
Interaction test	p=0.483			
< 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 28: Adjusted Mean Change (SE)	3.75 (2.19)	4.50 (1.84)		
Week 52: Adjusted Mean Change (SE)	10.52 (2.63)	4.44 (2.15)	6.08 [-0.62; 12.78]	0.075
≥ 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 28: Adjusted Mean Change (SE)	4.60 (1.79)	4.96 (2.14)		
Week 52: Adjusted Mean Change (SE)	6.72 (2.22)	6.12 (2.57)	0.60 [-6.07; 7.27]	0.861
KITE: General Health				
Interaction test	p=0.970			
< 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 28: Adjusted Mean Change (SE)	3.38 (2.07)	4.32 (1.90)		
Week 52: Adjusted Mean Change (SE)	5.92 (2.48)	5.09 (2.24)	0.83 [-5.74; 7.40]	0.804
≥ 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 28: Adjusted Mean Change (SE)	3.81 (1.88)	4.48 (2.02)		
Week 52: Adjusted Mean Change (SE)	5.11 (2.22)	4.81 (2.36)	0.30 [-6.08; 6.68]	0.926

	Treatment Groups		Comparison	
VFQ by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: General Health				
Interaction test	p=0.658			
< 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 28: Adjusted Mean Change (SE)	3.34 (1.50)	4.51 (1.32)		
Week 52: Adjusted Mean Change (SE)	7.95 (1.80)	4.82 (1.55)	3.13 [-1.53; 7.79]	0.188
≥ 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 28: Adjusted Mean Change (SE)	4.19 (1.30)	4.83 (1.47)		
Week 52: Adjusted Mean Change (SE)	5.95 (1.57)	5.57 (1.74)	0.39 [-4.21; 4.98]	0.869

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 52

	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=0.071**				
KESTREL: Composite Score				
Interaction test	p=0.558			
≤ 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 28: Adjusted Mean Change (SE)	6.40 (0.99)	8.95 (1.04)		
Week 52: Adjusted Mean Change (SE)	7.49 (1.03)	9.52 (1.06)	-2.03 [-4.93; 0.87]	0.170
> 3 - < 12 months				
N'/ N	30 / 30	39 / 39		
Baseline Mean (SD)	77.40 (13.15)	75.14 (13.31)		
Week 52 Mean (SD)	85.78 (10.96)	83.60 (13.07)		
Week 28: Adjusted Mean Change (SE)	3.98 (2.04)	7.57 (1.75)		
Week 52: Adjusted Mean Change (SE)	7.79 (2.20)	7.47 (1.84)	0.32 [-5.32; 5.96]	0.911
≥ 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 28: Adjusted Mean Change (SE)	5.28 (1.78)	4.20 (1.79)		
Week 52: Adjusted Mean Change (SE)	5.70 (1.94)	5.75 (1.81)	-0.05 [-5.25; 5.15]	0.985
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 28: Adjusted Mean Change (SE)	6.19 (1.12)	5.44 (1.07)		
Week 52: Adjusted Mean Change (SE)	10.12 (1.21)	6.18 (1.16)	3.94 [0.63; 7.24]	0.020 *

	Treatment Groups		Comparison	
VFQ 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)	75.12 (15.84)	70.23 (18.41)		
Week 52 Mean (SD)	82.07 (16.37)	78.33 (17.81)		
Week 28: Adjusted Mean Change (SE)	5.98 (1.42)	6.51 (1.49)		
Week 52: Adjusted Mean Change (SE)	7.53 (1.53)	5.55 (1.57)	1.98 [-2.31; 6.27]	0.364
≥ 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 28: Adjusted Mean Change (SE)	5.04 (1.57)	6.90 (1.64)		
Week 52: Adjusted Mean Change (SE)	8.25 (1.71)	8.53 (1.74)	-0.28 [-5.07; 4.51]	0.908
Pooled Analysis: Composite Score				
Interaction test	p=0.979			
≤ 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 28: Adjusted Mean Change (SE)	6.50 (0.75)	7.32 (0.76)		
Week 52: Adjusted Mean Change (SE)	8.70 (0.79)	8.01 (0.79)	0.69 [-1.50; 2.88]	0.536
> 3 - < 12 months				
N'/ N	81 / 81	88 / 88		
Baseline Mean (SD)	75.97 (14.86)	72.41 (16.44)		
Week 52 Mean (SD)	83.29 (14.83)	80.56 (16.09)		
Week 28: Adjusted Mean Change (SE)	4.96 (1.20)	6.76 (1.15)		
Week 52: Adjusted Mean Change (SE)	7.18 (1.28)	6.20 (1.20)	0.98 [-2.46; 4.42]	0.576

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 28: Adjusted Mean Change (SE)	5.27 (1.20)	5.77 (1.23)		
Week 52: Adjusted Mean Change (SE)	7.23 (1.29)	7.34 (1.26)	-0.10 [-3.64; 3.44]	0.954
General Vision				
Test of heterogeneity in main analysis: **p_H=0.986**				
KESTREL: General Vision				
Interaction test	p=0.699			
≤ 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 28: Adjusted Mean Change (SE)	12.64 (1.19)	12.90 (1.26)		
Week 52: Adjusted Mean Change (SE)	12.61 (1.25)	12.11 (1.30)	0.50 [-3.04; 4.04]	0.782
> 3 - < 12 months				
N'/ N	30 / 30	39 / 39		
Baseline Mean (SD)	62.67 (14.61)	56.41 (14.42)		
Week 52 Mean (SD)	72.38 (13.38)	69.68 (17.03)		
Week 28: Adjusted Mean Change (SE)	8.50 (2.47)	8.30 (2.11)		
Week 52: Adjusted Mean Change (SE)	10.75 (2.72)	10.55 (2.26)	0.20 [-6.77; 7.17]	0.955
≥ 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 28: Adjusted Mean Change (SE)	9.22 (2.14)	6.48 (2.17)		
Week 52: Adjusted Mean Change (SE)	8.98 (2.40)	6.56 (2.20)	2.42 [-3.96; 8.81]	0.456
KITE: General Vision				
Interaction test	p=0.911			
≤ 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 28: Adjusted Mean Change (SE)	9.54 (1.51)	9.60 (1.44)		
Week 52: Adjusted Mean Change (SE)	10.93 (1.68)	8.90 (1.60)	2.04 [-2.53; 6.61]	0.380

	Treatment Groups		Comparison	
VFQ 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)	59.22 (17.87)	55.51 (18.83)		
Week 52 Mean (SD)	70.23 (14.72)	68.10 (17.70)		
Week 28: Adjusted Mean Change (SE)	10.52 (1.90)	9.41 (2.00)		
Week 52: Adjusted Mean Change (SE)	11.11 (2.10)	10.84 (2.15)	0.28 [-5.63; 6.18]	0.927
≥ 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 28: Adjusted Mean Change (SE)	7.93 (2.11)	10.10 (2.20)		
Week 52: Adjusted Mean Change (SE)	13.96 (2.36)	12.66 (2.39)	1.30 [-5.30; 7.90]	0.698
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 28: Adjusted Mean Change (SE)	11.36 (0.95)	11.37 (0.96)		
Week 52: Adjusted Mean Change (SE)	11.89 (1.03)	10.71 (1.03)	1.19 [-1.66; 4.03]	0.413
> 3 - < 12 months				
N'/ N	81 / 81	88 / 88		
Baseline Mean (SD)	60.49 (16.73)	55.91 (16.93)		
Week 52 Mean (SD)	70.94 (14.22)	68.77 (17.32)		
Week 28: Adjusted Mean Change (SE)	9.72 (1.52)	8.84 (1.46)		
Week 52: Adjusted Mean Change (SE)	10.83 (1.66)	10.65 (1.56)	0.18 [-4.31; 4.66]	0.939
≥ 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 28: Adjusted Mean Change (SE)	8.69 (1.51)	8.45 (1.56)		
Week 52: Adjusted Mean Change (SE)	11.97 (1.69)	9.71 (1.63)	2.26 [-2.34; 6.86]	0.336

	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=0.492**				
KESTREL: Ocular Pain				
Interaction test	p=0.066			
≤ 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 28: Adjusted Mean Change (SE)	1.79 (1.63)	6.25 (1.73)		
Week 52: Adjusted Mean Change (SE)	4.08 (1.49)	5.18 (1.54)	-1.10 [-5.30; 3.11]	0.608
> 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 28: Adjusted Mean Change (SE)	8.83 (3.37)	2.40 (2.88)		
Week 52: Adjusted Mean Change (SE)	8.91 (3.22)	2.29 (2.67)	6.62 [-1.60; 14.83]	0.114
≥ 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 28: Adjusted Mean Change (SE)	1.25 (2.93)	0.80 (2.96)		
Week 52: Adjusted Mean Change (SE)	6.29 (2.84)	4.02 (2.61)	2.27 [-5.28; 9.82]	0.555
KITE: Ocular Pain				
Interaction test	p=0.952			
≤ 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 28: Adjusted Mean Change (SE)	5.31 (1.74)	4.45 (1.65)		
Week 52: Adjusted Mean Change (SE)	5.65 (1.79)	5.29 (1.71)	0.36 [-4.52; 5.24]	0.884
> 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 28: Adjusted Mean Change (SE)	3.27 (2.18)	2.21 (2.27)		
Week 52: Adjusted Mean Change (SE)	2.18 (2.24)	0.13 (2.28)	2.04 [-4.24; 8.33]	0.523

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 28: Adjusted Mean Change (SE)	5.09 (2.41)	5.25 (2.52)		
Week 52: Adjusted Mean Change (SE)	7.46 (2.52)	6.13 (2.54)	1.33 [-5.70; 8.37]	0.709
Pooled Analysis: Ocular Pain				
Interaction test	p=0.227			
≤ 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 28: Adjusted Mean Change (SE)	3.31 (1.19)	5.38 (1.20)		
Week 52: Adjusted Mean Change (SE)	4.86 (1.15)	5.23 (1.15)	-0.36 [-3.56; 2.84]	0.824
> 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 28: Adjusted Mean Change (SE)	5.08 (1.90)	2.17 (1.82)		
Week 52: Adjusted Mean Change (SE)	4.29 (1.87)	0.91 (1.75)	3.38 [-1.65; 8.40]	0.187
≥ 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 28: Adjusted Mean Change (SE)	3.36 (1.89)	3.14 (1.95)		
Week 52: Adjusted Mean Change (SE)	6.86 (1.90)	5.20 (1.83)	1.66 [-3.50; 6.83]	0.528
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.456**				
KESTREL: Near Activities				
Interaction test	p=0.592			
≤ 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 28: Adjusted Mean Change (SE)	15.20 (1.66)	15.54 (1.76)		
Week 52: Adjusted Mean Change (SE)	14.61 (1.83)	15.52 (1.90)	-0.92 [-6.11; 4.28]	0.729

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 3 - < 12 months				
N'/ N	30 / 30	39 / 39		
Baseline Mean (SD)	64.72 (25.30)	59.40 (21.02)		
Week 52 Mean (SD)	80.56 (20.97)	73.92 (23.74)		
Week 28: Adjusted Mean Change (SE)	4.76 (3.44)	16.35 (2.94)		
Week 52: Adjusted Mean Change (SE)	13.24 (3.97)	11.91 (3.30)	1.33 [-8.83; 11.49]	0.797
≥ 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 28: Adjusted Mean Change (SE)	9.14 (2.99)	9.49 (3.02)		
Week 52: Adjusted Mean Change (SE)	10.00 (3.51)	10.34 (3.22)	-0.34 [-9.68; 9.00]	0.943
KITE: Near Activities				
Interaction test	p=0.392			
≤ 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 28: Adjusted Mean Change (SE)	6.54 (2.03)	4.59 (1.93)		
Week 52: Adjusted Mean Change (SE)	12.60 (2.04)	8.43 (1.95)	4.17 [-1.39; 9.73]	0.141
> 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 28: Adjusted Mean Change (SE)	7.32 (2.55)	7.01 (2.66)		
Week 52: Adjusted Mean Change (SE)	7.08 (2.57)	8.29 (2.62)	-1.22 [-8.40; 5.97]	0.739
≥ 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 28: Adjusted Mean Change (SE)	5.32 (2.83)	8.45 (2.94)		
Week 52: Adjusted Mean Change (SE)	10.12 (2.88)	12.19 (2.91)	-2.07 [-10.12; 5.99]	0.614

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Near Activities				
Interaction test	p=0.358			
≤ 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 28: Adjusted Mean Change (SE)	11.55 (1.32)	10.22 (1.32)		
Week 52: Adjusted Mean Change (SE)	13.54 (1.38)	12.06 (1.38)	1.48 [-2.34; 5.31]	0.447
> 3 - < 12 months				
N'/ N	81 / 81	88 / 88		
Baseline Mean (SD)	64.81 (23.53)	61.70 (22.87)		
Week 52 Mean (SD)	74.74 (23.66)	74.03 (22.87)		
Week 28: Adjusted Mean Change (SE)	6.80 (2.10)	11.38 (2.01)		
Week 52: Adjusted Mean Change (SE)	9.13 (2.24)	10.27 (2.10)	-1.14 [-7.15; 4.87]	0.711
≥ 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 28: Adjusted Mean Change (SE)	7.75 (2.08)	9.04 (2.14)		
Week 52: Adjusted Mean Change (SE)	10.81 (2.26)	11.27 (2.20)	-0.46 [-6.64; 5.73]	0.884
Distance Activities				
Test of heterogeneity in main analysis: **p_H=0.136**				
KESTREL: Distance Activities				
Interaction test	p=0.839			
≤ 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 28: Adjusted Mean Change (SE)	8.33 (1.48)	11.16 (1.57)		
Week 52: Adjusted Mean Change (SE)	10.07 (1.40)	10.99 (1.45)	-0.93 [-4.88; 3.03]	0.646
> 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 28: Adjusted Mean Change (SE)	5.10 (3.07)	7.18 (2.62)		
Week 52: Adjusted Mean Change (SE)	6.79 (3.01)	5.74 (2.51)	1.05 [-6.65; 8.75]	0.789

	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)	72.70 (25.11)	71.71 (18.91)		
Week 52 Mean (SD)	80.56 (19.85)	82.70 (16.61)		
Week 28: Adjusted Mean Change (SE)	6.39 (2.67)	4.31 (2.69)		
Week 52: Adjusted Mean Change (SE)	7.59 (2.66)	9.38 (2.47)	-1.80 [-8.89; 5.30]	0.619
KITE: Distance Activities				
Interaction test	p=0.363			
≤ 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 28: Adjusted Mean Change (SE)	7.03 (1.76)	5.63 (1.67)		
Week 52: Adjusted Mean Change (SE)	12.32 (1.68)	7.77 (1.60)	4.55 [-0.01; 9.12]	0.050
> 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 28: Adjusted Mean Change (SE)	6.65 (2.21)	4.28 (2.32)		
Week 52: Adjusted Mean Change (SE)	11.75 (2.10)	7.39 (2.15)	4.36 [-1.53; 10.25]	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 28: Adjusted Mean Change (SE)	4.51 (2.44)	6.73 (2.55)		
Week 52: Adjusted Mean Change (SE)	9.09 (2.35)	10.13 (2.38)	-1.04 [-7.63; 5.55]	0.757
Pooled Analysis: Distance Activities				
Interaction test	p=0.655			
≤ 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 28: Adjusted Mean Change (SE)	8.06 (1.15)	8.61 (1.16)		
Week 52: Adjusted Mean Change (SE)	11.21 (1.08)	9.51 (1.08)	1.69 [-1.30; 4.68]	0.267

	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 28: Adjusted Mean Change (SE)	5.69 (1.83)	5.35 (1.75)		
Week 52: Adjusted Mean Change (SE)	9.67 (1.75)	6.51 (1.64)	3.16 [-1.54; 7.86]	0.188
≥ 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 28: Adjusted Mean Change (SE)	5.39 (1.82)	5.80 (1.87)		
Week 52: Adjusted Mean Change (SE)	8.36 (1.77)	10.01 (1.72)	-1.65 [-6.48; 3.18]	0.502
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.037 ***				
KESTREL: Social Functioning				
Interaction test	p=0.423			
≤ 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 28: Adjusted Mean Change (SE)	2.02 (1.13)	5.39 (1.20)		
Week 52: Adjusted Mean Change (SE)	4.36 (1.25)	3.39 (1.30)	0.98 [-2.58; 4.53]	0.589
> 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 28: Adjusted Mean Change (SE)	1.10 (2.35)	4.34 (2.00)		
Week 52: Adjusted Mean Change (SE)	-1.26 (2.73)	5.86 (2.25)	-7.12 [-14.08; -0.16]	0.045 *
≥ 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 28: Adjusted Mean Change (SE)	0.87 (2.04)	-0.23 (2.06)		
Week 52: Adjusted Mean Change (SE)	-0.54 (2.41)	4.66 (2.20)	-5.20 [-11.59; 1.18]	0.110

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Social Functioning				
Interaction test	p=0.564			
≤ 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 28: Adjusted Mean Change (SE)	5.01 (1.56)	3.23 (1.48)		
Week 52: Adjusted Mean Change (SE)	8.62 (1.33)	5.02 (1.27)	3.60 [-0.01; 7.21]	0.051
> 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 28: Adjusted Mean Change (SE)	1.61 (1.95)	4.18 (2.05)		
Week 52: Adjusted Mean Change (SE)	4.52 (1.66)	1.60 (1.69)	2.92 [-1.73; 7.58]	0.217
≥ 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 28: Adjusted Mean Change (SE)	4.24 (2.16)	5.46 (2.25)		
Week 52: Adjusted Mean Change (SE)	8.85 (1.86)	6.80 (1.88)	2.05 [-3.16; 7.25]	0.440
Pooled Analysis: Social Functioning				
Interaction test	p=0.192			
≤ 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 28: Adjusted Mean Change (SE)	3.69 (0.94)	4.30 (0.95)		
Week 52: Adjusted Mean Change (SE)	6.60 (0.92)	4.02 (0.92)	2.59 [0.04; 5.13]	0.046 *
> 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 28: Adjusted Mean Change (SE)	0.71 (1.50)	4.22 (1.44)		
Week 52: Adjusted Mean Change (SE)	1.82 (1.49)	3.36 (1.39)	-1.54 [-5.54; 2.45]	0.449

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 28: Adjusted Mean Change (SE)	2.46 (1.49)	2.76 (1.53)		
Week 52: Adjusted Mean Change (SE)	4.34 (1.51)	5.85 (1.45)	-1.51 [-5.62; 2.60]	0.471
Mental Health				
Test of heterogeneity in main analysis: **p_H=0.300**				
KESTREL: Mental Health				
Interaction test	p=0.397			
≤ 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 28: Adjusted Mean Change (SE)	8.31 (1.59)	11.17 (1.69)		
Week 52: Adjusted Mean Change (SE)	10.76 (1.61)	13.78 (1.67)	-3.02 [-7.57; 1.54]	0.194
> 3 - < 12 months				
N'/ N	30 / 30	39 / 39		
Baseline Mean (SD)	65.42 (22.19)	64.74 (24.14)		
Week 52 Mean (SD)	81.85 (11.16)	74.60 (20.60)		
Week 28: Adjusted Mean Change (SE)	6.15 (3.29)	8.01 (2.81)		
Week 52: Adjusted Mean Change (SE)	14.63 (3.49)	8.92 (2.89)	5.72 [-3.21; 14.64]	0.208
≥ 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 28: Adjusted Mean Change (SE)	5.21 (2.86)	4.02 (2.89)		
Week 52: Adjusted Mean Change (SE)	6.16 (3.08)	5.90 (2.83)	0.26 [-7.94; 8.46]	0.950
KITE: Mental Health				
Interaction test	p=0.383			
≤ 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 28: Adjusted Mean Change (SE)	10.41 (1.89)	8.68 (1.80)		
Week 52: Adjusted Mean Change (SE)	15.41 (2.28)	10.44 (2.18)	4.97 [-1.23; 11.18]	0.116

	Treatment Groups		Comparison	
VFQ 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)	66.05 (21.15)	55.99 (25.96)		
Week 52 Mean (SD)	75.44 (25.93)	72.32 (26.63)		
Week 28: Adjusted Mean Change (SE)	8.05 (2.38)	11.17 (2.52)		
Week 52: Adjusted Mean Change (SE)	9.15 (2.86)	10.61 (2.94)	-1.46 [-9.52; 6.60]	0.722
≥ 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 28: Adjusted Mean Change (SE)	6.17 (2.64)	8.60 (2.76)		
Week 52: Adjusted Mean Change (SE)	13.04 (3.21)	6.57 (3.26)	6.47 [-2.51; 15.45]	0.157
Pooled Analysis: Mental Health				
Interaction test	p=0.809			
≤ 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 28: Adjusted Mean Change (SE)	9.50 (1.22)	9.99 (1.23)		
Week 52: Adjusted Mean Change (SE)	12.92 (1.36)	12.23 (1.35)	0.69 [-3.07; 4.45]	0.717
> 3 - < 12 months				
N'/ N	81 / 81	88 / 88		
Baseline Mean (SD)	65.82 (21.40)	59.87 (25.40)		
Week 52 Mean (SD)	77.54 (22.29)	73.29 (24.12)		
Week 28: Adjusted Mean Change (SE)	7.01 (1.95)	9.54 (1.87)		
Week 52: Adjusted Mean Change (SE)	10.49 (2.20)	9.70 (2.07)	0.79 [-5.13; 6.70]	0.794
≥ 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 28: Adjusted Mean Change (SE)	5.69 (1.93)	6.51 (1.99)		
Week 52: Adjusted Mean Change (SE)	9.91 (2.23)	6.34 (2.16)	3.57 [-2.51; 9.65]	0.250

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.072**				
KESTREL: Role Difficulties				
Interaction test	p=0.077			
≤ 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 28: Adjusted Mean Change (SE)	5.45 (2.00)	10.28 (2.12)		
Week 52: Adjusted Mean Change (SE)	4.97 (2.15)	13.64 (2.22)	-8.68 [-14.76; -2.60]	0.005 *
> 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 28: Adjusted Mean Change (SE)	4.07 (4.14)	9.46 (3.53)		
Week 52: Adjusted Mean Change (SE)	9.65 (4.65)	8.56 (3.86)	1.10 [-10.79; 12.98]	0.856
≥ 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 28: Adjusted Mean Change (SE)	9.01 (3.59)	5.41 (3.63)		
Week 52: Adjusted Mean Change (SE)	12.37 (4.11)	6.45 (3.77)	5.92 [-5.02; 16.85]	0.288
KITE: Role Difficulties				
Interaction test	p=0.229			
≤ 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 28: Adjusted Mean Change (SE)	6.76 (2.32)	8.84 (2.20)		
Week 52: Adjusted Mean Change (SE)	14.53 (2.48)	7.69 (2.37)	6.84 [0.09; 13.59]	0.047 *
> 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 28: Adjusted Mean Change (SE)	8.04 (2.92)	3.50 (3.06)		
Week 52: Adjusted Mean Change (SE)	10.57 (3.12)	5.50 (3.17)	5.08 [-3.63; 13.79]	0.252

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 28: Adjusted Mean Change (SE)	8.50 (3.22)	13.22 (3.36)		
Week 52: Adjusted Mean Change (SE)	10.20 (3.49)	13.96 (3.52)	-3.76 [-13.50; 5.99]	0.449
Pooled Analysis: Role Difficulties				
Interaction test	p=0.454			
≤ 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 28: Adjusted Mean Change (SE)	6.34 (1.52)	9.68 (1.53)		
Week 52: Adjusted Mean Change (SE)	9.07 (1.63)	11.05 (1.62)	-1.98 [-6.49; 2.54]	0.390
> 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 28: Adjusted Mean Change (SE)	6.01 (2.43)	5.92 (2.32)		
Week 52: Adjusted Mean Change (SE)	9.49 (2.64)	6.66 (2.47)	2.83 [-4.26; 9.92]	0.433
≥ 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 28: Adjusted Mean Change (SE)	8.77 (2.41)	9.51 (2.48)		
Week 52: Adjusted Mean Change (SE)	11.16 (2.68)	10.33 (2.59)	0.83 [-6.47; 8.13]	0.824
Dependency				
Test of heterogeneity in main analysis: **p_H=0.029 ***				
KESTREL: Dependency				
Interaction test	p=0.753			
≤ 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 28: Adjusted Mean Change (SE)	6.23 (1.72)	7.41 (1.82)		
Week 52: Adjusted Mean Change (SE)	5.36 (1.76)	9.97 (1.83)	-4.62 [-9.61; 0.37]	0.070

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 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 28: Adjusted Mean Change (SE)	3.96 (3.56)	7.59 (3.04)		
Week 52: Adjusted Mean Change (SE)	9.77 (3.82)	10.24 (3.16)	-0.47 [-10.22; 9.28]	0.924
≥ 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 28: Adjusted Mean Change (SE)	4.87 (3.09)	4.27 (3.12)		
Week 52: Adjusted Mean Change (SE)	3.87 (3.37)	3.75 (3.10)	0.12 [-8.85; 9.09]	0.979
KITE: Dependency				
Interaction test	p=0.634			
≤ 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 28: Adjusted Mean Change (SE)	7.45 (1.89)	3.27 (1.81)		
Week 52: Adjusted Mean Change (SE)	9.74 (2.05)	4.18 (1.96)	5.56 [-0.03; 11.15]	0.051
> 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 28: Adjusted Mean Change (SE)	2.57 (2.39)	1.69 (2.51)		
Week 52: Adjusted Mean Change (SE)	4.30 (2.58)	1.30 (2.64)	3.00 [-4.24; 10.24]	0.416
≥ 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 28: Adjusted Mean Change (SE)	5.95 (2.64)	5.59 (2.76)		
Week 52: Adjusted Mean Change (SE)	7.19 (2.89)	4.51 (2.93)	2.68 [-5.40; 10.75]	0.515

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Dependency				
Interaction test	p=0.937			
≤ 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 28: Adjusted Mean Change (SE)	6.87 (1.28)	5.45 (1.29)		
Week 52: Adjusted Mean Change (SE)	7.20 (1.35)	7.30 (1.35)	-0.10 [-3.84; 3.64]	0.958
> 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 28: Adjusted Mean Change (SE)	2.83 (2.04)	4.14 (1.96)		
Week 52: Adjusted Mean Change (SE)	5.85 (2.19)	5.00 (2.05)	0.85 [-5.03; 6.73]	0.777
≥ 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 28: Adjusted Mean Change (SE)	5.69 (2.03)	5.27 (2.09)		
Week 52: Adjusted Mean Change (SE)	5.96 (2.21)	4.41 (2.15)	1.55 [-4.50; 7.60]	0.615
Driving				
Test of heterogeneity in main analysis: **p_H=0.778**				
KESTREL: Driving				
Interaction test	p=0.464			
≤ 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 28: Adjusted Mean Change (SE)	2.30 (1.65)	6.07 (1.86)		
Week 52: Adjusted Mean Change (SE)	4.92 (1.83)	8.60 (2.09)	-3.68 [-9.15; 1.79]	0.186
> 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 28: Adjusted Mean Change (SE)	3.51 (4.06)	5.67 (2.96)		
Week 52: Adjusted Mean Change (SE)	6.07 (4.79)	0.74 (3.36)	5.33 [-6.20; 16.86]	0.363

	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 28: Adjusted Mean Change (SE)	-0.09 (3.42)	4.50 (3.49)		
Week 52: Adjusted Mean Change (SE)	-3.74 (3.86)	4.66 (3.79)	-8.40 [-19.04; 2.24]	0.121
KITE: Driving				
Interaction test	p=0.762			
≤ 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 28: Adjusted Mean Change (SE)	-2.10 (2.10)	5.92 (2.16)		
Week 52: Adjusted Mean Change (SE)	6.30 (1.83)	4.77 (1.93)	1.54 [-3.72; 6.79]	0.565
> 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 28: Adjusted Mean Change (SE)	1.35 (2.64)	7.89 (3.04)		
Week 52: Adjusted Mean Change (SE)	6.61 (2.30)	3.52 (2.59)	3.09 [-3.73; 9.92]	0.372
≥ 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 28: Adjusted Mean Change (SE)	5.55 (2.98)	2.54 (2.86)		
Week 52: Adjusted Mean Change (SE)	4.22 (2.58)	7.72 (2.52)	-3.50 [-10.62; 3.63]	0.334
Pooled Analysis: Driving				
Interaction test	p=0.603			
≤ 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 28: Adjusted Mean Change (SE)	0.74 (1.31)	6.02 (1.41)		
Week 52: Adjusted Mean Change (SE)	5.53 (1.32)	7.11 (1.45)	-1.58 [-5.43; 2.27]	0.420

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
> 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 28: Adjusted Mean Change (SE)	1.96 (2.27)	6.81 (2.12)		
Week 52: Adjusted Mean Change (SE)	6.54 (2.36)	2.16 (2.15)	4.38 [-1.88; 10.64]	0.170
≥ 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 28: Adjusted Mean Change (SE)	2.89 (2.26)	3.35 (2.23)		
Week 52: Adjusted Mean Change (SE)	0.41 (2.30)	6.38 (2.25)	-5.98 [-12.30; 0.35]	0.064
Color Vision				
Test of heterogeneity in main analysis: **p_H=0.691**				
KESTREL: Color Vision				
Interaction test	p=0.805			
≤ 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 28: Adjusted Mean Change (SE)	2.94 (1.04)	1.83 (1.11)		
Week 52: Adjusted Mean Change (SE)	2.84 (1.05)	2.38 (1.10)	0.46 [-2.54; 3.46]	0.763
> 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 28: Adjusted Mean Change (SE)	-1.21 (2.15)	2.92 (1.89)		
Week 52: Adjusted Mean Change (SE)	3.69 (2.29)	1.17 (1.99)	2.53 [-3.44; 8.49]	0.405
≥ 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 28: Adjusted Mean Change (SE)	1.85 (1.89)	0.65 (1.89)		
Week 52: Adjusted Mean Change (SE)	-1.30 (2.06)	0.55 (1.85)	-1.85 [-7.28; 3.57]	0.502

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Color Vision				
Interaction test	p=0.433			
≤ 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 28: Adjusted Mean Change (SE)	3.57 (1.22)	3.53 (1.16)		
Week 52: Adjusted Mean Change (SE)	6.43 (1.10)	3.85 (1.05)	2.58 [-0.42; 5.58]	0.092
> 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 28: Adjusted Mean Change (SE)	4.79 (1.52)	5.48 (1.61)		
Week 52: Adjusted Mean Change (SE)	5.37 (1.37)	1.09 (1.42)	4.29 [0.42; 8.15]	0.030 *
≥ 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 28: Adjusted Mean Change (SE)	2.16 (1.68)	4.23 (1.75)		
Week 52: Adjusted Mean Change (SE)	4.93 (1.54)	5.44 (1.57)	-0.51 [-4.84; 3.82]	0.817
Pooled Analysis: Color Vision				
Interaction test	p=0.554			
≤ 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 28: Adjusted Mean Change (SE)	3.52 (0.80)	2.73 (0.81)		
Week 52: Adjusted Mean Change (SE)	4.58 (0.76)	3.17 (0.76)	1.41 [-0.70; 3.53]	0.190
> 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 28: Adjusted Mean Change (SE)	2.19 (1.27)	3.92 (1.24)		
Week 52: Adjusted Mean Change (SE)	4.15 (1.23)	0.63 (1.18)	3.52 [0.18; 6.86]	0.039 *

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 28: Adjusted Mean Change (SE)	2.01 (1.28)	2.53 (1.30)		
Week 52: Adjusted Mean Change (SE)	2.11 (1.26)	3.10 (1.21)	-0.99 [-4.41; 2.43]	0.569
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.021 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.636			
≤ 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 28: Adjusted Mean Change (SE)	3.39 (1.68)	9.16 (1.77)		
Week 52: Adjusted Mean Change (SE)	7.51 (1.68)	7.07 (1.75)	0.44 [-4.33; 5.20]	0.857
> 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 28: Adjusted Mean Change (SE)	2.26 (3.53)	7.69 (2.95)		
Week 52: Adjusted Mean Change (SE)	4.14 (3.66)	11.83 (3.02)	-7.69 [-17.03; 1.64]	0.106
≥ 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 28: Adjusted Mean Change (SE)	1.54 (3.00)	3.93 (3.06)		
Week 52: Adjusted Mean Change (SE)	0.93 (3.23)	3.76 (2.96)	-2.82 [-11.41; 5.76]	0.518
KITE: Peripheral Vision				
Interaction test	p=0.087			
≤ 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 28: Adjusted Mean Change (SE)	4.70 (1.76)	4.86 (1.69)		
Week 52: Adjusted Mean Change (SE)	8.92 (1.86)	4.08 (1.79)	4.84 [-0.24; 9.92]	0.062

	Treatment Groups		Comparison	
VFQ 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)	82.35 (18.90)	79.59 (22.05)		
Week 52 Mean (SD)	86.05 (20.63)	80.95 (23.30)		
Week 28: Adjusted Mean Change (SE)	6.15 (2.21)	2.51 (2.31)		
Week 52: Adjusted Mean Change (SE)	4.39 (2.33)	-1.43 (2.36)	5.83 [-0.70; 12.35]	0.080
≥ 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 28: Adjusted Mean Change (SE)	3.11 (2.45)	6.64 (2.55)		
Week 52: Adjusted Mean Change (SE)	4.33 (2.61)	8.82 (2.64)	-4.49 [-11.79; 2.81]	0.227
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.428			
≤ 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 28: Adjusted Mean Change (SE)	3.99 (1.22)	7.17 (1.23)		
Week 52: Adjusted Mean Change (SE)	8.17 (1.26)	5.70 (1.26)	2.47 [-1.03; 5.98]	0.166
> 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 28: Adjusted Mean Change (SE)	4.35 (1.96)	4.89 (1.86)		
Week 52: Adjusted Mean Change (SE)	3.65 (2.05)	4.46 (1.91)	-0.81 [-6.30; 4.68]	0.771
≥ 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 28: Adjusted Mean Change (SE)	2.25 (1.93)	5.79 (1.99)		
Week 52: Adjusted Mean Change (SE)	2.65 (2.07)	6.76 (2.00)	-4.11 [-9.76; 1.54]	0.153

	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=0.700**				
KESTREL: General Health				
Interaction test	p=0.760			
≤ 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 28: Adjusted Mean Change (SE)	6.04 (1.72)	5.63 (1.82)		
Week 52: Adjusted Mean Change (SE)	10.48 (2.07)	6.56 (2.13)	3.92 [-1.94; 9.77]	0.189
> 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 28: Adjusted Mean Change (SE)	0.75 (3.55)	2.25 (3.02)		
Week 52: Adjusted Mean Change (SE)	5.79 (4.47)	3.71 (3.70)	2.08 [-9.35; 13.50]	0.721
≥ 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 28: Adjusted Mean Change (SE)	1.72 (3.07)	4.45 (3.12)		
Week 52: Adjusted Mean Change (SE)	3.02 (3.95)	2.38 (3.61)	0.63 [-9.87; 11.14]	0.905
KITE: General Health				
Interaction test	p=0.562			
≤ 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 28: Adjusted Mean Change (SE)	5.77 (2.03)	6.29 (1.93)		
Week 52: Adjusted Mean Change (SE)	3.10 (2.42)	4.92 (2.31)	-1.82 [-8.41; 4.78]	0.588
> 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 28: Adjusted Mean Change (SE)	1.87 (2.55)	2.52 (2.67)		
Week 52: Adjusted Mean Change (SE)	9.23 (3.03)	2.91 (3.08)	6.31 [-2.18; 14.81]	0.145

	Treatment Groups		Comparison	
VFQ by duration of DME (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 28: Adjusted Mean Change (SE)	1.63 (2.83)	2.31 (2.95)		
Week 52: Adjusted Mean Change (SE)	5.31 (3.40)	7.42 (3.43)	-2.11 [-11.61; 7.39]	0.662
Pooled Analysis: General Health				
Interaction test	p=0.617			
≤ 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 28: Adjusted Mean Change (SE)	5.60 (1.32)	6.04 (1.32)		
Week 52: Adjusted Mean Change (SE)	7.22 (1.57)	5.95 (1.57)	1.27 [-3.08; 5.63]	0.565
> 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 28: Adjusted Mean Change (SE)	1.72 (2.10)	2.36 (2.01)		
Week 52: Adjusted Mean Change (SE)	8.23 (2.54)	3.13 (2.38)	5.10 [-1.74; 11.95]	0.144
≥ 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 28: Adjusted Mean Change (SE)	1.69 (2.08)	3.62 (2.14)		
Week 52: Adjusted Mean Change (SE)	4.42 (2.59)	5.33 (2.49)	-0.91 [-7.95; 6.13]	0.800

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 52

	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=0.071**				
KESTREL: Composite Score				
Interaction test	p=0.821			
focal				
N'/ N	59 / 59	48 / 48		
Baseline Mean (SD)	77.65 (16.27)	80.21 (13.63)		
Week 52 Mean (SD)	85.75 (14.72)	86.50 (13.72)		
Week 28: Adjusted Mean Change (SE)	5.39 (1.41)	6.56 (1.57)		
Week 52: Adjusted Mean Change (SE)	7.17 (1.45)	8.58 (1.62)	-1.41 [-5.67; 2.86]	0.517
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 28: Adjusted Mean Change (SE)	6.14 (0.97)	8.12 (0.95)		
Week 52: Adjusted Mean Change (SE)	6.78 (1.03)	8.40 (0.97)	-1.62 [-4.40; 1.15]	0.251
KITE: Composite Score				
Interaction test	p=0.317			
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 28: Adjusted Mean Change (SE)	6.92 (1.29)	5.27 (1.24)		
Week 52: Adjusted Mean Change (SE)	9.92 (1.42)	6.54 (1.37)	3.39 [-0.49; 7.26]	0.086
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 28: Adjusted Mean Change (SE)	5.09 (0.95)	6.20 (0.98)		
Week 52: Adjusted Mean Change (SE)	8.29 (1.02)	6.28 (1.03)	2.01 [-0.84; 4.85]	0.166

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Composite Score				
Interaction test	p=0.514			
focal				
N'/ N	122 / 122	114 / 114		
Baseline Mean (SD)	78.02 (15.06)	80.22 (14.48)		
Week 52 Mean (SD)	86.86 (12.72)	86.18 (13.82)		
Week 28: Adjusted Mean Change (SE)	6.20 (0.97)	6.10 (1.00)		
Week 52: Adjusted Mean Change (SE)	8.53 (1.02)	7.75 (1.05)	0.78 [-2.09; 3.65]	0.592
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 28: Adjusted Mean Change (SE)	5.69 (0.69)	7.10 (0.69)		
Week 52: Adjusted Mean Change (SE)	7.56 (0.73)	7.29 (0.71)	0.27 [-1.72; 2.26]	0.789
General Vision				
Test of heterogeneity in main analysis: **p_H=0.986**				
KESTREL: General Vision				
Interaction test	p=0.581			
focal				
N'/ N	59 / 59	48 / 48		
Baseline Mean (SD)	64.75 (16.75)	63.33 (13.26)		
Week 52 Mean (SD)	75.20 (14.32)	74.00 (14.46)		
Week 28: Adjusted Mean Change (SE)	10.70 (1.73)	11.20 (1.92)		
Week 52: Adjusted Mean Change (SE)	12.48 (1.79)	12.63 (1.99)	-0.15 [-5.42; 5.12]	0.955
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 28: Adjusted Mean Change (SE)	11.58 (1.18)	10.40 (1.17)		
Week 52: Adjusted Mean Change (SE)	10.76 (1.27)	9.73 (1.19)	1.04 [-2.39; 4.47]	0.551

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Vision				
Interaction test	p=0.829			
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 28: Adjusted Mean Change (SE)	10.17 (1.75)	7.79 (1.68)		
Week 52: Adjusted Mean Change (SE)	11.25 (1.97)	11.86 (1.91)	-0.61 [-5.99; 4.77]	0.824
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 28: Adjusted Mean Change (SE)	8.78 (1.28)	10.56 (1.33)		
Week 52: Adjusted Mean Change (SE)	11.67 (1.41)	9.30 (1.42)	2.37 [-1.56; 6.30]	0.236
Pooled Analysis: General Vision				
Interaction test	p=0.808			
focal				
N'/ N	122 / 122	114 / 114		
Baseline Mean (SD)	64.10 (15.41)	62.63 (17.14)		
Week 52 Mean (SD)	74.08 (14.70)	73.41 (16.07)		
Week 28: Adjusted Mean Change (SE)	10.36 (1.24)	9.24 (1.27)		
Week 52: Adjusted Mean Change (SE)	11.72 (1.33)	12.25 (1.38)	-0.53 [-4.29; 3.23]	0.782
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 28: Adjusted Mean Change (SE)	10.25 (0.88)	10.48 (0.88)		
Week 52: Adjusted Mean Change (SE)	11.27 (0.95)	9.53 (0.92)	1.75 [-0.85; 4.34]	0.187

	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=0.492**				
KESTREL: Ocular Pain				
Interaction test	p=0.876			
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 28: Adjusted Mean Change (SE)	1.77 (2.33)	1.83 (2.60)		
Week 52: Adjusted Mean Change (SE)	3.29 (2.11)	3.00 (2.35)	0.29 [-5.93; 6.51]	0.927
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 28: Adjusted Mean Change (SE)	3.23 (1.60)	5.17 (1.58)		
Week 52: Adjusted Mean Change (SE)	5.86 (1.51)	4.74 (1.40)	1.12 [-2.94; 5.17]	0.588
KITE: Ocular Pain				
Interaction test	p=0.711			
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 28: Adjusted Mean Change (SE)	5.14 (2.00)	3.47 (1.92)		
Week 52: Adjusted Mean Change (SE)	5.77 (2.13)	4.40 (2.06)	1.37 [-4.45; 7.20]	0.643
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 28: Adjusted Mean Change (SE)	4.13 (1.47)	4.20 (1.52)		
Week 52: Adjusted Mean Change (SE)	4.81 (1.52)	3.84 (1.52)	0.97 [-3.26; 5.20]	0.652

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Ocular Pain				
Interaction test	p=0.760			
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 28: Adjusted Mean Change (SE)	3.48 (1.54)	2.77 (1.58)		
Week 52: Adjusted Mean Change (SE)	4.56 (1.50)	3.85 (1.56)	0.71 [-3.54; 4.96]	0.742
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 28: Adjusted Mean Change (SE)	3.71 (1.09)	4.69 (1.10)		
Week 52: Adjusted Mean Change (SE)	5.36 (1.07)	4.32 (1.04)	1.05 [-1.88; 3.98]	0.483
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.456**				
KESTREL: Near Activities				
Interaction test	p=0.441			
focal				
N'/ N	59 / 59	48 / 48		
Baseline Mean (SD)	65.11 (24.20)	70.23 (18.61)		
Week 52 Mean (SD)	83.00 (18.13)	81.04 (20.50)		
Week 28: Adjusted Mean Change (SE)	12.72 (2.41)	13.23 (2.70)		
Week 52: Adjusted Mean Change (SE)	16.35 (2.61)	14.60 (2.92)	1.75 [-5.96; 9.46]	0.656
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 28: Adjusted Mean Change (SE)	12.47 (1.66)	15.21 (1.63)		
Week 52: Adjusted Mean Change (SE)	11.86 (1.87)	13.72 (1.74)	-1.86 [-6.89; 3.16]	0.466

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Near Activities				
Interaction test	p=0.729			
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 28: Adjusted Mean Change (SE)	6.90 (2.37)	6.68 (2.26)		
Week 52: Adjusted Mean Change (SE)	12.85 (2.41)	9.72 (2.33)	3.13 [-3.45; 9.71]	0.351
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 28: Adjusted Mean Change (SE)	6.03 (1.73)	5.45 (1.79)		
Week 52: Adjusted Mean Change (SE)	8.88 (1.72)	8.61 (1.74)	0.26 [-4.55; 5.08]	0.914
Pooled Analysis: Near Activities				
Interaction test	p=0.536			
focal				
N'/ N	121 / 122	114 / 114		
Baseline Mean (SD)	68.80 (23.01)	72.62 (20.87)		
Week 52 Mean (SD)	83.42 (17.40)	81.96 (20.45)		
Week 28: Adjusted Mean Change (SE)	10.07 (1.71)	10.20 (1.76)		
Week 52: Adjusted Mean Change (SE)	14.64 (1.79)	12.65 (1.86)	1.99 [-3.08; 7.07]	0.441
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 28: Adjusted Mean Change (SE)	9.40 (1.21)	10.29 (1.22)		
Week 52: Adjusted Mean Change (SE)	10.44 (1.28)	10.96 (1.24)	-0.52 [-4.02; 2.98]	0.770

	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=0.136**				
KESTREL: Distance Activities				
Interaction test	p=0.516			
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 28: Adjusted Mean Change (SE)	4.84 (2.10)	8.35 (2.35)		
Week 52: Adjusted Mean Change (SE)	8.91 (1.99)	10.51 (2.22)	-1.59 [-7.46; 4.27]	0.593
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 28: Adjusted Mean Change (SE)	9.15 (1.45)	9.41 (1.42)		
Week 52: Adjusted Mean Change (SE)	9.15 (1.42)	9.83 (1.33)	-0.67 [-4.49; 3.14]	0.729
KITE: Distance Activities				
Interaction test	p=0.589			
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 28: Adjusted Mean Change (SE)	6.08 (2.04)	6.24 (1.96)		
Week 52: Adjusted Mean Change (SE)	11.38 (1.96)	9.04 (1.90)	2.34 [-3.02; 7.70]	0.392
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 28: Adjusted Mean Change (SE)	6.25 (1.50)	4.82 (1.54)		
Week 52: Adjusted Mean Change (SE)	11.26 (1.40)	7.34 (1.41)	3.92 [0.01; 7.83]	0.050 *

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Distance Activities				
Interaction test	p=0.326			
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 28: Adjusted Mean Change (SE)	5.47 (1.48)	7.48 (1.52)		
Week 52: Adjusted Mean Change (SE)	10.12 (1.40)	10.03 (1.45)	0.09 [-3.87; 4.04]	0.966
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 28: Adjusted Mean Change (SE)	7.82 (1.05)	7.16 (1.06)		
Week 52: Adjusted Mean Change (SE)	10.25 (1.00)	8.55 (0.97)	1.69 [-1.04; 4.42]	0.224
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.037 ***				
KESTREL: Social Functioning				
Interaction test	p=0.885			
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 28: Adjusted Mean Change (SE)	-0.00 (1.58)	3.01 (1.77)		
Week 52: Adjusted Mean Change (SE)	3.57 (1.79)	4.46 (2.03)	-0.90 [-6.23; 4.44]	0.741
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 28: Adjusted Mean Change (SE)	2.76 (1.09)	4.21 (1.07)		
Week 52: Adjusted Mean Change (SE)	2.22 (1.28)	3.96 (1.19)	-1.74 [-5.19; 1.71]	0.323

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Social Functioning				
Interaction test	p=0.698			
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 28: Adjusted Mean Change (SE)	5.53 (1.79)	4.63 (1.72)		
Week 52: Adjusted Mean Change (SE)	8.27 (1.58)	4.87 (1.53)	3.40 [-0.92; 7.72]	0.122
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 28: Adjusted Mean Change (SE)	2.71 (1.32)	3.09 (1.36)		
Week 52: Adjusted Mean Change (SE)	6.87 (1.12)	4.01 (1.13)	2.85 [-0.28; 5.99]	0.074
Pooled Analysis: Social Functioning				
Interaction test	p=0.956			
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 28: Adjusted Mean Change (SE)	2.82 (1.20)	4.08 (1.24)		
Week 52: Adjusted Mean Change (SE)	5.94 (1.20)	4.87 (1.25)	1.07 [-2.34; 4.47]	0.538
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 28: Adjusted Mean Change (SE)	2.83 (0.86)	3.57 (0.86)		
Week 52: Adjusted Mean Change (SE)	4.60 (0.86)	3.86 (0.83)	0.74 [-1.60; 3.08]	0.533

	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=0.300**				
KESTREL: Mental Health				
Interaction test	p=0.468			
focal				
N'/ N	59 / 59	48 / 48		
Baseline Mean (SD)	66.63 (24.77)	73.05 (20.55)		
Week 52 Mean (SD)	79.13 (22.18)	79.53 (18.83)		
Week 28: Adjusted Mean Change (SE)	8.00 (2.28)	7.40 (2.55)		
Week 52: Adjusted Mean Change (SE)	10.51 (2.26)	10.75 (2.53)	-0.23 [-6.91; 6.44]	0.945
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 28: Adjusted Mean Change (SE)	7.01 (1.57)	9.65 (1.54)		
Week 52: Adjusted Mean Change (SE)	9.64 (1.62)	11.54 (1.50)	-1.90 [-6.24; 2.45]	0.391
KITE: Mental Health				
Interaction test	p=0.217			
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 28: Adjusted Mean Change (SE)	12.31 (2.17)	7.92 (2.09)		
Week 52: Adjusted Mean Change (SE)	15.32 (2.69)	10.96 (2.61)	4.36 [-3.01; 11.72]	0.245
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 28: Adjusted Mean Change (SE)	6.57 (1.60)	9.81 (1.66)		
Week 52: Adjusted Mean Change (SE)	11.73 (1.93)	8.74 (1.95)	2.99 [-2.41; 8.38]	0.277

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Mental Health				
Interaction test	p=0.208			
focal				
N'/ N	122 / 122	114 / 114		
Baseline Mean (SD)	67.88 (23.61)	72.26 (21.89)		
Week 52 Mean (SD)	81.44 (19.69)	80.01 (20.29)		
Week 28: Adjusted Mean Change (SE)	10.21 (1.57)	7.81 (1.63)		
Week 52: Adjusted Mean Change (SE)	12.84 (1.75)	11.02 (1.82)	1.82 [-3.15; 6.78]	0.473
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 28: Adjusted Mean Change (SE)	6.92 (1.12)	9.61 (1.13)		
Week 52: Adjusted Mean Change (SE)	10.79 (1.25)	10.11 (1.21)	0.68 [-2.75; 4.10]	0.699
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.072**				
KESTREL: Role Difficulties				
Interaction test	p=0.904			
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 28: Adjusted Mean Change (SE)	6.98 (2.81)	9.22 (3.15)		
Week 52: Adjusted Mean Change (SE)	5.93 (3.04)	12.00 (3.40)	-6.07 [-15.04; 2.90]	0.184
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 28: Adjusted Mean Change (SE)	5.96 (1.94)	9.08 (1.91)		
Week 52: Adjusted Mean Change (SE)	6.93 (2.17)	11.04 (2.02)	-4.11 [-9.95; 1.73]	0.168

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Role Difficulties				
Interaction test	p=0.886			
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 28: Adjusted Mean Change (SE)	7.23 (2.70)	8.44 (2.60)		
Week 52: Adjusted Mean Change (SE)	12.55 (2.94)	7.72 (2.86)	4.83 [-3.21; 12.87]	0.238
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 28: Adjusted Mean Change (SE)	7.33 (1.99)	8.18 (2.06)		
Week 52: Adjusted Mean Change (SE)	12.19 (2.10)	8.91 (2.12)	3.29 [-2.57; 9.15]	0.271
Pooled Analysis: Role Difficulties				
Interaction test	p=0.992			
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 28: Adjusted Mean Change (SE)	7.12 (1.96)	8.93 (2.02)		
Week 52: Adjusted Mean Change (SE)	9.18 (2.11)	9.75 (2.19)	-0.57 [-6.53; 5.39]	0.851
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 28: Adjusted Mean Change (SE)	6.67 (1.39)	8.60 (1.40)		
Week 52: Adjusted Mean Change (SE)	9.51 (1.50)	10.01 (1.46)	-0.50 [-4.62; 3.61]	0.810

	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=0.029 ***				
KESTREL: Dependency				
Interaction test	p=0.708			
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 28: Adjusted Mean Change (SE)	7.53 (2.43)	5.59 (2.72)		
Week 52: Adjusted Mean Change (SE)	4.12 (2.46)	8.71 (2.75)	-4.59 [-11.85; 2.68]	0.215
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 28: Adjusted Mean Change (SE)	4.91 (1.68)	7.28 (1.65)		
Week 52: Adjusted Mean Change (SE)	6.16 (1.76)	9.21 (1.64)	-3.05 [-7.78; 1.68]	0.206
KITE: Dependency				
Interaction test	p=0.226			
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 28: Adjusted Mean Change (SE)	7.32 (2.19)	2.43 (2.11)		
Week 52: Adjusted Mean Change (SE)	10.14 (2.42)	2.59 (2.35)	7.55 [0.92; 14.18]	0.026 *
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 28: Adjusted Mean Change (SE)	4.62 (1.61)	3.20 (1.67)		
Week 52: Adjusted Mean Change (SE)	6.06 (1.73)	3.39 (1.75)	2.67 [-2.17; 7.52]	0.279

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Dependency				
Interaction test	p=0.356			
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 28: Adjusted Mean Change (SE)	7.43 (1.64)	4.38 (1.70)		
Week 52: Adjusted Mean Change (SE)	7.07 (1.74)	5.89 (1.81)	1.18 [-3.75; 6.10]	0.639
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 28: Adjusted Mean Change (SE)	4.84 (1.17)	5.16 (1.18)		
Week 52: Adjusted Mean Change (SE)	6.15 (1.24)	6.27 (1.20)	-0.12 [-3.52; 3.28]	0.945
Driving				
Test of heterogeneity in main analysis: **p_H=0.778**				
KESTREL: Driving				
Interaction test	p=0.939			
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 28: Adjusted Mean Change (SE)	6.16 (2.38)	9.43 (2.75)		
Week 52: Adjusted Mean Change (SE)	7.00 (2.70)	10.26 (3.23)	-3.26 [-11.56; 5.04]	0.440
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 28: Adjusted Mean Change (SE)	0.06 (1.67)	4.19 (1.67)		
Week 52: Adjusted Mean Change (SE)	1.91 (1.98)	4.94 (1.94)	-3.03 [-8.51; 2.44]	0.276

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Driving				
Interaction test	p=0.130			
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 28: Adjusted Mean Change (SE)	2.98 (2.45)	4.56 (2.21)		
Week 52: Adjusted Mean Change (SE)	8.39 (2.11)	4.84 (1.99)	3.56 [-2.17; 9.29]	0.222
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 28: Adjusted Mean Change (SE)	-0.80 (1.78)	6.60 (2.05)		
Week 52: Adjusted Mean Change (SE)	4.33 (1.58)	5.38 (1.80)	-1.05 [-5.77; 3.67]	0.661
Pooled Analysis: Driving				
Interaction test	p=0.314			
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 28: Adjusted Mean Change (SE)	4.59 (1.71)	6.80 (1.74)		
Week 52: Adjusted Mean Change (SE)	7.61 (1.74)	7.25 (1.84)	0.36 [-4.62; 5.33]	0.888
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 28: Adjusted Mean Change (SE)	-0.35 (1.22)	5.03 (1.30)		
Week 52: Adjusted Mean Change (SE)	3.12 (1.29)	5.06 (1.35)	-1.94 [-5.61; 1.73]	0.300

	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=0.691**				
KESTREL: Color Vision				
Interaction test	p=0.897			
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 28: Adjusted Mean Change (SE)	2.49 (1.49)	2.47 (1.67)		
Week 52: Adjusted Mean Change (SE)	2.89 (1.50)	1.58 (1.70)	1.31 [-3.16; 5.77]	0.565
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 28: Adjusted Mean Change (SE)	1.84 (1.03)	1.30 (1.02)		
Week 52: Adjusted Mean Change (SE)	1.78 (1.08)	1.57 (1.02)	0.21 [-2.70; 3.12]	0.887
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 28: Adjusted Mean Change (SE)	4.38 (1.39)	4.72 (1.36)		
Week 52: Adjusted Mean Change (SE)	6.65 (1.29)	4.24 (1.29)	2.41 [-1.17; 6.00]	0.187
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 28: Adjusted Mean Change (SE)	3.05 (1.03)	3.45 (1.06)		
Week 52: Adjusted Mean Change (SE)	5.20 (0.92)	2.80 (0.93)	2.41 [-0.17; 4.98]	0.067

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Color Vision				
Interaction test	p=0.975			
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 28: Adjusted Mean Change (SE)	3.52 (1.03)	3.71 (1.07)		
Week 52: Adjusted Mean Change (SE)	4.79 (0.99)	3.11 (1.04)	1.68 [-1.14; 4.50]	0.241
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 28: Adjusted Mean Change (SE)	2.48 (0.74)	2.27 (0.74)		
Week 52: Adjusted Mean Change (SE)	3.47 (0.71)	2.09 (0.69)	1.38 [-0.55; 3.31]	0.161
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.021 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.902			
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 28: Adjusted Mean Change (SE)	0.55 (2.33)	5.17 (2.60)		
Week 52: Adjusted Mean Change (SE)	5.92 (2.39)	7.13 (2.68)	-1.21 [-8.29; 5.87]	0.736
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 28: Adjusted Mean Change (SE)	4.38 (1.61)	8.77 (1.58)		
Week 52: Adjusted Mean Change (SE)	5.29 (1.72)	7.57 (1.60)	-2.28 [-6.90; 2.34]	0.332

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Peripheral Vision				
Interaction test	p=0.734			
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 28: Adjusted Mean Change (SE)	5.73 (2.04)	5.20 (1.96)		
Week 52: Adjusted Mean Change (SE)	6.85 (2.23)	5.75 (2.17)	1.10 [-5.03; 7.23]	0.724
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 28: Adjusted Mean Change (SE)	4.06 (1.50)	4.15 (1.55)		
Week 52: Adjusted Mean Change (SE)	6.10 (1.60)	2.30 (1.61)	3.80 [-0.66; 8.26]	0.095
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.663			
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 28: Adjusted Mean Change (SE)	3.06 (1.56)	5.89 (1.60)		
Week 52: Adjusted Mean Change (SE)	6.15 (1.65)	7.10 (1.71)	-0.95 [-5.61; 3.71]	0.690
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 28: Adjusted Mean Change (SE)	4.15 (1.11)	6.52 (1.12)		
Week 52: Adjusted Mean Change (SE)	5.64 (1.18)	5.04 (1.14)	0.60 [-2.62; 3.82]	0.714

	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=0.700**				
KESTREL: General Health				
Interaction test	p=0.786			
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 28: Adjusted Mean Change (SE)	4.25 (2.43)	3.77 (2.71)		
Week 52: Adjusted Mean Change (SE)	10.08 (2.94)	5.18 (3.28)	4.90 [-3.77; 13.57]	0.267
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 28: Adjusted Mean Change (SE)	4.68 (1.67)	4.22 (1.65)		
Week 52: Adjusted Mean Change (SE)	7.15 (2.10)	4.37 (1.96)	2.78 [-2.90; 8.46]	0.336
KITE: General Health				
Interaction test	p=0.241			
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 28: Adjusted Mean Change (SE)	4.24 (2.35)	7.04 (2.26)		
Week 52: Adjusted Mean Change (SE)	5.31 (2.82)	8.46 (2.74)	-3.15 [-10.88; 4.59]	0.424
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 28: Adjusted Mean Change (SE)	2.97 (1.73)	3.03 (1.78)		
Week 52: Adjusted Mean Change (SE)	4.96 (2.01)	2.58 (2.02)	2.38 [-3.22; 7.98]	0.403

	Treatment Groups		Comparison	
VFQ by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: General Health				
Interaction test	p=0.515			
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 28: Adjusted Mean Change (SE)	4.17 (1.69)	5.82 (1.75)		
Week 52: Adjusted Mean Change (SE)	7.68 (2.04)	7.20 (2.11)	0.48 [-5.28; 6.23]	0.871
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 28: Adjusted Mean Change (SE)	3.72 (1.20)	3.77 (1.21)		
Week 52: Adjusted Mean Change (SE)	5.95 (1.45)	3.63 (1.40)	2.32 [-1.64; 6.29]	0.251

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 52

	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=0.071**				
KESTREL: Composite Score				
Interaction test	p=0.089			
< 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 28: Adjusted Mean Change (SE)	7.07 (1.06)	7.01 (1.12)		
Week 52: Adjusted Mean Change (SE)	8.32 (1.11)	8.38 (1.15)	-0.06 [-3.20; 3.09]	0.971
≥ 450 - < 650 µm				
N'/ N	69 / 70	71 / 71		
Baseline Mean (SD)	74.53 (16.31)	75.38 (14.61)		
Week 52 Mean (SD)	83.35 (12.60)	84.31 (13.17)		
Week 28: Adjusted Mean Change (SE)	4.97 (1.30)	8.19 (1.31)		
Week 52: Adjusted Mean Change (SE)	6.25 (1.37)	8.24 (1.33)	-1.99 [-5.75; 1.76]	0.297
≥ 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 28: Adjusted Mean Change (SE)	-0.45 (3.17)	9.43 (2.48)		
Week 52: Adjusted Mean Change (SE)	2.27 (3.40)	8.53 (2.59)	-6.26 [-14.63; 2.12]	0.143
KITE: Composite Score				
Interaction test	p=0.915			
< 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 28: Adjusted Mean Change (SE)	5.20 (1.14)	5.21 (1.17)		
Week 52: Adjusted Mean Change (SE)	7.21 (1.25)	5.59 (1.28)	1.62 [-1.89; 5.13]	0.364

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 28: Adjusted Mean Change (SE)	6.39 (1.18)	6.34 (1.13)		
Week 52: Adjusted Mean Change (SE)	9.93 (1.24)	6.76 (1.19)	3.16 [-0.23; 6.56]	0.068
≥ 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 28: Adjusted Mean Change (SE)	6.69 (2.22)	8.10 (2.40)		
Week 52: Adjusted Mean Change (SE)	11.74 (2.53)	9.12 (2.53)	2.63 [-4.41; 9.66]	0.463
Pooled Analysis: Composite Score				
Interaction test	p=0.280			
< 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 28: Adjusted Mean Change (SE)	6.32 (0.78)	6.07 (0.82)		
Week 52: Adjusted Mean Change (SE)	7.90 (0.84)	7.04 (0.86)	0.86 [-1.50; 3.21]	0.475
≥ 450 - < 650 µm				
N'/ N	143 / 144	150 / 150		
Baseline Mean (SD)	75.88 (15.98)	74.86 (16.42)		
Week 52 Mean (SD)	85.23 (12.35)	83.08 (14.93)		
Week 28: Adjusted Mean Change (SE)	5.84 (0.89)	7.15 (0.87)		
Week 52: Adjusted Mean Change (SE)	8.31 (0.93)	7.40 (0.90)	0.91 [-1.63; 3.44]	0.483

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 28: Adjusted Mean Change (SE)	3.78 (1.87)	9.29 (1.75)		
Week 52: Adjusted Mean Change (SE)	7.87 (2.06)	9.39 (1.82)	-1.52 [-6.90; 3.85]	0.578
General Vision				
Test of heterogeneity in main analysis: **p_H=0.986**				
KESTREL: General Vision				
Interaction test	p=0.107			
< 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 28: Adjusted Mean Change (SE)	12.32 (1.29)	10.16 (1.38)		
Week 52: Adjusted Mean Change (SE)	13.00 (1.36)	11.15 (1.40)	1.86 [-1.97; 5.68]	0.341
≥ 450 - < 650 µm				
N'/ N	69 / 70	71 / 71		
Baseline Mean (SD)	59.71 (16.62)	56.06 (14.59)		
Week 52 Mean (SD)	72.00 (11.93)	69.18 (12.42)		
Week 28: Adjusted Mean Change (SE)	10.86 (1.58)	10.93 (1.61)		
Week 52: Adjusted Mean Change (SE)	11.03 (1.68)	9.89 (1.62)	1.14 [-3.45; 5.73]	0.625
≥ 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 28: Adjusted Mean Change (SE)	5.31 (3.87)	11.83 (3.02)		
Week 52: Adjusted Mean Change (SE)	2.71 (4.16)	11.01 (3.14)	-8.30 [-18.52; 1.93]	0.111
KITE: General Vision				
Interaction test	p=0.333			
< 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 28: Adjusted Mean Change (SE)	9.00 (1.53)	8.71 (1.57)		
Week 52: Adjusted Mean Change (SE)	11.06 (1.73)	10.46 (1.77)	0.60 [-4.26; 5.45]	0.809

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 28: Adjusted Mean Change (SE)	10.42 (1.59)	10.15 (1.51)		
Week 52: Adjusted Mean Change (SE)	12.94 (1.71)	9.29 (1.64)	3.65 [-1.02; 8.33]	0.125
≥ 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 28: Adjusted Mean Change (SE)	7.84 (2.99)	11.79 (3.25)		
Week 52: Adjusted Mean Change (SE)	9.48 (3.53)	14.71 (3.49)	-5.23 [-14.96; 4.50]	0.291
Pooled Analysis: General Vision				
Interaction test	p=0.077			
< 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 28: Adjusted Mean Change (SE)	10.79 (1.00)	9.36 (1.04)		
Week 52: Adjusted Mean Change (SE)	12.09 (1.09)	10.70 (1.12)	1.39 [-1.66; 4.44]	0.371
≥ 450 - < 650 µm				
N'/ N	143 / 144	150 / 150		
Baseline Mean (SD)	60.84 (16.59)	57.20 (16.87)		
Week 52 Mean (SD)	72.89 (11.79)	69.02 (15.27)		
Week 28: Adjusted Mean Change (SE)	10.75 (1.13)	10.66 (1.11)		
Week 52: Adjusted Mean Change (SE)	12.16 (1.20)	9.73 (1.16)	2.43 [-0.85; 5.70]	0.147
≥ 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 28: Adjusted Mean Change (SE)	6.88 (2.37)	11.81 (2.22)		
Week 52: Adjusted Mean Change (SE)	6.94 (2.68)	12.91 (2.35)	-5.97 [-12.95; 1.01]	0.094

	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=0.492**				
KESTREL: Ocular Pain				
Interaction test	p=0.077			
< 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 28: Adjusted Mean Change (SE)	3.27 (1.74)	2.15 (1.84)		
Week 52: Adjusted Mean Change (SE)	5.37 (1.61)	4.32 (1.65)	1.05 [-3.49; 5.59]	0.650
≥ 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 28: Adjusted Mean Change (SE)	3.35 (2.13)	4.95 (2.15)		
Week 52: Adjusted Mean Change (SE)	5.07 (1.99)	2.93 (1.91)	2.14 [-3.29; 7.58]	0.439
≥ 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 28: Adjusted Mean Change (SE)	-5.53 (5.20)	12.65 (4.04)		
Week 52: Adjusted Mean Change (SE)	4.31 (4.93)	9.90 (3.71)	-5.60 [-17.71; 6.51]	0.364
KITE: Ocular Pain				
Interaction test	p=0.796			
< 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 28: Adjusted Mean Change (SE)	4.31 (1.75)	4.17 (1.80)		
Week 52: Adjusted Mean Change (SE)	4.13 (1.86)	2.26 (1.90)	1.87 [-3.37; 7.10]	0.484
≥ 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 28: Adjusted Mean Change (SE)	3.93 (1.83)	3.70 (1.73)		
Week 52: Adjusted Mean Change (SE)	5.70 (1.84)	5.55 (1.76)	0.16 [-4.85; 5.16]	0.951

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 28: Adjusted Mean Change (SE)	8.60 (3.42)	4.32 (3.71)		
Week 52: Adjusted Mean Change (SE)	5.85 (3.81)	3.42 (3.72)	2.43 [-8.04; 12.90]	0.648
Pooled Analysis: Ocular Pain				
Interaction test	p=0.470			
< 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 28: Adjusted Mean Change (SE)	3.81 (1.24)	3.04 (1.30)		
Week 52: Adjusted Mean Change (SE)	4.97 (1.23)	3.47 (1.26)	1.51 [-1.94; 4.96]	0.392
≥ 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 28: Adjusted Mean Change (SE)	3.60 (1.41)	4.18 (1.37)		
Week 52: Adjusted Mean Change (SE)	5.33 (1.36)	4.24 (1.30)	1.09 [-2.61; 4.79]	0.564
≥ 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 28: Adjusted Mean Change (SE)	3.68 (2.95)	8.77 (2.76)		
Week 52: Adjusted Mean Change (SE)	5.42 (3.03)	7.05 (2.64)	-1.62 [-9.52; 6.27]	0.687
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.456**				
KESTREL: Near Activities				
Interaction test	p=0.251			
< 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 28: Adjusted Mean Change (SE)	14.06 (1.80)	15.73 (1.92)		
Week 52: Adjusted Mean Change (SE)	16.36 (1.98)	13.01 (2.04)	3.35 [-2.23; 8.93]	0.238

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 450 - < 650 µm				
N'/ N	69 / 70	71 / 71		
Baseline Mean (SD)	59.00 (24.10)	63.15 (19.84)		
Week 52 Mean (SD)	75.53 (19.61)	79.30 (20.10)		
Week 28: Adjusted Mean Change (SE)	11.40 (2.21)	14.77 (2.22)		
Week 52: Adjusted Mean Change (SE)	11.02 (2.45)	15.47 (2.35)	-4.45 [-11.12; 2.22]	0.190
≥ 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 28: Adjusted Mean Change (SE)	3.30 (5.39)	7.99 (4.21)		
Week 52: Adjusted Mean Change (SE)	1.26 (6.05)	11.35 (4.58)	-10.09 [-24.98; 4.80]	0.183
KITE: Near Activities				
Interaction test	p=0.869			
< 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 28: Adjusted Mean Change (SE)	6.98 (2.06)	7.03 (2.11)		
Week 52: Adjusted Mean Change (SE)	9.67 (2.11)	9.95 (2.16)	-0.28 [-6.21; 5.66]	0.927
≥ 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 28: Adjusted Mean Change (SE)	6.59 (2.13)	6.12 (2.03)		
Week 52: Adjusted Mean Change (SE)	11.52 (2.10)	9.13 (2.01)	2.39 [-3.35; 8.14]	0.413
≥ 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 28: Adjusted Mean Change (SE)	4.72 (4.01)	1.95 (4.33)		
Week 52: Adjusted Mean Change (SE)	8.63 (4.30)	6.78 (4.27)	1.85 [-10.05; 13.76]	0.760

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Near Activities				
Interaction test	p=0.731			
< 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 28: Adjusted Mean Change (SE)	10.75 (1.37)	11.41 (1.43)		
Week 52: Adjusted Mean Change (SE)	13.19 (1.46)	11.25 (1.50)	1.94 [-2.17; 6.04]	0.356
≥ 450 - < 650 µm				
N'/ N	143 / 144	150 / 150		
Baseline Mean (SD)	64.83 (24.21)	64.28 (21.02)		
Week 52 Mean (SD)	78.75 (19.45)	77.38 (21.60)		
Week 28: Adjusted Mean Change (SE)	9.52 (1.55)	10.11 (1.51)		
Week 52: Adjusted Mean Change (SE)	11.84 (1.62)	12.09 (1.56)	-0.24 [-4.66; 4.17]	0.913
≥ 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 28: Adjusted Mean Change (SE)	4.35 (3.26)	5.69 (3.04)		
Week 52: Adjusted Mean Change (SE)	5.85 (3.61)	9.88 (3.16)	-4.02 [-13.41; 5.36]	0.400
Distance Activities				
Test of heterogeneity in main analysis: **p_H=0.136**				
KESTREL: Distance Activities				
Interaction test	p=0.388			
< 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 28: Adjusted Mean Change (SE)	9.57 (1.59)	6.97 (1.68)		
Week 52: Adjusted Mean Change (SE)	9.26 (1.52)	10.14 (1.57)	-0.88 [-5.18; 3.42]	0.688
≥ 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 28: Adjusted Mean Change (SE)	4.31 (1.95)	11.06 (1.96)		
Week 52: Adjusted Mean Change (SE)	8.40 (1.88)	8.33 (1.82)	0.07 [-5.07; 5.20]	0.980

	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)	67.01 (23.60)	65.00 (20.30)		
Week 52 Mean (SD)	84.26 (22.61)	83.07 (14.47)		
Week 28: Adjusted Mean Change (SE)	7.24 (4.76)	11.04 (3.71)		
Week 52: Adjusted Mean Change (SE)	12.45 (4.65)	12.08 (3.53)	0.37 [-11.06; 11.80]	0.949
KITE: Distance Activities				
Interaction test	p=0.998			
< 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 28: Adjusted Mean Change (SE)	6.45 (1.77)	5.90 (1.83)		
Week 52: Adjusted Mean Change (SE)	11.30 (1.72)	7.75 (1.77)	3.55 [-1.31; 8.40]	0.152
≥ 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 28: Adjusted Mean Change (SE)	7.16 (1.85)	4.83 (1.76)		
Week 52: Adjusted Mean Change (SE)	10.87 (1.71)	8.79 (1.64)	2.08 [-2.59; 6.75]	0.382
≥ 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 28: Adjusted Mean Change (SE)	3.02 (3.47)	6.60 (3.75)		
Week 52: Adjusted Mean Change (SE)	14.47 (3.52)	7.04 (3.47)	7.43 [-2.28; 17.15]	0.133
Pooled Analysis: Distance Activities				
Interaction test	p=0.663			
< 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 28: Adjusted Mean Change (SE)	8.22 (1.20)	6.36 (1.25)		
Week 52: Adjusted Mean Change (SE)	10.10 (1.15)	8.99 (1.18)	1.11 [-2.11; 4.34]	0.499

	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 28: Adjusted Mean Change (SE)	5.98 (1.35)	7.67 (1.32)		
Week 52: Adjusted Mean Change (SE)	9.86 (1.27)	8.56 (1.22)	1.30 [-2.16; 4.77]	0.461
≥ 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 28: Adjusted Mean Change (SE)	4.28 (2.85)	9.35 (2.66)		
Week 52: Adjusted Mean Change (SE)	13.36 (2.83)	10.11 (2.48)	3.25 [-4.11; 10.61]	0.386
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.037 ***				
KESTREL: Social Functioning				
Interaction test	p=0.943			
< 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 28: Adjusted Mean Change (SE)	3.48 (1.21)	4.32 (1.29)		
Week 52: Adjusted Mean Change (SE)	3.35 (1.36)	5.97 (1.40)	-2.62 [-6.46; 1.23]	0.182
≥ 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 28: Adjusted Mean Change (SE)	-1.12 (1.49)	3.61 (1.50)		
Week 52: Adjusted Mean Change (SE)	1.86 (1.69)	2.17 (1.63)	-0.31 [-4.93; 4.30]	0.893
≥ 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 28: Adjusted Mean Change (SE)	1.39 (3.62)	4.17 (2.83)		
Week 52: Adjusted Mean Change (SE)	1.43 (4.18)	2.42 (3.15)	-0.99 [-11.29; 9.30]	0.850

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Social Functioning				
Interaction test	p=0.205			
< 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 28: Adjusted Mean Change (SE)	4.80 (1.57)	4.08 (1.61)		
Week 52: Adjusted Mean Change (SE)	7.05 (1.38)	4.03 (1.41)	3.03 [-0.85; 6.91]	0.126
≥ 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 28: Adjusted Mean Change (SE)	3.44 (1.63)	3.15 (1.55)		
Week 52: Adjusted Mean Change (SE)	8.21 (1.36)	3.85 (1.31)	4.36 [0.64; 8.08]	0.022 *
≥ 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 28: Adjusted Mean Change (SE)	1.67 (3.06)	7.40 (3.32)		
Week 52: Adjusted Mean Change (SE)	6.00 (2.83)	8.96 (2.76)	-2.96 [-10.72; 4.81]	0.454
Pooled Analysis: Social Functioning				
Interaction test	p=0.366			
< 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 28: Adjusted Mean Change (SE)	4.21 (0.98)	4.19 (1.02)		
Week 52: Adjusted Mean Change (SE)	5.16 (0.98)	5.16 (1.00)	-0.01 [-2.75; 2.74]	0.996
≥ 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 28: Adjusted Mean Change (SE)	1.34 (1.11)	3.18 (1.08)		
Week 52: Adjusted Mean Change (SE)	5.28 (1.08)	2.87 (1.04)	2.40 [-0.54; 5.35]	0.110

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 28: Adjusted Mean Change (SE)	0.93 (2.32)	5.99 (2.18)		
Week 52: Adjusted Mean Change (SE)	3.66 (2.42)	5.99 (2.11)	-2.33 [-8.63; 3.96]	0.466
Mental Health				
Test of heterogeneity in main analysis: **p_H=0.300**				
KESTREL: Mental Health				
Interaction test	p=0.242			
< 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 28: Adjusted Mean Change (SE)	8.97 (1.70)	8.06 (1.81)		
Week 52: Adjusted Mean Change (SE)	10.95 (1.77)	10.13 (1.81)	0.82 [-4.15; 5.80]	0.746
≥ 450 - < 650 µm				
N'/ N	69 / 70	71 / 71		
Baseline Mean (SD)	62.50 (23.82)	68.84 (22.45)		
Week 52 Mean (SD)	75.91 (20.88)	81.45 (16.46)		
Week 28: Adjusted Mean Change (SE)	6.62 (2.09)	9.81 (2.10)		
Week 52: Adjusted Mean Change (SE)	10.17 (2.19)	13.54 (2.09)	-3.37 [-9.33; 2.58]	0.266
≥ 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 28: Adjusted Mean Change (SE)	-2.61 (5.09)	11.53 (3.99)		
Week 52: Adjusted Mean Change (SE)	7.41 (5.40)	7.54 (4.10)	-0.12 [-13.43; 13.18]	0.986
KITE: Mental Health				
Interaction test	p=0.734			
< 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 28: Adjusted Mean Change (SE)	8.82 (1.91)	7.74 (1.96)		
Week 52: Adjusted Mean Change (SE)	11.73 (2.35)	8.21 (2.40)	3.53 [-3.09; 10.14]	0.295

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 28: Adjusted Mean Change (SE)	7.84 (1.99)	10.05 (1.90)		
Week 52: Adjusted Mean Change (SE)	14.39 (2.34)	9.30 (2.24)	5.08 [-1.29; 11.46]	0.118
≥ 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 28: Adjusted Mean Change (SE)	11.57 (3.73)	12.18 (4.04)		
Week 52: Adjusted Mean Change (SE)	11.87 (4.78)	15.93 (4.75)	-4.06 [-17.32; 9.19]	0.547
Pooled Analysis: Mental Health				
Interaction test	p=0.320			
< 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 28: Adjusted Mean Change (SE)	9.05 (1.27)	7.82 (1.33)		
Week 52: Adjusted Mean Change (SE)	11.42 (1.45)	9.21 (1.48)	2.21 [-1.85; 6.27]	0.285
≥ 450 - < 650 µm				
N'/ N	143 / 144	150 / 150		
Baseline Mean (SD)	65.38 (23.45)	65.92 (24.96)		
Week 52 Mean (SD)	79.13 (20.33)	77.87 (22.09)		
Week 28: Adjusted Mean Change (SE)	7.35 (1.44)	9.82 (1.41)		
Week 52: Adjusted Mean Change (SE)	12.48 (1.60)	11.13 (1.54)	1.35 [-3.01; 5.70]	0.544
≥ 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 28: Adjusted Mean Change (SE)	6.20 (3.03)	12.22 (2.83)		
Week 52: Adjusted Mean Change (SE)	10.03 (3.56)	12.05 (3.12)	-2.02 [-11.30; 7.27]	0.670

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.072**				
KESTREL: Role Difficulties				
Interaction test	p=0.540			
< 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 28: Adjusted Mean Change (SE)	6.79 (2.14)	10.19 (2.26)		
Week 52: Adjusted Mean Change (SE)	10.33 (2.31)	11.47 (2.38)	-1.14 [-7.66; 5.38]	0.730
≥ 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 28: Adjusted Mean Change (SE)	6.12 (2.62)	9.05 (2.64)		
Week 52: Adjusted Mean Change (SE)	4.48 (2.86)	12.98 (2.74)	-8.49 [-16.29; -0.70]	0.033 *
≥ 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 28: Adjusted Mean Change (SE)	-2.69 (6.39)	4.38 (5.01)		
Week 52: Adjusted Mean Change (SE)	-8.83 (7.08)	2.58 (5.37)	-11.41 [-28.85; 6.03]	0.199
KITE: Role Difficulties				
Interaction test	p=0.842			
< 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 28: Adjusted Mean Change (SE)	6.19 (2.36)	7.39 (2.42)		
Week 52: Adjusted Mean Change (SE)	9.88 (2.57)	8.03 (2.62)	1.85 [-5.35; 9.05]	0.614
≥ 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 28: Adjusted Mean Change (SE)	8.49 (2.45)	8.25 (2.33)		
Week 52: Adjusted Mean Change (SE)	12.72 (2.53)	8.09 (2.43)	4.63 [-2.27; 11.54]	0.188

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 28: Adjusted Mean Change (SE)	9.56 (4.62)	12.45 (4.97)		
Week 52: Adjusted Mean Change (SE)	20.75 (5.26)	11.52 (5.14)	9.23 [-5.23; 23.69]	0.210
Pooled Analysis: Role Difficulties				
Interaction test	p=0.962			
< 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 28: Adjusted Mean Change (SE)	6.84 (1.59)	8.79 (1.66)		
Week 52: Adjusted Mean Change (SE)	10.42 (1.73)	9.86 (1.77)	0.55 [-4.30; 5.41]	0.823
≥ 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 28: Adjusted Mean Change (SE)	7.39 (1.80)	8.58 (1.76)		
Week 52: Adjusted Mean Change (SE)	8.86 (1.91)	10.28 (1.83)	-1.42 [-6.63; 3.78]	0.592
≥ 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 28: Adjusted Mean Change (SE)	4.00 (3.79)	8.74 (3.54)		
Week 52: Adjusted Mean Change (SE)	8.51 (4.28)	7.52 (3.73)	0.99 [-10.12; 12.09]	0.862
Dependency				
Test of heterogeneity in main analysis: **p_H=0.029 ***				
KESTREL: Dependency				
Interaction test	p=0.081			
< 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 28: Adjusted Mean Change (SE)	7.05 (1.82)	5.03 (1.93)		
Week 52: Adjusted Mean Change (SE)	6.57 (1.91)	8.85 (1.97)	-2.28 [-7.67; 3.11]	0.407

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 28: Adjusted Mean Change (SE)	5.63 (2.23)	9.09 (2.25)		
Week 52: Adjusted Mean Change (SE)	6.31 (2.37)	8.96 (2.27)	-2.65 [-9.10; 3.80]	0.419
≥ 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 28: Adjusted Mean Change (SE)	-7.34 (5.44)	7.46 (4.27)		
Week 52: Adjusted Mean Change (SE)	-6.48 (5.85)	7.52 (4.44)	-14.00 [-28.44; 0.44]	0.057
KITE: Dependency				
Interaction test	p=0.758			
< 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 28: Adjusted Mean Change (SE)	5.47 (1.92)	1.70 (1.98)		
Week 52: Adjusted Mean Change (SE)	6.20 (2.12)	1.22 (2.17)	4.98 [-0.98; 10.94]	0.101
≥ 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 28: Adjusted Mean Change (SE)	6.01 (2.00)	4.03 (1.90)		
Week 52: Adjusted Mean Change (SE)	8.64 (2.11)	4.89 (2.02)	3.75 [-2.00; 9.49]	0.200
≥ 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 28: Adjusted Mean Change (SE)	5.42 (3.76)	7.39 (4.07)		
Week 52: Adjusted Mean Change (SE)	8.58 (4.32)	5.81 (4.28)	2.77 [-9.18; 14.72]	0.649

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Dependency				
Interaction test	p=0.129			
< 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 28: Adjusted Mean Change (SE)	6.53 (1.33)	3.31 (1.39)		
Week 52: Adjusted Mean Change (SE)	6.60 (1.43)	5.29 (1.47)	1.30 [-2.72; 5.33]	0.524
≥ 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 28: Adjusted Mean Change (SE)	5.92 (1.51)	6.40 (1.47)		
Week 52: Adjusted Mean Change (SE)	7.58 (1.59)	6.82 (1.52)	0.76 [-3.56; 5.08]	0.730
≥ 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 28: Adjusted Mean Change (SE)	0.37 (3.16)	8.03 (2.96)		
Week 52: Adjusted Mean Change (SE)	2.52 (3.53)	7.20 (3.10)	-4.67 [-13.87; 4.53]	0.319
Driving				
Test of heterogeneity in main analysis: **p_H=0.778**				
KESTREL: Driving				
Interaction test	p=0.972			
< 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 28: Adjusted Mean Change (SE)	3.28 (1.81)	6.57 (1.97)		
Week 52: Adjusted Mean Change (SE)	5.21 (2.08)	7.53 (2.27)	-2.32 [-8.39; 3.75]	0.452
≥ 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 28: Adjusted Mean Change (SE)	0.72 (2.29)	3.13 (2.33)		
Week 52: Adjusted Mean Change (SE)	0.89 (2.66)	5.97 (2.71)	-5.08 [-12.56; 2.39]	0.182

	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 28: Adjusted Mean Change (SE)	-1.60 (5.90)	11.40 (4.50)		
Week 52: Adjusted Mean Change (SE)	4.31 (7.01)	-1.30 (5.22)	5.61 [-11.61; 22.83]	0.521
KITE: Driving				
Interaction test	p=0.608			
< 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 28: Adjusted Mean Change (SE)	-0.43 (2.02)	4.64 (2.16)		
Week 52: Adjusted Mean Change (SE)	3.43 (1.78)	5.27 (1.89)	-1.84 [-6.96; 3.28]	0.478
≥ 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 28: Adjusted Mean Change (SE)	2.68 (2.46)	5.88 (2.29)		
Week 52: Adjusted Mean Change (SE)	7.67 (2.03)	5.20 (1.97)	2.47 [-3.09; 8.04]	0.382
≥ 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 28: Adjusted Mean Change (SE)	0.25 (4.11)	6.45 (6.34)		
Week 52: Adjusted Mean Change (SE)	10.30 (3.64)	2.12 (5.71)	8.18 [-5.18; 21.54]	0.229
Pooled Analysis: Driving				
Interaction test	p=0.852			
< 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 28: Adjusted Mean Change (SE)	1.67 (1.35)	5.79 (1.46)		
Week 52: Adjusted Mean Change (SE)	4.37 (1.40)	6.60 (1.50)	-2.23 [-6.26; 1.80]	0.277

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 28: Adjusted Mean Change (SE)	1.56 (1.67)	4.53 (1.64)		
Week 52: Adjusted Mean Change (SE)	4.36 (1.70)	5.62 (1.69)	-1.26 [-5.96; 3.45]	0.600
≥ 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 28: Adjusted Mean Change (SE)	-0.56 (3.40)	9.72 (3.66)		
Week 52: Adjusted Mean Change (SE)	8.62 (3.60)	-0.04 (3.83)	8.66 [-1.66; 18.98]	0.100
Color Vision				
Test of heterogeneity in main analysis: **p_H=0.691**				
KESTREL: Color Vision				
Interaction test	p=0.734			
< 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 28: Adjusted Mean Change (SE)	3.57 (1.10)	4.11 (1.17)		
Week 52: Adjusted Mean Change (SE)	2.92 (1.15)	3.00 (1.19)	-0.09 [-3.35; 3.18]	0.959
≥ 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 28: Adjusted Mean Change (SE)	0.90 (1.34)	0.02 (1.36)		
Week 52: Adjusted Mean Change (SE)	1.71 (1.42)	0.43 (1.37)	1.28 [-2.60; 5.16]	0.517
≥ 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 28: Adjusted Mean Change (SE)	-3.72 (3.27)	-3.08 (2.63)		
Week 52: Adjusted Mean Change (SE)	-1.28 (3.51)	0.64 (2.82)	-1.91 [-10.77; 6.94]	0.671

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Color Vision				
Interaction test	p=0.120			
< 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 28: Adjusted Mean Change (SE)	3.17 (1.22)	3.57 (1.25)		
Week 52: Adjusted Mean Change (SE)	4.90 (1.13)	2.50 (1.15)	2.40 [-0.78; 5.58]	0.138
≥ 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 28: Adjusted Mean Change (SE)	4.95 (1.27)	4.04 (1.22)		
Week 52: Adjusted Mean Change (SE)	6.15 (1.11)	2.90 (1.07)	3.25 [0.21; 6.29]	0.036 *
≥ 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 28: Adjusted Mean Change (SE)	0.63 (2.37)	7.74 (2.57)		
Week 52: Adjusted Mean Change (SE)	8.01 (2.29)	9.40 (2.24)	-1.39 [-7.69; 4.92]	0.665
Pooled Analysis: Color Vision				
Interaction test	p=0.232			
< 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 28: Adjusted Mean Change (SE)	3.58 (0.84)	3.96 (0.87)		
Week 52: Adjusted Mean Change (SE)	3.95 (0.81)	2.93 (0.83)	1.02 [-1.26; 3.30]	0.379
≥ 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 28: Adjusted Mean Change (SE)	3.00 (0.94)	2.02 (0.93)		
Week 52: Adjusted Mean Change (SE)	4.00 (0.89)	1.57 (0.86)	2.43 [-0.00; 4.86]	0.050

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 28: Adjusted Mean Change (SE)	-1.33 (1.97)	2.32 (1.88)		
Week 52: Adjusted Mean Change (SE)	4.14 (1.99)	5.15 (1.79)	-1.01 [-6.25; 4.24]	0.706
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.021 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.328			
< 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 28: Adjusted Mean Change (SE)	4.34 (1.81)	6.60 (1.89)		
Week 52: Adjusted Mean Change (SE)	7.12 (1.84)	8.37 (1.88)	-1.25 [-6.42; 3.91]	0.634
≥ 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 28: Adjusted Mean Change (SE)	1.26 (2.19)	8.33 (2.21)		
Week 52: Adjusted Mean Change (SE)	3.91 (2.27)	4.67 (2.18)	-0.76 [-6.96; 5.44]	0.810
≥ 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 28: Adjusted Mean Change (SE)	-1.30 (5.33)	11.92 (4.19)		
Week 52: Adjusted Mean Change (SE)	4.74 (5.62)	12.29 (4.28)	-7.56 [-21.42; 6.31]	0.285
KITE: Peripheral Vision				
Interaction test	p=0.251			
< 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 28: Adjusted Mean Change (SE)	4.44 (1.78)	5.06 (1.84)		
Week 52: Adjusted Mean Change (SE)	3.63 (1.93)	4.81 (1.99)	-1.18 [-6.64; 4.28]	0.670

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 28: Adjusted Mean Change (SE)	4.08 (1.85)	3.92 (1.76)		
Week 52: Adjusted Mean Change (SE)	7.36 (1.91)	2.43 (1.83)	4.93 [-0.28; 10.13]	0.064
≥ 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 28: Adjusted Mean Change (SE)	8.80 (3.48)	5.83 (3.76)		
Week 52: Adjusted Mean Change (SE)	14.55 (3.95)	4.22 (3.88)	10.33 [-0.57; 21.23]	0.063
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.907			
< 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 28: Adjusted Mean Change (SE)	4.27 (1.27)	5.83 (1.33)		
Week 52: Adjusted Mean Change (SE)	5.62 (1.34)	6.78 (1.38)	-1.16 [-4.93; 2.61]	0.547
≥ 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 28: Adjusted Mean Change (SE)	2.78 (1.44)	6.06 (1.40)		
Week 52: Adjusted Mean Change (SE)	5.69 (1.48)	3.59 (1.42)	2.10 [-1.94; 6.13]	0.308
≥ 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 28: Adjusted Mean Change (SE)	4.59 (3.01)	9.75 (2.82)		
Week 52: Adjusted Mean Change (SE)	10.24 (3.31)	9.18 (2.89)	1.07 [-7.55; 9.68]	0.808

	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=0.700**				
KESTREL: General Health				
Interaction test	p=0.918			
< 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 28: Adjusted Mean Change (SE)	5.64 (1.83)	5.85 (1.94)		
Week 52: Adjusted Mean Change (SE)	8.62 (2.24)	7.42 (2.31)	1.20 [-5.14; 7.54]	0.709
≥ 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 28: Adjusted Mean Change (SE)	2.82 (2.24)	5.07 (2.26)		
Week 52: Adjusted Mean Change (SE)	8.56 (2.78)	2.53 (2.66)	6.02 [-1.56; 13.61]	0.119
≥ 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 28: Adjusted Mean Change (SE)	1.64 (5.48)	-1.97 (4.26)		
Week 52: Adjusted Mean Change (SE)	4.95 (6.87)	3.94 (5.16)	1.01 [-15.89; 17.90]	0.907
KITE: General Health				
Interaction test	p=0.862			
< 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 28: Adjusted Mean Change (SE)	3.64 (2.05)	3.35 (2.12)		
Week 52: Adjusted Mean Change (SE)	7.09 (2.50)	5.55 (2.55)	1.54 [-5.49; 8.58]	0.666
≥ 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 28: Adjusted Mean Change (SE)	4.84 (2.14)	6.05 (2.03)		
Week 52: Adjusted Mean Change (SE)	5.21 (2.46)	5.42 (2.35)	-0.21 [-6.91; 6.49]	0.951

	Treatment Groups		Comparison	
VFQ by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 28: Adjusted Mean Change (SE)	-0.46 (4.01)	1.13 (4.35)		
Week 52: Adjusted Mean Change (SE)	0.52 (5.12)	2.17 (4.99)	-1.65 [-15.72; 12.41]	0.818
Pooled Analysis: General Health				
Interaction test	p=0.993			
< 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 28: Adjusted Mean Change (SE)	4.61 (1.37)	4.88 (1.43)		
Week 52: Adjusted Mean Change (SE)	7.80 (1.66)	6.81 (1.70)	0.98 [-3.69; 5.66]	0.680
≥ 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 28: Adjusted Mean Change (SE)	3.79 (1.55)	5.62 (1.52)		
Week 52: Adjusted Mean Change (SE)	6.66 (1.84)	4.08 (1.76)	2.58 [-2.43; 7.59]	0.312
≥ 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 28: Adjusted Mean Change (SE)	0.34 (3.26)	-0.31 (3.05)		
Week 52: Adjusted Mean Change (SE)	2.17 (4.12)	3.07 (3.58)	-0.90 [-11.62; 9.81]	0.869

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 52

	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=0.071**				
KESTREL: Composite Score				
Interaction test	p=0.037 *			
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 28: Adjusted Mean Change (SE)	5.17 (1.37)	10.31 (1.39)		
Week 52: Adjusted Mean Change (SE)	5.90 (1.50)	9.84 (1.44)	-3.94 [-8.00; 0.11]	0.057
absence				
N'/ N	127 / 127	126 / 126		
Baseline Mean (SD)	78.38 (15.95)	78.80 (13.44)		
Week 52 Mean (SD)	86.17 (12.49)	85.05 (12.36)		
Week 28: Adjusted Mean Change (SE)	6.14 (0.97)	6.39 (0.99)		
Week 52: Adjusted Mean Change (SE)	7.77 (1.01)	7.58 (1.01)	0.18 [-2.62; 2.99]	0.899
KITE: Composite Score				
Interaction test	p=0.284			
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 28: Adjusted Mean Change (SE)	7.24 (1.36)	5.69 (1.23)		
Week 52: Adjusted Mean Change (SE)	11.44 (1.49)	7.63 (1.31)	3.81 [-0.09; 7.70]	0.055
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 28: Adjusted Mean Change (SE)	5.23 (0.93)	6.28 (0.97)		
Week 52: Adjusted Mean Change (SE)	7.77 (0.99)	5.83 (1.04)	1.94 [-0.88; 4.76]	0.177

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Composite Score				
Interaction test	p=0.390			
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 28: Adjusted Mean Change (SE)	6.26 (0.98)	8.04 (0.94)		
Week 52: Adjusted Mean Change (SE)	8.66 (1.06)	8.85 (0.98)	-0.19 [-3.01; 2.63]	0.895
absence				
N'/ N	249 / 250	240 / 240		
Baseline Mean (SD)	78.86 (15.29)	78.06 (15.49)		
Week 52 Mean (SD)	86.12 (12.84)	84.23 (13.85)		
Week 28: Adjusted Mean Change (SE)	5.72 (0.68)	6.21 (0.70)		
Week 52: Adjusted Mean Change (SE)	7.77 (0.72)	6.65 (0.73)	1.12 [-0.88; 3.12]	0.272
General Vision				
Test of heterogeneity in main analysis: **p_H=0.986**				
KESTREL: General Vision				
Interaction test	p=0.105			
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 28: Adjusted Mean Change (SE)	11.08 (1.67)	12.90 (1.70)		
Week 52: Adjusted Mean Change (SE)	9.82 (1.85)	11.73 (1.76)	-1.91 [-6.90; 3.07]	0.451
absence				
N'/ N	127 / 127	126 / 126		
Baseline Mean (SD)	62.99 (17.29)	61.75 (14.76)		
Week 52 Mean (SD)	74.17 (13.90)	70.94 (13.28)		
Week 28: Adjusted Mean Change (SE)	11.45 (1.19)	9.48 (1.21)		
Week 52: Adjusted Mean Change (SE)	12.46 (1.24)	10.11 (1.23)	2.35 [-1.09; 5.78]	0.180

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Vision				
Interaction test	p=0.943			
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 28: Adjusted Mean Change (SE)	10.77 (1.83)	10.55 (1.66)		
Week 52: Adjusted Mean Change (SE)	12.83 (2.07)	11.40 (1.83)	1.43 [-3.98; 6.84]	0.603
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 28: Adjusted Mean Change (SE)	8.81 (1.25)	9.12 (1.31)		
Week 52: Adjusted Mean Change (SE)	11.17 (1.38)	9.60 (1.44)	1.57 [-2.34; 5.48]	0.431
Pooled Analysis: General Vision				
Interaction test	p=0.323			
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 28: Adjusted Mean Change (SE)	10.96 (1.24)	11.65 (1.20)		
Week 52: Adjusted Mean Change (SE)	11.33 (1.39)	11.58 (1.27)	-0.25 [-3.93; 3.43]	0.895
absence				
N'/ N	249 / 250	240 / 240		
Baseline Mean (SD)	63.13 (16.50)	62.08 (15.97)		
Week 52 Mean (SD)	73.60 (14.23)	70.91 (14.18)		
Week 28: Adjusted Mean Change (SE)	10.13 (0.87)	9.31 (0.89)		
Week 52: Adjusted Mean Change (SE)	11.80 (0.93)	9.88 (0.95)	1.92 [-0.68; 4.52]	0.148

	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=0.492**				
KESTREL: Ocular Pain				
Interaction test	p=0.242			
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 28: Adjusted Mean Change (SE)	3.49 (2.26)	7.57 (2.29)		
Week 52: Adjusted Mean Change (SE)	4.16 (2.18)	5.89 (2.07)	-1.73 [-7.62; 4.16]	0.563
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 28: Adjusted Mean Change (SE)	2.36 (1.61)	2.69 (1.64)		
Week 52: Adjusted Mean Change (SE)	5.64 (1.46)	3.60 (1.46)	2.05 [-2.01; 6.10]	0.322
KITE: Ocular Pain				
Interaction test	p=0.724			
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 28: Adjusted Mean Change (SE)	5.88 (2.10)	2.56 (1.90)		
Week 52: Adjusted Mean Change (SE)	6.09 (2.22)	6.26 (1.95)	-0.17 [-5.97; 5.63]	0.953
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 28: Adjusted Mean Change (SE)	4.09 (1.43)	4.95 (1.50)		
Week 52: Adjusted Mean Change (SE)	4.58 (1.48)	2.63 (1.54)	1.95 [-2.24; 6.15]	0.360

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Ocular Pain				
Interaction test	p=0.521			
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 28: Adjusted Mean Change (SE)	4.66 (1.55)	4.93 (1.49)		
Week 52: Adjusted Mean Change (SE)	5.14 (1.56)	6.10 (1.43)	-0.97 [-5.11; 3.18]	0.647
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 28: Adjusted Mean Change (SE)	3.25 (1.08)	3.70 (1.12)		
Week 52: Adjusted Mean Change (SE)	5.16 (1.04)	3.14 (1.06)	2.01 [-0.91; 4.94]	0.177
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.456**				
KESTREL: Near Activities				
Interaction test	p=0.527			
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 28: Adjusted Mean Change (SE)	12.37 (2.35)	15.14 (2.38)		
Week 52: Adjusted Mean Change (SE)	10.24 (2.70)	13.05 (2.57)	-2.81 [-10.09; 4.47]	0.448
absence				
N'/ N	127 / 127	126 / 126		
Baseline Mean (SD)	65.65 (25.33)	68.22 (20.97)		
Week 52 Mean (SD)	81.15 (19.94)	79.60 (19.59)		
Week 28: Adjusted Mean Change (SE)	12.41 (1.67)	14.19 (1.70)		
Week 52: Adjusted Mean Change (SE)	14.88 (1.81)	14.10 (1.80)	0.78 [-4.24; 5.79]	0.761

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Near Activities				
Interaction test	p=0.397			
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 28: Adjusted Mean Change (SE)	8.17 (2.45)	4.84 (2.22)		
Week 52: Adjusted Mean Change (SE)	12.90 (2.52)	10.48 (2.22)	2.41 [-4.17; 9.00]	0.471
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 28: Adjusted Mean Change (SE)	5.72 (1.68)	6.88 (1.75)		
Week 52: Adjusted Mean Change (SE)	9.22 (1.68)	8.41 (1.76)	0.81 [-3.97; 5.58]	0.740
Pooled Analysis: Near Activities				
Interaction test	p=0.998			
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 28: Adjusted Mean Change (SE)	10.36 (1.72)	9.96 (1.64)		
Week 52: Adjusted Mean Change (SE)	11.50 (1.87)	11.99 (1.71)	-0.49 [-5.44; 4.47]	0.847
absence				
N'/ N	248 / 250	240 / 240		
Baseline Mean (SD)	69.25 (23.26)	69.70 (22.19)		
Week 52 Mean (SD)	80.79 (20.35)	79.25 (20.28)		
Week 28: Adjusted Mean Change (SE)	9.31 (1.20)	10.42 (1.23)		
Week 52: Adjusted Mean Change (SE)	12.19 (1.25)	11.18 (1.28)	1.01 [-2.49; 4.51]	0.571

	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=0.136**				
KESTREL: Distance Activities				
Interaction test	p=0.176			
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 28: Adjusted Mean Change (SE)	7.20 (2.07)	12.34 (2.10)		
Week 52: Adjusted Mean Change (SE)	8.34 (2.05)	10.76 (1.97)	-2.42 [-7.97; 3.13]	0.392
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 28: Adjusted Mean Change (SE)	7.59 (1.47)	7.24 (1.49)		
Week 52: Adjusted Mean Change (SE)	9.46 (1.39)	9.04 (1.38)	0.42 [-3.42; 4.26]	0.831
KITE: Distance Activities				
Interaction test	p=0.824			
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 28: Adjusted Mean Change (SE)	6.55 (2.12)	5.69 (1.92)		
Week 52: Adjusted Mean Change (SE)	12.56 (2.06)	10.08 (1.81)	2.49 [-2.89; 7.86]	0.363
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 28: Adjusted Mean Change (SE)	6.21 (1.45)	5.40 (1.52)		
Week 52: Adjusted Mean Change (SE)	10.86 (1.37)	7.02 (1.43)	3.85 [-0.04; 7.74]	0.053

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Distance Activities				
Interaction test	p=0.284			
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 28: Adjusted Mean Change (SE)	7.08 (1.49)	8.96 (1.43)		
Week 52: Adjusted Mean Change (SE)	10.56 (1.46)	10.53 (1.34)	0.03 [-3.85; 3.90]	0.990
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 28: Adjusted Mean Change (SE)	6.90 (1.04)	6.27 (1.07)		
Week 52: Adjusted Mean Change (SE)	10.13 (0.98)	8.02 (1.00)	2.11 [-0.63; 4.85]	0.130
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.037 ***				
KESTREL: Social Functioning				
Interaction test	p=0.673			
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 28: Adjusted Mean Change (SE)	1.09 (1.58)	4.35 (1.61)		
Week 52: Adjusted Mean Change (SE)	0.55 (1.85)	2.59 (1.75)	-2.05 [-7.03; 2.94]	0.420
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 28: Adjusted Mean Change (SE)	1.90 (1.12)	3.90 (1.15)		
Week 52: Adjusted Mean Change (SE)	3.62 (1.24)	4.94 (1.23)	-1.31 [-4.74; 2.12]	0.452

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Social Functioning				
Interaction test	p=0.863			
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 28: Adjusted Mean Change (SE)	3.96 (1.88)	4.08 (1.70)		
Week 52: Adjusted Mean Change (SE)	9.20 (1.64)	6.55 (1.44)	2.65 [-1.63; 6.94]	0.224
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 28: Adjusted Mean Change (SE)	3.77 (1.28)	3.93 (1.35)		
Week 52: Adjusted Mean Change (SE)	6.67 (1.09)	3.15 (1.14)	3.52 [0.42; 6.62]	0.026 *
Pooled Analysis: Social Functioning				
Interaction test	p=0.648			
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 28: Adjusted Mean Change (SE)	2.64 (1.22)	4.23 (1.17)		
Week 52: Adjusted Mean Change (SE)	4.90 (1.25)	4.69 (1.14)	0.21 [-3.10; 3.52]	0.902
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 28: Adjusted Mean Change (SE)	2.82 (0.85)	3.80 (0.88)		
Week 52: Adjusted Mean Change (SE)	5.16 (0.84)	4.02 (0.85)	1.14 [-1.20; 3.47]	0.341

	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=0.300**				
KESTREL: Mental Health				
Interaction test	p=0.293			
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 28: Adjusted Mean Change (SE)	5.22 (2.22)	10.94 (2.25)		
Week 52: Adjusted Mean Change (SE)	11.24 (2.39)	12.45 (2.27)	-1.21 [-7.67; 5.24]	0.712
absence				
N'/ N	127 / 127	126 / 126		
Baseline Mean (SD)	68.41 (24.27)	70.98 (20.55)		
Week 52 Mean (SD)	79.43 (19.33)	78.83 (17.96)		
Week 28: Adjusted Mean Change (SE)	8.48 (1.57)	8.13 (1.60)		
Week 52: Adjusted Mean Change (SE)	10.13 (1.61)	10.55 (1.59)	-0.43 [-4.87; 4.01]	0.850
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 28: Adjusted Mean Change (SE)	9.82 (2.29)	7.83 (2.07)		
Week 52: Adjusted Mean Change (SE)	17.29 (2.81)	8.26 (2.47)	9.03 [1.69; 16.37]	0.016 *
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 28: Adjusted Mean Change (SE)	8.23 (1.57)	10.27 (1.64)		
Week 52: Adjusted Mean Change (SE)	11.10 (1.87)	10.43 (1.95)	0.67 [-4.65; 5.99]	0.803

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Mental Health				
Interaction test	p=0.611			
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 28: Adjusted Mean Change (SE)	7.52 (1.59)	9.37 (1.53)		
Week 52: Adjusted Mean Change (SE)	14.24 (1.84)	10.29 (1.68)	3.95 [-0.92; 8.83]	0.112
absence				
N'/ N	249 / 250	240 / 240		
Baseline Mean (SD)	69.93 (22.82)	68.93 (23.30)		
Week 52 Mean (SD)	80.02 (20.10)	78.38 (19.43)		
Week 28: Adjusted Mean Change (SE)	8.41 (1.11)	9.04 (1.14)		
Week 52: Adjusted Mean Change (SE)	10.64 (1.23)	10.40 (1.25)	0.25 [-3.20; 3.69]	0.889
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.072**				
KESTREL: Role Difficulties				
Interaction test	p=0.056			
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 28: Adjusted Mean Change (SE)	2.64 (2.77)	10.43 (2.80)		
Week 52: Adjusted Mean Change (SE)	3.82 (3.16)	14.20 (3.00)	-10.38 [-18.91; -1.85]	0.017 *
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 28: Adjusted Mean Change (SE)	7.64 (1.97)	8.47 (2.00)		
Week 52: Adjusted Mean Change (SE)	8.49 (2.13)	9.63 (2.11)	-1.14 [-7.01; 4.74]	0.704

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Role Difficulties				
Interaction test	p=0.564			
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 28: Adjusted Mean Change (SE)	8.69 (2.82)	9.09 (2.55)		
Week 52: Adjusted Mean Change (SE)	17.09 (3.06)	10.20 (2.68)	6.89 [-1.09; 14.87]	0.090
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 28: Adjusted Mean Change (SE)	7.05 (1.93)	7.98 (2.02)		
Week 52: Adjusted Mean Change (SE)	10.18 (2.04)	7.46 (2.12)	2.72 [-3.06; 8.49]	0.355
Pooled Analysis: Role Difficulties				
Interaction test	p=0.295			
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 28: Adjusted Mean Change (SE)	5.56 (1.98)	9.80 (1.90)		
Week 52: Adjusted Mean Change (SE)	10.22 (2.20)	12.13 (2.01)	-1.91 [-7.74; 3.92]	0.521
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 28: Adjusted Mean Change (SE)	7.41 (1.38)	8.16 (1.42)		
Week 52: Adjusted Mean Change (SE)	9.35 (1.47)	8.59 (1.50)	0.76 [-3.36; 4.88]	0.717

	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=0.029 ***				
KESTREL: Dependency				
Interaction test	p=0.063			
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 28: Adjusted Mean Change (SE)	2.74 (2.37)	9.37 (2.41)		
Week 52: Adjusted Mean Change (SE)	4.58 (2.59)	10.98 (2.47)	-6.41 [-13.40; 0.59]	0.073
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 28: Adjusted Mean Change (SE)	7.10 (1.68)	5.51 (1.71)		
Week 52: Adjusted Mean Change (SE)	6.25 (1.74)	7.62 (1.73)	-1.37 [-6.19; 3.45]	0.577
KITE: Dependency				
Interaction test	p=0.558			
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 28: Adjusted Mean Change (SE)	5.16 (2.30)	2.24 (2.08)		
Week 52: Adjusted Mean Change (SE)	9.78 (2.54)	3.59 (2.23)	6.19 [-0.44; 12.82]	0.067
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 28: Adjusted Mean Change (SE)	5.92 (1.57)	4.07 (1.65)		
Week 52: Adjusted Mean Change (SE)	6.55 (1.69)	3.34 (1.77)	3.20 [-1.60; 8.00]	0.190

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Dependency				
Interaction test	p=0.357			
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 28: Adjusted Mean Change (SE)	4.15 (1.67)	5.94 (1.60)		
Week 52: Adjusted Mean Change (SE)	7.35 (1.82)	7.39 (1.67)	-0.04 [-4.88; 4.80]	0.987
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 28: Adjusted Mean Change (SE)	6.49 (1.16)	4.64 (1.20)		
Week 52: Adjusted Mean Change (SE)	6.35 (1.22)	5.43 (1.24)	0.93 [-2.49; 4.34]	0.595
Driving				
Test of heterogeneity in main analysis: **p_H=0.778**				
KESTREL: Driving				
Interaction test	p=0.129			
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 28: Adjusted Mean Change (SE)	-1.24 (2.51)	8.78 (2.34)		
Week 52: Adjusted Mean Change (SE)	2.53 (3.06)	6.86 (2.74)	-4.32 [-12.37; 3.72]	0.291
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 28: Adjusted Mean Change (SE)	3.49 (1.64)	3.92 (1.80)		
Week 52: Adjusted Mean Change (SE)	4.12 (1.87)	5.62 (2.09)	-1.49 [-7.02; 4.03]	0.594

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Driving				
Interaction test	p=0.996			
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 28: Adjusted Mean Change (SE)	0.34 (2.66)	5.79 (2.49)		
Week 52: Adjusted Mean Change (SE)	7.52 (2.33)	6.01 (2.19)	1.51 [-4.80; 7.82]	0.638
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 28: Adjusted Mean Change (SE)	0.91 (1.73)	5.23 (1.90)		
Week 52: Adjusted Mean Change (SE)	5.20 (1.48)	4.79 (1.65)	0.41 [-3.98; 4.79]	0.855
Pooled Analysis: Driving				
Interaction test	p=0.244			
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 28: Adjusted Mean Change (SE)	-0.39 (1.82)	7.52 (1.70)		
Week 52: Adjusted Mean Change (SE)	5.26 (1.95)	6.63 (1.78)	-1.37 [-6.54; 3.81]	0.603
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 28: Adjusted Mean Change (SE)	2.22 (1.19)	4.51 (1.31)		
Week 52: Adjusted Mean Change (SE)	4.57 (1.21)	5.21 (1.35)	-0.64 [-4.21; 2.93]	0.724

	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=0.691**				
KESTREL: Color Vision				
Interaction test	p=0.250			
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 28: Adjusted Mean Change (SE)	0.17 (1.45)	1.85 (1.49)		
Week 52: Adjusted Mean Change (SE)	0.77 (1.57)	1.68 (1.52)	-0.91 [-5.20; 3.37]	0.675
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 28: Adjusted Mean Change (SE)	3.07 (1.03)	1.81 (1.05)		
Week 52: Adjusted Mean Change (SE)	2.86 (1.04)	1.83 (1.05)	1.04 [-1.86; 3.94]	0.482
KITE: Color Vision				
Interaction test	p=0.617			
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 28: Adjusted Mean Change (SE)	5.15 (1.47)	5.18 (1.33)		
Week 52: Adjusted Mean Change (SE)	6.61 (1.37)	3.43 (1.20)	3.19 [-0.39; 6.76]	0.081
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 28: Adjusted Mean Change (SE)	2.89 (1.00)	3.59 (1.05)		
Week 52: Adjusted Mean Change (SE)	5.37 (0.90)	3.44 (0.95)	1.93 [-0.64; 4.51]	0.141

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Color Vision				
Interaction test	p=0.546			
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 28: Adjusted Mean Change (SE)	2.69 (1.05)	3.65 (1.01)		
Week 52: Adjusted Mean Change (SE)	3.71 (1.04)	2.58 (0.96)	1.13 [-1.64; 3.90]	0.423
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 28: Adjusted Mean Change (SE)	2.99 (0.73)	2.59 (0.75)		
Week 52: Adjusted Mean Change (SE)	4.09 (0.69)	2.57 (0.71)	1.52 [-0.41; 3.45]	0.122
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.021 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.108			
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 28: Adjusted Mean Change (SE)	3.82 (2.30)	11.61 (2.34)		
Week 52: Adjusted Mean Change (SE)	3.08 (2.49)	9.02 (2.37)	-5.94 [-12.67; 0.78]	0.083
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 28: Adjusted Mean Change (SE)	2.28 (1.66)	5.89 (1.67)		
Week 52: Adjusted Mean Change (SE)	6.97 (1.67)	6.53 (1.66)	0.44 [-4.18; 5.06]	0.851

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Peripheral Vision				
Interaction test	p=0.254			
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 28: Adjusted Mean Change (SE)	6.17 (2.12)	2.62 (1.94)		
Week 52: Adjusted Mean Change (SE)	8.80 (2.33)	4.58 (2.06)	4.22 [-1.88; 10.33]	0.174
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 28: Adjusted Mean Change (SE)	4.13 (1.45)	5.83 (1.52)		
Week 52: Adjusted Mean Change (SE)	5.45 (1.55)	2.98 (1.62)	2.47 [-1.92; 6.86]	0.269
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.568			
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 28: Adjusted Mean Change (SE)	4.87 (1.58)	7.34 (1.52)		
Week 52: Adjusted Mean Change (SE)	5.73 (1.71)	7.16 (1.57)	-1.43 [-5.98; 3.12]	0.536
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 28: Adjusted Mean Change (SE)	3.11 (1.11)	5.77 (1.14)		
Week 52: Adjusted Mean Change (SE)	6.14 (1.15)	4.80 (1.17)	1.34 [-1.87; 4.54]	0.413

	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=0.700**				
KESTREL: General Health				
Interaction test	p=0.683			
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 28: Adjusted Mean Change (SE)	3.85 (2.37)	4.33 (2.42)		
Week 52: Adjusted Mean Change (SE)	4.15 (3.02)	3.00 (2.87)	1.15 [-7.01; 9.31]	0.781
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 28: Adjusted Mean Change (SE)	4.59 (1.70)	4.90 (1.73)		
Week 52: Adjusted Mean Change (SE)	10.28 (2.04)	6.20 (2.01)	4.08 [-1.57; 9.73]	0.156
KITE: General Health				
Interaction test	p=0.840			
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 28: Adjusted Mean Change (SE)	2.54 (2.46)	7.02 (2.22)		
Week 52: Adjusted Mean Change (SE)	4.89 (2.98)	1.73 (2.61)	3.16 [-4.62; 10.94]	0.425
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 28: Adjusted Mean Change (SE)	4.11 (1.68)	2.73 (1.76)		
Week 52: Adjusted Mean Change (SE)	5.73 (1.98)	6.98 (2.07)	-1.26 [-6.88; 4.37]	0.661

	Treatment Groups		Comparison	
VFQ by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: General Health				
Interaction test	p=0.700			
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 28: Adjusted Mean Change (SE)	3.23 (1.71)	5.88 (1.64)		
Week 52: Adjusted Mean Change (SE)	4.51 (2.12)	2.42 (1.93)	2.09 [-3.53; 7.71]	0.465
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 28: Adjusted Mean Change (SE)	4.18 (1.20)	3.95 (1.23)		
Week 52: Adjusted Mean Change (SE)	7.88 (1.42)	6.67 (1.44)	1.21 [-2.75; 5.17]	0.549

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 8.12 VFQ by exposure (FAS), continuous analysis, week 52

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Composite Score				
Test of heterogeneity in main analysis: **p_H=0.071**				
KESTREL: Composite Score				
Interaction test	p=0.682			
Non-exposed				
N'/ N	71 / 71	75 / 75		
Baseline Mean (SD)	77.45 (18.18)	79.98 (14.03)		
Week 52 Mean (SD)	86.71 (12.33)	87.27 (11.65)		
Week 28: Adjusted Mean Change (SE)	6.00 (1.33)	8.64 (1.32)		
Week 52: Adjusted Mean Change (SE)	7.80 (1.38)	9.31 (1.34)	-1.51 [-5.28; 2.26]	0.432
Exposed				
N'/ N	117 / 118	112 / 112		
Baseline Mean (SD)	76.15 (17.07)	74.69 (14.63)		
Week 52 Mean (SD)	84.01 (14.73)	83.83 (12.52)		
Week 28: Adjusted Mean Change (SE)	5.69 (1.00)	7.15 (1.02)		
Week 52: Adjusted Mean Change (SE)	6.80 (1.06)	7.75 (1.05)	-0.95 [-3.88; 1.97]	0.522
KITE: Composite Score				
Interaction test	p=0.311			
Non-exposed				
N'/ N	84 / 85	90 / 90		
Baseline Mean (SD)	78.79 (14.62)	75.51 (17.91)		
Week 52 Mean (SD)	86.86 (12.81)	83.61 (15.63)		
Week 28: Adjusted Mean Change (SE)	5.70 (1.13)	7.08 (1.12)		
Week 52: Adjusted Mean Change (SE)	8.29 (1.21)	6.90 (1.18)	1.40 [-1.93; 4.72]	0.409
Exposed				
N'/ N	94 / 94	91 / 91		
Baseline Mean (SD)	76.96 (15.34)	77.40 (17.48)		
Week 52 Mean (SD)	86.13 (13.03)	83.48 (15.78)		
Week 28: Adjusted Mean Change (SE)	5.99 (1.04)	5.14 (1.04)		
Week 52: Adjusted Mean Change (SE)	9.45 (1.15)	6.22 (1.15)	3.23 [0.03; 6.43]	0.048 *

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Composite Score				
Interaction test	p=0.396			
Non-exposed				
N'/ N	155 / 156	165 / 165		
Baseline Mean (SD)	78.17 (16.30)	77.54 (16.37)		
Week 52 Mean (SD)	86.79 (12.55)	85.25 (14.06)		
Week 28: Adjusted Mean Change (SE)	5.83 (0.88)	7.73 (0.87)		
Week 52: Adjusted Mean Change (SE)	8.04 (0.92)	7.95 (0.89)	0.09 [-2.42; 2.60]	0.943
Exposed				
N'/ N	211 / 212	203 / 203		
Baseline Mean (SD)	76.51 (16.29)	75.91 (15.98)		
Week 52 Mean (SD)	84.96 (14.00)	83.68 (13.99)		
Week 28: Adjusted Mean Change (SE)	5.93 (0.73)	6.24 (0.74)		
Week 52: Adjusted Mean Change (SE)	8.06 (0.78)	7.07 (0.78)	0.99 [-1.18; 3.15]	0.370
General Vision				
Test of heterogeneity in main analysis: **p_H=0.986**				
KESTREL: General Vision				
Interaction test	p=0.414			
Non-exposed				
N'/ N	71 / 71	75 / 75		
Baseline Mean (SD)	61.97 (17.94)	64.27 (13.67)		
Week 52 Mean (SD)	73.21 (12.81)	72.46 (12.74)		
Week 28: Adjusted Mean Change (SE)	11.19 (1.62)	12.02 (1.61)		
Week 52: Adjusted Mean Change (SE)	11.24 (1.69)	11.21 (1.63)	0.03 [-4.58; 4.63]	0.991
Exposed				
N'/ N	117 / 118	112 / 112		
Baseline Mean (SD)	60.85 (16.90)	57.50 (14.73)		
Week 52 Mean (SD)	72.69 (14.97)	70.31 (12.95)		
Week 28: Adjusted Mean Change (SE)	11.41 (1.21)	9.81 (1.25)		
Week 52: Adjusted Mean Change (SE)	11.88 (1.30)	10.32 (1.29)	1.56 [-2.04; 5.16]	0.394

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: General Vision				
Interaction test	p=0.070			
Non-exposed				
N'/ N	84 / 85	90 / 90		
Baseline Mean (SD)	63.81 (16.27)	58.00 (18.00)		
Week 52 Mean (SD)	73.33 (14.42)	70.93 (16.86)		
Week 28: Adjusted Mean Change (SE)	7.37 (1.51)	10.96 (1.50)		
Week 52: Adjusted Mean Change (SE)	11.42 (1.66)	11.75 (1.61)	-0.34 [-4.90; 4.22]	0.884
Exposed				
N'/ N	94 / 94	91 / 91		
Baseline Mean (SD)	60.00 (15.79)	61.76 (18.53)		
Week 52 Mean (SD)	72.27 (14.67)	70.13 (17.51)		
Week 28: Adjusted Mean Change (SE)	11.16 (1.39)	8.53 (1.40)		
Week 52: Adjusted Mean Change (SE)	11.86 (1.58)	8.91 (1.59)	2.95 [-1.46; 7.36]	0.189
Pooled Analysis: General Vision				
Interaction test	p=0.121			
Non-exposed				
N'/ N	155 / 156	165 / 165		
Baseline Mean (SD)	62.97 (17.02)	60.85 (16.43)		
Week 52 Mean (SD)	73.28 (13.67)	71.62 (15.12)		
Week 28: Adjusted Mean Change (SE)	9.21 (1.12)	11.16 (1.10)		
Week 52: Adjusted Mean Change (SE)	11.42 (1.19)	11.29 (1.15)	0.13 [-3.12; 3.37]	0.939
Exposed				
N'/ N	211 / 212	203 / 203		
Baseline Mean (SD)	60.47 (16.38)	59.41 (16.64)		
Week 52 Mean (SD)	72.50 (14.79)	70.23 (15.06)		
Week 28: Adjusted Mean Change (SE)	11.22 (0.92)	9.43 (0.94)		
Week 52: Adjusted Mean Change (SE)	11.82 (1.02)	9.88 (1.01)	1.94 [-0.88; 4.75]	0.177

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Ocular Pain				
Test of heterogeneity in main analysis: **p_H=0.492**				
KESTREL: Ocular Pain				
Interaction test	p=0.491			
Non-exposed				
N'/ N	71 / 71	75 / 75		
Baseline Mean (SD)	84.86 (18.65)	83.50 (18.17)		
Week 52 Mean (SD)	91.52 (13.51)	86.27 (17.49)		
Week 28: Adjusted Mean Change (SE)	2.86 (2.20)	4.55 (2.18)		
Week 52: Adjusted Mean Change (SE)	7.16 (1.99)	3.57 (1.91)	3.59 [-1.84; 9.02]	0.194
Exposed				
N'/ N	117 / 118	112 / 112		
Baseline Mean (SD)	82.48 (20.70)	81.25 (21.94)		
Week 52 Mean (SD)	86.83 (16.93)	86.98 (15.41)		
Week 28: Adjusted Mean Change (SE)	2.66 (1.64)	4.22 (1.68)		
Week 52: Adjusted Mean Change (SE)	4.01 (1.53)	4.87 (1.51)	-0.86 [-5.08; 3.37]	0.690
KITE: Ocular Pain				
Interaction test	p=0.425			
Non-exposed				
N'/ N	84 / 85	90 / 90		
Baseline Mean (SD)	86.31 (15.23)	82.50 (21.27)		
Week 52 Mean (SD)	89.31 (17.32)	87.33 (17.74)		
Week 28: Adjusted Mean Change (SE)	4.24 (1.75)	5.39 (1.73)		
Week 52: Adjusted Mean Change (SE)	4.05 (1.79)	3.68 (1.72)	0.37 [-4.52; 5.26]	0.881
Exposed				
N'/ N	94 / 94	91 / 91		
Baseline Mean (SD)	82.45 (20.02)	82.42 (19.98)		
Week 52 Mean (SD)	88.33 (15.96)	87.33 (17.97)		
Week 28: Adjusted Mean Change (SE)	5.00 (1.60)	2.84 (1.61)		
Week 52: Adjusted Mean Change (SE)	5.95 (1.71)	4.45 (1.71)	1.51 [-3.25; 6.26]	0.534

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Ocular Pain				
Interaction test	p=0.963			
Non-exposed				
N'/ N	155 / 156	165 / 165		
Baseline Mean (SD)	85.65 (16.84)	82.95 (19.86)		
Week 52 Mean (SD)	90.30 (15.70)	86.86 (17.57)		
Week 28: Adjusted Mean Change (SE)	3.67 (1.40)	4.95 (1.38)		
Week 52: Adjusted Mean Change (SE)	5.45 (1.34)	3.59 (1.29)	1.87 [-1.79; 5.52]	0.317
Exposed				
N'/ N	211 / 212	203 / 203		
Baseline Mean (SD)	82.46 (20.35)	81.77 (21.04)		
Week 52 Mean (SD)	87.50 (16.47)	87.14 (16.53)		
Week 28: Adjusted Mean Change (SE)	3.73 (1.15)	3.57 (1.17)		
Week 52: Adjusted Mean Change (SE)	4.93 (1.15)	4.71 (1.14)	0.22 [-2.95; 3.40]	0.889
Near Activities				
Test of heterogeneity in main analysis: **p_H=0.456**				
KESTREL: Near Activities				
Interaction test	p=0.636			
Non-exposed				
N'/ N	71 / 71	75 / 75		
Baseline Mean (SD)	64.03 (25.45)	70.28 (21.38)		
Week 52 Mean (SD)	82.29 (18.12)	80.05 (20.99)		
Week 28: Adjusted Mean Change (SE)	11.56 (2.27)	13.88 (2.26)		
Week 52: Adjusted Mean Change (SE)	15.79 (2.46)	13.82 (2.38)	1.97 [-4.77; 8.70]	0.566
Exposed				
N'/ N	117 / 118	112 / 112		
Baseline Mean (SD)	63.18 (26.67)	62.54 (21.65)		
Week 52 Mean (SD)	77.28 (22.86)	77.84 (19.60)		
Week 28: Adjusted Mean Change (SE)	12.87 (1.69)	14.88 (1.74)		
Week 52: Adjusted Mean Change (SE)	12.02 (1.90)	13.71 (1.87)	-1.69 [-6.93; 3.55]	0.527

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Near Activities				
Interaction test	p=0.096			
Non-exposed				
N'/ N	84 / 85	90 / 90		
Baseline Mean (SD)	71.28 (22.10)	67.96 (24.13)		
Week 52 Mean (SD)	79.59 (22.07)	78.78 (21.77)		
Week 28: Adjusted Mean Change (SE)	5.23 (2.02)	8.94 (2.00)		
Week 52: Adjusted Mean Change (SE)	9.19 (2.03)	10.10 (1.97)	-0.90 [-6.48; 4.67]	0.750
Exposed				
N'/ N	93 / 94	91 / 91		
Baseline Mean (SD)	69.13 (22.72)	70.83 (23.68)		
Week 52 Mean (SD)	80.56 (19.39)	78.50 (22.53)		
Week 28: Adjusted Mean Change (SE)	7.57 (1.87)	3.60 (1.87)		
Week 52: Adjusted Mean Change (SE)	11.38 (1.93)	8.50 (1.94)	2.88 [-2.50; 8.26]	0.293
Pooled Analysis: Near Activities				
Interaction test	p=0.504			
Non-exposed				
N'/ N	155 / 156	165 / 165		
Baseline Mean (SD)	67.96 (23.89)	69.02 (22.88)		
Week 52 Mean (SD)	80.80 (20.36)	79.35 (21.35)		
Week 28: Adjusted Mean Change (SE)	8.51 (1.53)	11.17 (1.52)		
Week 52: Adjusted Mean Change (SE)	12.48 (1.60)	11.88 (1.55)	0.60 [-3.77; 4.97]	0.788
Exposed				
N'/ N	210 / 212	203 / 203		
Baseline Mean (SD)	65.81 (25.12)	66.26 (22.90)		
Week 52 Mean (SD)	78.75 (21.38)	78.12 (20.87)		
Week 28: Adjusted Mean Change (SE)	10.45 (1.27)	9.59 (1.29)		
Week 52: Adjusted Mean Change (SE)	11.59 (1.37)	11.17 (1.36)	0.41 [-3.37; 4.20]	0.830

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Distance Activities				
Test of heterogeneity in main analysis: **p_H=0.136**				
KESTREL: Distance Activities				
Interaction test	p=0.463			
Non-exposed				
N'/ N	71 / 71	75 / 75		
Baseline Mean (SD)	77.11 (23.63)	78.72 (21.21)		
Week 52 Mean (SD)	87.43 (15.33)	87.70 (15.89)		
Week 28: Adjusted Mean Change (SE)	8.46 (2.00)	12.11 (1.98)		
Week 52: Adjusted Mean Change (SE)	10.20 (1.88)	11.32 (1.82)	-1.13 [-6.26; 4.01]	0.666
Exposed				
N'/ N	117 / 118	112 / 112		
Baseline Mean (SD)	74.15 (24.00)	73.10 (20.89)		
Week 52 Mean (SD)	84.18 (18.22)	83.42 (17.64)		
Week 28: Adjusted Mean Change (SE)	6.86 (1.49)	7.10 (1.53)		
Week 52: Adjusted Mean Change (SE)	8.47 (1.44)	8.61 (1.43)	-0.15 [-4.13; 3.84]	0.943
KITE: Distance Activities				
Interaction test	p=0.554			
Non-exposed				
N'/ N	84 / 85	90 / 90		
Baseline Mean (SD)	76.49 (22.29)	75.46 (22.96)		
Week 52 Mean (SD)	88.10 (17.88)	83.06 (19.32)		
Week 28: Adjusted Mean Change (SE)	7.43 (1.77)	6.26 (1.75)		
Week 52: Adjusted Mean Change (SE)	11.73 (1.66)	7.19 (1.60)	4.54 [0.01; 9.07]	0.050 *
Exposed				
N'/ N	94 / 94	91 / 91		
Baseline Mean (SD)	77.26 (20.82)	76.92 (22.01)		
Week 52 Mean (SD)	87.78 (17.24)	85.72 (18.13)		
Week 28: Adjusted Mean Change (SE)	5.38 (1.62)	4.86 (1.63)		
Week 52: Adjusted Mean Change (SE)	11.10 (1.57)	9.24 (1.58)	1.87 [-2.53; 6.26]	0.404

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Distance Activities				
Interaction test	p=0.896			
Non-exposed				
N'/ N	155 / 156	165 / 165		
Baseline Mean (SD)	76.77 (22.84)	76.94 (22.17)		
Week 52 Mean (SD)	87.80 (16.73)	85.14 (17.95)		
Week 28: Adjusted Mean Change (SE)	7.83 (1.34)	8.92 (1.33)		
Week 52: Adjusted Mean Change (SE)	10.94 (1.25)	9.11 (1.21)	1.83 [-1.59; 5.25]	0.294
Exposed				
N'/ N	211 / 212	203 / 203		
Baseline Mean (SD)	75.53 (22.64)	74.82 (21.43)		
Week 52 Mean (SD)	85.79 (17.83)	84.42 (17.84)		
Week 28: Adjusted Mean Change (SE)	6.35 (1.11)	6.03 (1.12)		
Week 52: Adjusted Mean Change (SE)	9.78 (1.07)	8.82 (1.07)	0.96 [-2.00; 3.93]	0.524
Social Functioning				
Test of heterogeneity in main analysis: **p_H=0.037 ***				
KESTREL: Social Functioning				
Interaction test	p=0.447			
Non-exposed				
N'/ N	71 / 71	75 / 75		
Baseline Mean (SD)	90.49 (16.56)	92.67 (13.65)		
Week 52 Mean (SD)	93.08 (13.68)	95.70 (11.15)		
Week 28: Adjusted Mean Change (SE)	2.07 (1.53)	5.18 (1.52)		
Week 52: Adjusted Mean Change (SE)	2.13 (1.69)	5.07 (1.62)	-2.94 [-7.54; 1.66]	0.209
Exposed				
N'/ N	117 / 118	112 / 112		
Baseline Mean (SD)	87.82 (20.20)	87.95 (16.60)		
Week 52 Mean (SD)	92.20 (15.74)	92.45 (14.68)		
Week 28: Adjusted Mean Change (SE)	1.40 (1.14)	3.36 (1.17)		
Week 52: Adjusted Mean Change (SE)	2.99 (1.30)	3.59 (1.29)	-0.59 [-4.19; 3.01]	0.746

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Social Functioning				
Interaction test	p=0.999			
Non-exposed				
N'/ N	84 / 85	90 / 90		
Baseline Mean (SD)	87.20 (18.71)	84.86 (20.91)		
Week 52 Mean (SD)	95.65 (12.47)	91.33 (15.24)		
Week 28: Adjusted Mean Change (SE)	3.36 (1.56)	4.19 (1.55)		
Week 52: Adjusted Mean Change (SE)	8.46 (1.32)	4.81 (1.28)	3.65 [0.03; 7.26]	0.048 *
Exposed				
N'/ N	94 / 94	91 / 91		
Baseline Mean (SD)	89.49 (16.01)	87.91 (18.95)		
Week 52 Mean (SD)	94.67 (11.47)	91.83 (14.31)		
Week 28: Adjusted Mean Change (SE)	4.22 (1.44)	3.80 (1.44)		
Week 52: Adjusted Mean Change (SE)	6.52 (1.27)	4.13 (1.27)	2.39 [-1.13; 5.92]	0.183
Pooled Analysis: Social Functioning				
Interaction test	p=0.554			
Non-exposed				
N'/ N	155 / 156	165 / 165		
Baseline Mean (SD)	88.71 (17.78)	88.41 (18.34)		
Week 52 Mean (SD)	94.50 (13.03)	93.29 (13.69)		
Week 28: Adjusted Mean Change (SE)	2.55 (1.10)	4.58 (1.09)		
Week 52: Adjusted Mean Change (SE)	5.40 (1.07)	4.86 (1.03)	0.54 [-2.37; 3.45]	0.715
Exposed				
N'/ N	211 / 212	203 / 203		
Baseline Mean (SD)	88.57 (18.43)	87.93 (17.65)		
Week 52 Mean (SD)	93.30 (14.01)	92.18 (14.48)		
Week 28: Adjusted Mean Change (SE)	2.91 (0.91)	3.51 (0.92)		
Week 52: Adjusted Mean Change (SE)	4.84 (0.92)	3.80 (0.91)	1.03 [-1.50; 3.57]	0.424

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Mental Health				
Test of heterogeneity in main analysis: **p_H=0.300**				
KESTREL: Mental Health				
Interaction test	p=0.799			
Non-exposed				
N'/ N	71 / 71	75 / 75		
Baseline Mean (SD)	66.99 (25.40)	71.92 (20.71)		
Week 52 Mean (SD)	80.47 (18.50)	81.56 (16.24)		
Week 28: Adjusted Mean Change (SE)	7.57 (2.15)	9.03 (2.13)		
Week 52: Adjusted Mean Change (SE)	10.83 (2.18)	12.82 (2.10)	-1.99 [-7.94; 3.95]	0.510
Exposed				
N'/ N	117 / 118	112 / 112		
Baseline Mean (SD)	64.64 (24.70)	65.79 (24.24)		
Week 52 Mean (SD)	77.22 (20.91)	76.87 (18.69)		
Week 28: Adjusted Mean Change (SE)	7.24 (1.60)	9.11 (1.64)		
Week 52: Adjusted Mean Change (SE)	10.20 (1.68)	10.16 (1.66)	0.04 [-4.60; 4.68]	0.987
KITE: Mental Health				
Interaction test	p=0.765			
Non-exposed				
N'/ N	84 / 85	90 / 90		
Baseline Mean (SD)	69.79 (20.58)	64.03 (25.34)		
Week 52 Mean (SD)	82.61 (20.13)	77.17 (24.54)		
Week 28: Adjusted Mean Change (SE)	9.56 (1.90)	11.16 (1.88)		
Week 52: Adjusted Mean Change (SE)	13.52 (2.27)	10.22 (2.20)	3.30 [-2.93; 9.52]	0.298
Exposed				
N'/ N	94 / 94	91 / 91		
Baseline Mean (SD)	68.15 (22.49)	67.51 (26.68)		
Week 52 Mean (SD)	80.25 (21.31)	76.25 (22.74)		
Week 28: Adjusted Mean Change (SE)	8.02 (1.74)	7.73 (1.76)		
Week 52: Adjusted Mean Change (SE)	12.57 (2.16)	9.08 (2.17)	3.49 [-2.52; 9.51]	0.254

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Mental Health				
Interaction test	p=0.722			
Non-exposed				
N'/ N	155 / 156	165 / 165		
Baseline Mean (SD)	68.51 (22.88)	67.61 (23.61)		
Week 52 Mean (SD)	81.65 (19.37)	79.14 (21.26)		
Week 28: Adjusted Mean Change (SE)	8.61 (1.43)	10.12 (1.41)		
Week 52: Adjusted Mean Change (SE)	12.25 (1.58)	11.34 (1.52)	0.91 [-3.39; 5.21]	0.679
Exposed				
N'/ N	211 / 212	203 / 203		
Baseline Mean (SD)	66.20 (23.75)	66.56 (25.32)		
Week 52 Mean (SD)	78.57 (21.08)	76.60 (20.49)		
Week 28: Adjusted Mean Change (SE)	7.76 (1.18)	8.46 (1.20)		
Week 52: Adjusted Mean Change (SE)	11.38 (1.35)	9.61 (1.34)	1.77 [-1.96; 5.50]	0.352
Role Difficulties				
Test of heterogeneity in main analysis: **p_H=0.072**				
KESTREL: Role Difficulties				
Interaction test	p=0.101			
Non-exposed				
N'/ N	71 / 71	75 / 75		
Baseline Mean (SD)	74.12 (26.08)	74.00 (27.55)		
Week 52 Mean (SD)	79.91 (26.62)	87.30 (20.98)		
Week 28: Adjusted Mean Change (SE)	6.59 (2.67)	12.65 (2.65)		
Week 52: Adjusted Mean Change (SE)	5.52 (2.88)	15.18 (2.77)	-9.66 [-17.51; -1.80]	0.016 *
Exposed				
N'/ N	117 / 118	112 / 112		
Baseline Mean (SD)	70.73 (30.09)	70.31 (26.05)		
Week 52 Mean (SD)	81.18 (24.63)	80.54 (23.66)		
Week 28: Adjusted Mean Change (SE)	5.60 (1.99)	7.04 (2.04)		
Week 52: Adjusted Mean Change (SE)	7.89 (2.22)	8.66 (2.18)	-0.77 [-6.89; 5.35]	0.804

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Role Difficulties				
Interaction test	p=0.256			
Non-exposed				
N'/ N	84 / 85	90 / 90		
Baseline Mean (SD)	72.32 (25.45)	66.11 (30.92)		
Week 52 Mean (SD)	84.42 (19.93)	80.17 (23.44)		
Week 28: Adjusted Mean Change (SE)	6.42 (2.34)	9.61 (2.32)		
Week 52: Adjusted Mean Change (SE)	12.63 (2.46)	11.09 (2.38)	1.54 [-5.19; 8.28]	0.653
Exposed				
N'/ N	94 / 94	91 / 91		
Baseline Mean (SD)	69.95 (28.89)	68.27 (27.78)		
Week 52 Mean (SD)	81.50 (23.73)	76.17 (26.96)		
Week 28: Adjusted Mean Change (SE)	8.52 (2.15)	7.30 (2.16)		
Week 52: Adjusted Mean Change (SE)	11.96 (2.34)	5.99 (2.35)	5.97 [-0.56; 12.51]	0.073
Pooled Analysis: Role Difficulties				
Interaction test	p=0.053			
Non-exposed				
N'/ N	155 / 156	165 / 165		
Baseline Mean (SD)	73.15 (25.67)	69.70 (29.61)		
Week 52 Mean (SD)	82.40 (23.17)	83.36 (22.57)		
Week 28: Adjusted Mean Change (SE)	6.29 (1.78)	11.02 (1.76)		
Week 52: Adjusted Mean Change (SE)	9.21 (1.88)	12.99 (1.81)	-3.78 [-8.90; 1.35]	0.149
Exposed				
N'/ N	211 / 212	203 / 203		
Baseline Mean (SD)	70.38 (29.49)	69.40 (26.80)		
Week 52 Mean (SD)	81.32 (24.16)	78.63 (25.17)		
Week 28: Adjusted Mean Change (SE)	7.14 (1.47)	7.11 (1.49)		
Week 52: Adjusted Mean Change (SE)	9.88 (1.61)	7.44 (1.60)	2.44 [-2.01; 6.89]	0.282

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Dependency				
Test of heterogeneity in main analysis: **p_H=0.029 ***				
KESTREL: Dependency				
Interaction test	p=0.608			
Non-exposed				
N'/ N	71 / 71	75 / 75		
Baseline Mean (SD)	79.81 (28.51)	85.56 (21.02)		
Week 52 Mean (SD)	92.11 (16.32)	96.17 (9.57)		
Week 28: Adjusted Mean Change (SE)	7.17 (2.30)	9.21 (2.28)		
Week 52: Adjusted Mean Change (SE)	8.38 (2.34)	12.73 (2.26)	-4.35 [-10.75; 2.06]	0.183
Exposed				
N'/ N	117 / 118	112 / 112		
Baseline Mean (SD)	82.55 (25.07)	80.88 (25.40)		
Week 52 Mean (SD)	87.10 (24.53)	89.43 (19.97)		
Week 28: Adjusted Mean Change (SE)	4.74 (1.71)	5.38 (1.76)		
Week 52: Adjusted Mean Change (SE)	4.07 (1.81)	6.27 (1.78)	-2.20 [-7.19; 2.79]	0.387
KITE: Dependency				
Interaction test	p=0.467			
Non-exposed				
N'/ N	84 / 85	90 / 90		
Baseline Mean (SD)	85.02 (20.85)	81.48 (27.93)		
Week 52 Mean (SD)	90.22 (21.00)	87.56 (21.33)		
Week 28: Adjusted Mean Change (SE)	5.15 (1.92)	3.29 (1.89)		
Week 52: Adjusted Mean Change (SE)	5.55 (2.04)	3.56 (1.97)	1.99 [-3.59; 7.57]	0.483
Exposed				
N'/ N	94 / 94	91 / 91		
Baseline Mean (SD)	82.00 (25.76)	82.33 (26.17)		
Week 52 Mean (SD)	91.89 (17.49)	85.89 (24.12)		
Week 28: Adjusted Mean Change (SE)	6.09 (1.76)	3.42 (1.77)		
Week 52: Adjusted Mean Change (SE)	9.33 (1.93)	3.33 (1.95)	6.00 [0.60; 11.40]	0.029 *

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Dependency				
Interaction test	p=0.424			
Non-exposed				
N'/ N	155 / 156	165 / 165		
Baseline Mean (SD)	82.63 (24.71)	83.33 (25.03)		
Week 52 Mean (SD)	91.07 (19.00)	91.42 (17.57)		
Week 28: Adjusted Mean Change (SE)	6.17 (1.49)	6.17 (1.48)		
Week 52: Adjusted Mean Change (SE)	6.91 (1.56)	7.97 (1.51)	-1.06 [-5.32; 3.21]	0.627
Exposed				
N'/ N	211 / 212	203 / 203		
Baseline Mean (SD)	82.31 (25.32)	81.53 (25.69)		
Week 52 Mean (SD)	89.24 (21.74)	87.89 (21.88)		
Week 28: Adjusted Mean Change (SE)	5.40 (1.24)	4.33 (1.25)		
Week 52: Adjusted Mean Change (SE)	6.45 (1.33)	4.71 (1.33)	1.74 [-1.96; 5.43]	0.356
Driving				
Test of heterogeneity in main analysis: **p_H=0.778**				
KESTREL: Driving				
Interaction test	p=0.789			
Non-exposed				
N'/ N	51 / 71	50 / 75		
Baseline Mean (SD)	79.25 (19.61)	82.00 (18.70)		
Week 52 Mean (SD)	85.16 (17.03)	87.88 (17.06)		
Week 28: Adjusted Mean Change (SE)	2.48 (2.14)	7.11 (2.33)		
Week 52: Adjusted Mean Change (SE)	3.67 (2.47)	6.52 (2.74)	-2.85 [-10.12; 4.41]	0.440
Exposed				
N'/ N	69 / 118	70 / 112		
Baseline Mean (SD)	80.43 (17.95)	73.69 (19.78)		
Week 52 Mean (SD)	83.62 (22.13)	82.34 (18.38)		
Week 28: Adjusted Mean Change (SE)	1.78 (1.80)	4.90 (1.82)		
Week 52: Adjusted Mean Change (SE)	3.57 (2.09)	5.83 (2.09)	-2.25 [-8.08; 3.57]	0.447

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Driving				
Interaction test	p=0.605			
Non-exposed				
N'/ N	51 / 85	47 / 90		
Baseline Mean (SD)	81.62 (18.97)	80.41 (21.33)		
Week 52 Mean (SD)	87.02 (18.03)	87.18 (16.65)		
Week 28: Adjusted Mean Change (SE)	1.78 (2.07)	6.87 (2.22)		
Week 52: Adjusted Mean Change (SE)	4.59 (1.76)	5.42 (1.87)	-0.82 [-5.90; 4.26]	0.750
Exposed				
N'/ N	52 / 94	49 / 91		
Baseline Mean (SD)	76.44 (21.50)	83.67 (22.26)		
Week 52 Mean (SD)	86.79 (16.56)	88.51 (14.97)		
Week 28: Adjusted Mean Change (SE)	-0.29 (2.03)	4.22 (2.06)		
Week 52: Adjusted Mean Change (SE)	7.23 (1.79)	5.14 (1.88)	2.09 [-3.04; 7.21]	0.423
Pooled Analysis: Driving				
Interaction test	p=0.619			
Non-exposed				
N'/ N	102 / 156	97 / 165		
Baseline Mean (SD)	80.43 (19.23)	81.23 (19.93)		
Week 52 Mean (SD)	86.11 (17.47)	87.50 (16.73)		
Week 28: Adjusted Mean Change (SE)	2.11 (1.49)	7.07 (1.61)		
Week 52: Adjusted Mean Change (SE)	4.20 (1.53)	5.98 (1.65)	-1.78 [-6.21; 2.64]	0.429
Exposed				
N'/ N	121 / 212	119 / 203		
Baseline Mean (SD)	78.72 (19.57)	77.80 (21.32)		
Week 52 Mean (SD)	84.93 (19.98)	84.72 (17.33)		
Week 28: Adjusted Mean Change (SE)	0.89 (1.34)	4.61 (1.36)		
Week 52: Adjusted Mean Change (SE)	5.16 (1.40)	5.59 (1.42)	-0.43 [-4.36; 3.49]	0.828

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Color Vision				
Test of heterogeneity in main analysis: **p_H=0.691**				
KESTREL: Color Vision				
Interaction test	p=0.418			
Non-exposed				
N'/ N	70 / 71	75 / 75		
Baseline Mean (SD)	93.93 (15.01)	94.00 (15.29)		
Week 52 Mean (SD)	98.18 (8.13)	96.67 (10.76)		
Week 28: Adjusted Mean Change (SE)	2.40 (1.40)	4.79 (1.38)		
Week 52: Adjusted Mean Change (SE)	3.39 (1.43)	2.39 (1.38)	1.00 [-2.90; 4.90]	0.614
Exposed				
N'/ N	116 / 118	109 / 112		
Baseline Mean (SD)	92.46 (17.51)	94.04 (14.79)		
Week 52 Mean (SD)	95.70 (12.57)	95.43 (12.74)		
Week 28: Adjusted Mean Change (SE)	1.93 (1.04)	0.05 (1.07)		
Week 52: Adjusted Mean Change (SE)	1.49 (1.09)	1.42 (1.10)	0.07 [-2.98; 3.12]	0.965
KITE: Color Vision				
Interaction test	p=0.387			
Non-exposed				
N'/ N	84 / 85	89 / 90		
Baseline Mean (SD)	92.56 (17.26)	90.45 (16.65)		
Week 52 Mean (SD)	97.46 (8.73)	94.59 (11.90)		
Week 28: Adjusted Mean Change (SE)	4.11 (1.21)	5.41 (1.21)		
Week 52: Adjusted Mean Change (SE)	4.95 (1.09)	3.62 (1.06)	1.33 [-1.65; 4.32]	0.380
Exposed				
N'/ N	94 / 94	90 / 91		
Baseline Mean (SD)	91.76 (16.55)	93.06 (15.46)		
Week 52 Mean (SD)	97.64 (8.45)	95.21 (12.95)		
Week 28: Adjusted Mean Change (SE)	3.15 (1.12)	3.15 (1.13)		
Week 52: Adjusted Mean Change (SE)	6.51 (1.04)	3.29 (1.06)	3.22 [0.30; 6.14]	0.031 *

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Color Vision				
Interaction test	p=0.241			
Non-exposed				
N'/ N	154 / 156	164 / 165		
Baseline Mean (SD)	93.18 (16.24)	92.07 (16.09)		
Week 52 Mean (SD)	97.78 (8.44)	95.52 (11.41)		
Week 28: Adjusted Mean Change (SE)	3.20 (0.93)	4.98 (0.93)		
Week 52: Adjusted Mean Change (SE)	4.07 (0.88)	2.87 (0.85)	1.20 [-1.21; 3.61]	0.330
Exposed				
N'/ N	210 / 212	199 / 203		
Baseline Mean (SD)	92.14 (17.05)	93.59 (15.07)		
Week 52 Mean (SD)	96.56 (10.95)	95.33 (12.79)		
Week 28: Adjusted Mean Change (SE)	2.68 (0.77)	1.53 (0.79)		
Week 52: Adjusted Mean Change (SE)	3.90 (0.76)	2.38 (0.76)	1.52 [-0.58; 3.63]	0.155
Peripheral Vision				
Test of heterogeneity in main analysis: **p_H=0.021 ***				
KESTREL: Peripheral Vision				
Interaction test	p=0.256			
Non-exposed				
N'/ N	71 / 71	75 / 75		
Baseline Mean (SD)	82.75 (23.75)	85.00 (23.25)		
Week 52 Mean (SD)	91.52 (17.37)	89.75 (18.47)		
Week 28: Adjusted Mean Change (SE)	4.31 (2.24)	6.95 (2.23)		
Week 52: Adjusted Mean Change (SE)	7.49 (2.27)	6.82 (2.18)	0.67 [-5.51; 6.85]	0.832
Exposed				
N'/ N	116 / 118	111 / 112		
Baseline Mean (SD)	84.70 (20.53)	76.80 (22.79)		
Week 52 Mean (SD)	87.90 (20.72)	87.76 (17.39)		
Week 28: Adjusted Mean Change (SE)	1.97 (1.69)	8.34 (1.72)		
Week 52: Adjusted Mean Change (SE)	4.77 (1.75)	7.69 (1.74)	-2.92 [-7.79; 1.95]	0.240

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
KITE: Peripheral Vision				
Interaction test	p=0.145			
Non-exposed				
N'/ N	84 / 85	90 / 90		
Baseline Mean (SD)	84.52 (20.50)	85.28 (19.79)		
Week 52 Mean (SD)	90.22 (17.79)	86.33 (20.26)		
Week 28: Adjusted Mean Change (SE)	6.07 (1.77)	2.80 (1.75)		
Week 52: Adjusted Mean Change (SE)	6.05 (1.86)	1.77 (1.80)	4.28 [-0.81; 9.37]	0.099
Exposed				
N'/ N	94 / 94	90 / 91		
Baseline Mean (SD)	81.91 (19.88)	84.17 (22.93)		
Week 52 Mean (SD)	89.33 (16.53)	89.19 (18.54)		
Week 28: Adjusted Mean Change (SE)	3.69 (1.62)	6.19 (1.64)		
Week 52: Adjusted Mean Change (SE)	6.92 (1.77)	5.37 (1.79)	1.55 [-3.41; 6.51]	0.539
Pooled Analysis: Peripheral Vision				
Interaction test	p=0.055			
Non-exposed				
N'/ N	155 / 156	165 / 165		
Baseline Mean (SD)	83.71 (21.99)	85.15 (21.37)		
Week 52 Mean (SD)	90.80 (17.54)	87.87 (19.48)		
Week 28: Adjusted Mean Change (SE)	5.19 (1.42)	4.91 (1.41)		
Week 52: Adjusted Mean Change (SE)	6.59 (1.46)	4.29 (1.41)	2.30 [-1.69; 6.28]	0.258
Exposed				
N'/ N	210 / 212	201 / 203		
Baseline Mean (SD)	83.45 (20.24)	80.10 (23.09)		
Week 52 Mean (SD)	88.54 (18.93)	88.38 (17.86)		
Week 28: Adjusted Mean Change (SE)	2.66 (1.18)	7.37 (1.19)		
Week 52: Adjusted Mean Change (SE)	5.63 (1.25)	6.70 (1.25)	-1.07 [-4.55; 2.41]	0.547

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
General Health				
Test of heterogeneity in main analysis: **p_H=0.700**				
KESTREL: General Health				
Interaction test	p=0.888			
Non-exposed				
N'/ N	71 / 71	75 / 75		
Baseline Mean (SD)	45.42 (24.39)	39.00 (20.65)		
Week 52 Mean (SD)	54.46 (25.27)	46.72 (22.58)		
Week 28: Adjusted Mean Change (SE)	4.99 (2.31)	5.65 (2.29)		
Week 52: Adjusted Mean Change (SE)	9.30 (2.78)	6.37 (2.66)	2.93 [-4.65; 10.51]	0.448
Exposed				
N'/ N	117 / 118	112 / 112		
Baseline Mean (SD)	43.38 (18.97)	38.17 (19.84)		
Week 52 Mean (SD)	50.27 (23.46)	45.10 (20.93)		
Week 28: Adjusted Mean Change (SE)	4.00 (1.72)	4.14 (1.77)		
Week 52: Adjusted Mean Change (SE)	7.83 (2.14)	4.39 (2.11)	3.45 [-2.46; 9.35]	0.251
KITE: General Health				
Interaction test	p=0.031 *			
Non-exposed				
N'/ N	84 / 85	90 / 90		
Baseline Mean (SD)	45.83 (22.57)	43.33 (22.11)		
Week 52 Mean (SD)	48.91 (24.79)	51.00 (23.05)		
Week 28: Adjusted Mean Change (SE)	2.29 (2.04)	6.89 (2.02)		
Week 52: Adjusted Mean Change (SE)	3.10 (2.39)	6.54 (2.30)	-3.44 [-9.96; 3.08]	0.301
Exposed				
N'/ N	94 / 94	91 / 91		
Baseline Mean (SD)	42.29 (17.97)	45.88 (23.65)		
Week 52 Mean (SD)	50.00 (18.83)	49.33 (23.96)		
Week 28: Adjusted Mean Change (SE)	4.73 (1.88)	2.22 (1.89)		
Week 52: Adjusted Mean Change (SE)	7.63 (2.29)	3.45 (2.29)	4.18 [-2.20; 10.55]	0.198

	Treatment Groups		Comparison	
VFQ by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: General Health				
Interaction test	p=0.115			
Non-exposed				
N'/ N	155 / 156	165 / 165		
Baseline Mean (SD)	45.65 (23.35)	41.36 (21.50)		
Week 52 Mean (SD)	51.40 (25.06)	49.08 (22.85)		
Week 28: Adjusted Mean Change (SE)	3.47 (1.54)	6.43 (1.52)		
Week 52: Adjusted Mean Change (SE)	5.81 (1.82)	6.54 (1.75)	-0.73 [-5.68; 4.23]	0.774
Exposed				
N'/ N	211 / 212	203 / 203		
Baseline Mean (SD)	42.89 (18.50)	41.63 (21.91)		
Week 52 Mean (SD)	50.15 (21.45)	46.95 (22.33)		
Week 28: Adjusted Mean Change (SE)	4.15 (1.27)	3.39 (1.29)		
Week 52: Adjusted Mean Change (SE)	7.59 (1.56)	4.11 (1.55)	3.48 [-0.82; 7.79]	0.113

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 value + exposure + treatment * exposure + visit * exposure + treatment * exposure * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline value + study + treatment * study + exposure + treatment * exposure + visit * exposure + treatment * exposure * visit.

9 VFQ: Binary analysis (Gain)

Table 9.1 VFQ - Gain of 4 respectively 15 points (FAS), binary analysis, week 52

	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 (%) p_H=0.178	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
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

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 + 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 52

	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 ≥ 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 = 0.804				
< 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

	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	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

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 52

	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 ≥ 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

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 52

	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 ≥ 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

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 + 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 52

	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 ≥ 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 = 0.045 *				
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 *

	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 ≥ 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
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

	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	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 *

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 + 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 52

	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 ≥ 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

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 + 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).

Table 9.7 VFQ - Gain of 4 respectively 15 points by HbA1c (FAS), binary analysis, week 52

	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 ≥ 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

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 52

	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 ≥ 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 = 0.245				
≤ 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 *

	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 ≥ 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
> 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

	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	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

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 52

	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 ≥ 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

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 52

	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 ≥ 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 = 0.225				
< 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

	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 ≥ 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
≥ 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

	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	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

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 + 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 52

	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 ≥ 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

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 + 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 (FAS), binary analysis, week 52

	Treatment Groups		Comparison		
VFQ - Gain of 4 respectively 15 points by exposure (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 (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 (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
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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 + treatment * exposure.
RR and RD calculated directly (with Wald 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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

10 CSFT: Continuous analysis

Table 10.0 CSFT (FAS), return rates, Week 52

	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)
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)
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)

	Treatment Groups		
CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Total**
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)
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)
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)

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 52

	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 52: Adjusted Mean Change (SE)	-164.83 (6.41)	-162.69 (6.42)	-2.15 [-20.01; 15.72]	0.814
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 52: Adjusted Mean Change (SE)	-202.38 (6.98)	-167.05 (6.94)	-35.33 [-54.69; -15.97]	<.001 *
Pooled Analysis: Central Subfield Thickness - Study Eye p_H=0.065				
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 52: Adjusted Mean Change (SE)	-183.80 (4.74)	-164.97 (4.73)	-18.83 [-31.97; -5.69]	0.005 *

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 10.2 CSFT by age (FAS), continuous analysis, week 52

	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=0.065**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.543			
< 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 52: Adjusted Mean Change (SE)	-169.19 (8.61)	-171.95 (9.02)	2.76 [-21.78; 27.29]	0.825
≥ 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 52: Adjusted Mean Change (SE)	-160.87 (9.59)	-152.81 (9.14)	-8.06 [-34.11; 17.98]	0.543
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.576			
< 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 52: Adjusted Mean Change (SE)	-209.45 (9.40)	-162.95 (9.27)	-46.49 [-72.50; -20.49]	<.001 *
≥ 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 52: Adjusted Mean Change (SE)	-193.56 (10.39)	-171.95 (10.43)	-21.61 [-50.60; 7.37]	0.143

	Treatment Groups		Comparison	
CSFT by age (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.977			
< 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 52: Adjusted Mean Change (SE)	-189.59 (6.38)	-167.42 (6.48)	-22.17 [-40.05; -4.30]	0.015 *
≥ 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 52: Adjusted Mean Change (SE)	-177.05 (7.06)	-161.96 (6.91)	-15.09 [-34.48; 4.30]	0.127

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.

Table 10.3 CSFT by gender (FAS), continuous analysis, week 52

	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=0.065**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.640			
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 52: Adjusted Mean Change (SE)	-159.69 (8.45)	-165.40 (7.89)	5.71 [-17.03; 28.46]	0.621
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 52: Adjusted Mean Change (SE)	-171.69 (9.89)	-157.90 (11.09)	-13.78 [-43.02; 15.46]	0.355
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.274			
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 52: Adjusted Mean Change (SE)	-195.54 (8.52)	-171.91 (8.73)	-23.63 [-47.63; 0.37]	0.054
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 52: Adjusted Mean Change (SE)	-216.65 (12.23)	-158.74 (11.52)	-57.91 [-90.97; -24.85]	<.001 *

	Treatment Groups		Comparison	
CSFT by gender (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.263			
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 52: Adjusted Mean Change (SE)	-178.01 (6.00)	-168.46 (5.86)	-9.55 [-26.02; 6.92]	0.255
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 52: Adjusted Mean Change (SE)	-193.34 (7.74)	-158.83 (7.99)	-34.52 [-56.39; -12.65]	0.002 *

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.

Table 10.4 CSFT by BCVA (FAS), continuous analysis, week 52

	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=0.065**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.067			
≤ 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 52: Adjusted Mean Change (SE)	-171.62 (10.24)	-196.71 (10.99)	25.09 [-4.25; 54.44]	0.094
> 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 52: Adjusted Mean Change (SE)	-159.58 (8.12)	-145.41 (7.80)	-14.17 [-36.20; 7.87]	0.207
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.175			
≤ 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 52: Adjusted Mean Change (SE)	-236.80 (11.69)	-173.23 (9.78)	-63.57 [-93.19; -33.95]	<.001 *
> 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 52: Adjusted Mean Change (SE)	-182.70 (8.75)	-160.40 (9.87)	-22.30 [-48.02; 3.43]	0.089

	Treatment Groups		Comparison	
CSFT by BCVA (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.945			
≤ 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 52: Adjusted Mean Change (SE)	-204.75 (7.73)	-183.06 (7.36)	-21.69 [-42.42; -0.96]	0.040 *
> 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 52: Adjusted Mean Change (SE)	-170.75 (5.99)	-151.95 (6.23)	-18.81 [-35.64; -1.97]	0.029 *

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.

Table 10.5 CSFT by region (FAS), continuous analysis, week 52

	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=0.065**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.109			
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 52: Adjusted Mean Change (SE)	-162.40 (9.29)	-152.19 (9.70)	-10.21 [-36.62; 16.20]	0.448
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 52: Adjusted Mean Change (SE)	-156.81 (10.62)	-172.69 (10.22)	15.87 [-13.14; 44.88]	0.283
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 52: Adjusted Mean Change (SE)	-190.18 (16.07)	-165.21 (16.44)	-24.98 [-70.13; 20.18]	0.277
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.758			
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 52: Adjusted Mean Change (SE)	-219.84 (18.88)	-177.31 (20.85)	-42.52 [-97.66; 12.62]	0.130

	Treatment Groups		Comparison	
CSFT by region (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
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 52: Adjusted Mean Change (SE)	-198.26 (8.06)	-167.61 (8.15)	-30.66 [-53.13; -8.18]	0.008 *
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 52: Adjusted Mean Change (SE)	-207.92 (21.93)	-155.96 (17.87)	-51.96 [-107.31; 3.38]	0.066
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.341			
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 52: Adjusted Mean Change (SE)	-177.12 (10.77)	-153.74 (11.08)	-23.39 [-53.71; 6.93]	0.130
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 52: Adjusted Mean Change (SE)	-203.88 (19.13)	-176.54 (20.90)	-27.35 [-82.91; 28.21]	0.334
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 52: Adjusted Mean Change (SE)	-180.48 (6.58)	-169.84 (6.49)	-10.64 [-28.77; 7.49]	0.250

	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 52: Adjusted Mean Change (SE)	-199.32 (13.10)	-158.63 (12.00)	-40.69 [-75.58; -5.81]	0.022 *

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.

Table 10.6 CSFT by diabetes type (FAS), continuous analysis, week 52

	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=0.065**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.751			
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 52: Adjusted Mean Change (SE)	-185.87 (25.69)	-185.35 (34.87)	-0.52 [-85.71; 84.66]	0.990
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 52: Adjusted Mean Change (SE)	-163.45 (6.62)	-161.92 (6.53)	-1.53 [-19.85; 16.79]	0.869
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.167			
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 52: Adjusted Mean Change (SE)	-207.28 (21.21)	-122.46 (34.50)	-84.82 [-164.45; -5.19]	0.037 *
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 52: Adjusted Mean Change (SE)	-201.80 (7.41)	-168.89 (7.08)	-32.91 [-53.07; -12.75]	0.001 *

	Treatment Groups		Comparison	
CSFT by diabetes type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.198			
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 52: Adjusted Mean Change (SE)	-196.10 (16.25)	-151.06 (24.53)	-45.04 [-102.83; 12.74]	0.126
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 52: Adjusted Mean Change (SE)	-182.67 (4.96)	-165.45 (4.82)	-17.22 [-30.80; -3.64]	0.013 *

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.

Table 10.7 CSFT by HbA1c (FAS), continuous analysis, week 52

	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=0.065**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.638			
< 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 52: Adjusted Mean Change (SE)	-159.97 (10.07)	-163.99 (8.45)	4.02 [-21.84; 29.88]	0.760
≥ 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 52: Adjusted Mean Change (SE)	-168.74 (8.39)	-161.22 (9.96)	-7.52 [-33.18; 18.13]	0.565
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.143			
< 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 52: Adjusted Mean Change (SE)	-211.93 (10.40)	-166.11 (9.50)	-45.82 [-73.48; -18.16]	0.001 *
≥ 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 52: Adjusted Mean Change (SE)	-194.53 (9.45)	-168.16 (10.19)	-26.37 [-53.69; 0.95]	0.058

	Treatment Groups		Comparison	
CSFT by HbA1c (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.423			
< 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 52: Adjusted Mean Change (SE)	-187.07 (7.25)	-165.03 (6.34)	-22.03 [-40.93; -3.13]	0.022 *
≥ 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 52: Adjusted Mean Change (SE)	-181.72 (6.30)	-165.10 (7.12)	-16.62 [-35.29; 2.05]	0.081

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.

Table 10.8 CSFT by duration of DME (FAS), continuous analysis, week 52

	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=0.065**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.751			
≤ 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 52: Adjusted Mean Change (SE)	-159.92 (8.05)	-159.59 (8.41)	-0.33 [-23.28; 22.62]	0.977
> 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 52: Adjusted Mean Change (SE)	-174.28 (16.17)	-169.63 (14.26)	-4.64 [-47.04; 37.76]	0.830
≥ 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 52: Adjusted Mean Change (SE)	-172.26 (14.50)	-164.35 (14.25)	-7.91 [-47.80; 31.99]	0.697
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.321			
≤ 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 52: Adjusted Mean Change (SE)	-196.37 (10.23)	-157.36 (9.82)	-39.01 [-66.91; -11.11]	0.006 *

	Treatment Groups		Comparison	
CSFT 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)	516.24 (138.13)	503.51 (132.81)		
Week 52 Mean (SD)	282.41 (65.61)	299.95 (78.38)		
Week 52: Adjusted Mean Change (SE)	-216.66 (13.08)	-184.64 (13.38)	-32.02 [-68.74; 4.70]	0.087
≥ 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 52: Adjusted Mean Change (SE)	-196.71 (14.37)	-167.78 (14.95)	-28.93 [-69.67; 11.81]	0.163
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.671			
≤ 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 52: Adjusted Mean Change (SE)	-177.75 (6.38)	-158.87 (6.40)	-18.89 [-36.62; -1.15]	0.037 *
> 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 52: Adjusted Mean Change (SE)	-196.58 (10.11)	-178.39 (9.69)	-18.19 [-45.67; 9.29]	0.194

	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 52: Adjusted Mean Change (SE)	-186.32 (10.15)	-165.48 (10.30)	-20.83 [-49.19; 7.52]	0.150

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.

Table 10.9 CSFT by DME type (FAS), continuous analysis, week 52

	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=0.065**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.182			
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 52: Adjusted Mean Change (SE)	-155.11 (11.42)	-130.09 (12.77)	-25.02 [-58.62; 8.58]	0.144
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 52: Adjusted Mean Change (SE)	-170.31 (7.85)	-175.89 (7.57)	5.58 [-15.87; 27.03]	0.609
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.712			
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 52: Adjusted Mean Change (SE)	-179.90 (11.99)	-157.43 (11.66)	-22.47 [-55.11; 10.17]	0.177
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 52: Adjusted Mean Change (SE)	-215.44 (8.73)	-173.59 (9.06)	-41.85 [-66.49; -17.22]	<.001 *

	Treatment Groups		Comparison	
CSFT by DME type (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.550			
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 52: Adjusted Mean Change (SE)	-167.00 (8.30)	-144.67 (8.61)	-22.33 [-45.67; 1.01]	0.061
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 52: Adjusted Mean Change (SE)	-193.54 (5.85)	-175.73 (5.85)	-17.81 [-34.01; -1.61]	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
*: $p < 0.05$
.....

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.

Table 10.10 CSFT by CSFT (FAS), continuous analysis, week 52

	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=0.065**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.003 *			
< 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 52: Adjusted Mean Change (SE)	-93.70 (8.37)	-91.04 (8.83)	-2.66 [-26.59; 21.27]	0.827
≥ 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 52: Adjusted Mean Change (SE)	-224.21 (10.33)	-201.54 (10.19)	-22.68 [-51.22; 5.86]	0.119
≥ 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 52: Adjusted Mean Change (SE)	-338.60 (25.13)	-434.56 (19.33)	95.97 [33.72; 158.22]	0.003 *
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.002 *			
< 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 52: Adjusted Mean Change (SE)	-101.83 (9.89)	-83.48 (10.07)	-18.35 [-46.13; 9.42]	0.195
≥ 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 52: Adjusted Mean Change (SE)	-234.00 (10.40)	-207.82 (10.00)	-26.18 [-54.61; 2.25]	0.071

	Treatment Groups		Comparison	
CSFT by CSFT (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
≥ 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 52: Adjusted Mean Change (SE)	-505.03 (20.11)	-364.51 (20.64)	-140.52 [-197.19; -83.86]	<.001 *
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.645			
< 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 52: Adjusted Mean Change (SE)	-98.61 (6.55)	-87.44 (6.79)	-11.16 [-29.70; 7.37]	0.237
≥ 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 52: Adjusted Mean Change (SE)	-229.48 (7.47)	-204.82 (7.26)	-24.67 [-45.12; -4.21]	0.018 *
≥ 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 52: Adjusted Mean Change (SE)	-444.01 (15.99)	-401.00 (14.39)	-43.01 [-85.21; -0.81]	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 + 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.

Table 10.11 CSFT by status of SRF (FAS), continuous analysis, week 52

	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=0.065**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.395			
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 52: Adjusted Mean Change (SE)	-182.70 (11.20)	-188.38 (11.67)	5.67 [-25.46; 36.80]	0.720
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 52: Adjusted Mean Change (SE)	-155.27 (7.85)	-151.13 (7.88)	-4.14 [-25.75; 17.48]	0.707
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.133			
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 52: Adjusted Mean Change (SE)	-220.38 (12.49)	-203.41 (11.60)	-16.97 [-49.88; 15.94]	0.311
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 52: Adjusted Mean Change (SE)	-194.16 (8.36)	-146.09 (8.73)	-48.07 [-71.63; -24.50]	<.001 *

	Treatment Groups		Comparison	
CSFT by status of SRF (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.078			
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 52: Adjusted Mean Change (SE)	-202.21 (8.38)	-197.38 (8.24)	-4.83 [-27.44; 17.78]	0.675
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 52: Adjusted Mean Change (SE)	-174.75 (5.74)	-148.26 (5.88)	-26.50 [-42.45; -10.54]	0.001 *

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.

Table 10.12 CSFT by exposure (FAS), continuous analysis, week 52

	Treatment Groups		Comparison	
CSFT by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Central Subfield Thickness - Study Eye				
Test of heterogeneity in main analysis: **p_H=0.065**				
KESTREL: Central Subfield Thickness - Study Eye				
Interaction test	p=0.983			
Non-exposed				
N'/ N	71 / 71	75 / 75		
Baseline Mean (SD)	465.96 (142.87)	450.05 (114.66)		
Week 52 Mean (SD)	298.67 (96.64)	304.98 (82.75)		
Week 52: Adjusted Mean Change (SE)	-159.78 (10.55)	-156.43 (10.35)	-3.35 [-32.45; 25.75]	0.821
Exposed				
N'/ N	118 / 118	112 / 112		
Baseline Mean (SD)	445.31 (110.01)	492.71 (146.35)		
Week 52 Mean (SD)	288.83 (62.91)	311.52 (73.66)		
Week 52: Adjusted Mean Change (SE)	-168.00 (8.10)	-166.64 (8.23)	-1.36 [-24.11; 21.40]	0.907
KITE: Central Subfield Thickness - Study Eye				
Interaction test	p=0.772			
Non-exposed				
N'/ N	85 / 85	89 / 90		
Baseline Mean (SD)	499.79 (138.12)	498.03 (151.22)		
Week 52 Mean (SD)	279.34 (50.87)	303.07 (71.73)		
Week 52: Adjusted Mean Change (SE)	-211.48 (10.15)	-176.35 (9.91)	-35.13 [-63.01; -7.25]	0.014 *
Exposed				
N'/ N	94 / 94	91 / 91		
Baseline Mean (SD)	464.27 (125.49)	470.97 (115.31)		
Week 52 Mean (SD)	279.36 (60.75)	316.58 (95.40)		
Week 52: Adjusted Mean Change (SE)	-194.19 (9.53)	-157.84 (9.68)	-36.35 [-63.07; -9.63]	0.008 *

	Treatment Groups		Comparison	
CSFT by exposure (FAS)	**Brolucizumab**	**Aflibercept**	**Mean Difference [95% CI]**	**p-value**
Pooled Analysis: Central Subfield Thickness - Study Eye				
Interaction test	p=0.779			
Non-exposed				
N'/ N	156 / 156	164 / 165		
Baseline Mean (SD)	484.39 (140.87)	476.09 (137.43)		
Week 52 Mean (SD)	288.03 (75.28)	303.93 (76.58)		
Week 52: Adjusted Mean Change (SE)	-187.50 (7.34)	-167.26 (7.19)	-20.24 [-40.43; -0.05]	0.049 *
Exposed				
N'/ N	212 / 212	203 / 203		
Baseline Mean (SD)	453.71 (117.22)	482.96 (133.46)		
Week 52 Mean (SD)	284.65 (61.97)	313.71 (83.58)		
Week 52: Adjusted Mean Change (SE)	-181.31 (6.23)	-163.09 (6.32)	-18.22 [-35.66; -0.78]	0.041 *

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 + exposure + treatment * exposure + visit * exposure + treatment * exposure * visit.
Pooled analysis: Change from baseline = treatment + visit + treatment * visit + age category + baseline category + study + treatment * study + exposure + treatment * exposure + visit * exposure + treatment * exposure * visit.

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 52

	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 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 *
Pooled Analysis, N''/N'/N	301 / 368 / 368	313 / 368 / 368			
Presence of IRF in the study eye, n (%)	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 *
p_H=0.503					
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 *

	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=0.574	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 *

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 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 11.2 Presence of SRF and/or IRF in the study eye by age (FAS), binary analysis, week 52

	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 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 *

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 + 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: logit(proportion) = treatment [by age].

Table 11.3 Presence of SRF and/or IRF in the study eye by gender (FAS), binary analysis, week 52

	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 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 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 *

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 11.4 Presence of SRF and/or IRF in the study eye by BCVA (FAS), binary analysis, week 52

	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 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 *

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: logit(proportion) = treatment [by BCVA].

Table 11.5 Presence of SRF and/or IRF in the study eye by region (FAS), binary analysis, week 52

	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 SRF and/or IRF in the study eye, Week 52					
Test of heterogeneity in main analysis: $\mathbf{p_H=0.574}$					
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 *

	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 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 *
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 *

	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 (%)	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 *

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 11.6 Presence of SRF and/or IRF in the study eye by diabetes type (FAS), binary analysis, week 52

	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 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 = 0.600				
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 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

	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 (%)	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 *

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):
Presence of SRF in the study eye / KESTREL, Presence of SRF in the study eye / KITE: logit(proportion) = treatment [by diabetes type].
Presence of SRF in the study eye / Pooled Analysis: 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 52

	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 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 *

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: logit(proportion) = treatment [by HbA1c].

Table 11.8 Presence of SRF and/or IRF in the study eye by duration of DME (FAS), binary analysis, week 52

	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 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 = 0.402				
≤ 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

	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 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 *
> 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

	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	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 *

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 11.9 Presence of SRF and/or IRF in the study eye by DME type (FAS), binary analysis, week 52

	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 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 *

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 11.10 Presence of SRF and/or IRF in the study eye by CSFT (FAS), binary analysis, week 52

	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 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 = 0.224				
< 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

	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 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 *
≥ 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 *

	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	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

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 + 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 11.11 Presence of SRF and/or IRF in the study eye by status of SRF (FAS), binary analysis, week 52

	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 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 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 *

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, Presence of SRF in the study eye / KITE: logit(proportion) = treatment [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 (FAS), binary analysis, week 52

	Treatment Groups		Comparison		
Presence of SRF and/or IRF in the study eye by exposure (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 (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 (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 (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
CI: Confidence interval
OR: 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 + treatment * exposure.
RR and RD calculated directly (with Wald 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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

12 Safety analysis: Any adverse event

Table 12-1.1 Any adverse event (SAF), binary analysis, week 52

	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 (%)	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
p_H=0.209					

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 52

	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

	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 (%)	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

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 52

	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

	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 (%)	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

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 52

	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

	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 (%)	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

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 12-1.5 Any adverse event by region (SAF), binary analysis, week 52

	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

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 52

	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 *

	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 (%)	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

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):
KESTREL, KITE: logit(proportion) = treatment [by diabetes type].
Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by diabetes type].

Table 12-1.7 Any adverse event by HbA1c (SAF), binary analysis, week 52

	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

	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 (%)	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

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 52

	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

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 52

	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

	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 (%)	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

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 52

	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 *

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 12-1.11 Any adverse event by status of SRF (SAF), binary analysis, week 52

	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

	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 (%)	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

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 12-1.12 Any adverse event by exposure (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any adverse event by exposure (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

	Treatment Groups		Comparison		
Any adverse event by exposure (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, 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

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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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 52

	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					

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 52

	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

	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 (%)	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

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 52

	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

	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 (%)	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

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 52

	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

	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 (%)	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

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 12-2.5 Any ocular adverse event by region (SAF), binary analysis, week 52

	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

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 52

	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

	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 (%)	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

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):
KESTREL: logit(proportion) = treatment [by diabetes type].

Table 12-2.7 Any ocular adverse event by HbA1c (SAF), binary analysis, week 52

	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

	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 (%)	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

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 52

	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

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 52

	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

	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 (%)	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

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 52

	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

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 12-2.11 Any ocular adverse event by status of SRF (SAF), binary analysis, week 52

	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

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 (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any ocular adverse event by exposure (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 (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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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 52

	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					

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 52

	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

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 52

	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

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 12-3.4 Any ocular adverse event at the study eye by BCVA (SAF), binary analysis, week 52

	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

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 12-3.5 Any ocular adverse event at the study eye by region (SAF), binary analysis, week 52

	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

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 12-3.6 Any ocular adverse event at the study eye by diabetes type (SAF), binary analysis, week 52

	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

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):
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 52

	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

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 52

	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

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 52

	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

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 52

	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

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 12-3.11 Any ocular adverse event at the study eye by status of SRF (SAF), binary analysis, week 52

	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

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 12-3.12 Any ocular adverse event at the study eye by exposure (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any ocular adverse event at the study eye by exposure (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 (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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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 52

	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					

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 12-4.2 Any ocular adverse event at the fellow eye by age (SAF), binary analysis, week 52

	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

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 52

	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

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 12-4.4 Any ocular adverse event at the fellow eye by BCVA (SAF), binary analysis, week 52

	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

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 12-4.5 Any ocular adverse event at the fellow eye by region (SAF), binary analysis, week 52

	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

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 12-4.6 Any ocular adverse event at the fellow eye by diabetes type (SAF), binary analysis, week 52

	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

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 52

	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

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 52

	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

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 12-4.9 Any ocular adverse event at the fellow eye by DME type (SAF), binary analysis, week 52

	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

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 52

	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

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 52

	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

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 12-4.12 Any ocular adverse event at the fellow eye by exposure (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any ocular adverse event at the fellow eye by exposure (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 (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
.....

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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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 52

	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					

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 52

	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

	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 (%)	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

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 52

	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

	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 (%)	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

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 52

	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

	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 (%)	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

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 52

	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

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 52

	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

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 12-5.7 Any non-ocular adverse event by HbA1c (SAF), binary analysis, week 52

	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

	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 (%)	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

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 52

	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

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 52

	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

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 52

	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

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 52

	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

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 (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any non-ocular adverse event by exposure (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 (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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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 52

	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					

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 52

	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

	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 (%)	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

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 52

	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

	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 (%)	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

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 52

	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

	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 (%)	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

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 52

	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

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 52

	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

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 52

	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

	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 (%)	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 *

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 52

	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

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 13-1.9 Any serious adverse event by DME type (SAF), binary analysis, week 52

	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

	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 (%)	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

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 13-1.10 Any serious adverse event by CSFT (SAF), binary analysis, week 52

	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

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 52

	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

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 (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any serious adverse event by exposure (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 (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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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 52

	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					

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 52

	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

	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 (%)	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

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):
KESTREL, KITE: logit(proportion) = treatment [by age].

Table 13-2.3 Any serious ocular adverse event by gender (SAF), binary analysis, week 52

	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

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):
KESTREL: logit(proportion) = treatment [by gender].

Table 13-2.4 Any serious ocular adverse event by BCVA (SAF), binary analysis, week 52

	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

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):
KESTREL: logit(proportion) = treatment [by BCVA].

Table 13-2.5 Any serious ocular adverse event by region (SAF), binary analysis, week 52

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

Table 13-2.6 Any serious ocular adverse event by diabetes type (SAF), binary analysis, week 52

	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.

	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 (%)	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

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):
KESTREL, KITE: logit(proportion) = treatment [by diabetes type].
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 52

	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 *

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):
KESTREL, KITE: logit(proportion) = treatment [by HbA1c].

Table 13-2.8 Any serious ocular adverse event by duration of DME (SAF), binary analysis, week 52

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

Table 13-2.9 Any serious ocular adverse event by DME type (SAF), binary analysis, week 52

	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

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):
KESTREL, KITE: logit(proportion) = treatment [by DME type].

Table 13-2.10 Any serious ocular adverse event by CSFT (SAF), binary analysis, week 52

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

Table 13-2.11 Any serious ocular adverse event by status of SRF (SAF), binary analysis, week 52

	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

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):
KESTREL: logit(proportion) = treatment [by status of SRF].

Table 13-2.12 Any serious ocular adverse event by exposure (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any serious ocular adverse event by exposure (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 (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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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):
KITE: logit(proportion) = treatment [by exposure].

Table 13-3.1 Any serious ocular adverse event at the study eye (SAF), binary analysis, week 52

	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 (%)	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
p_H=0.381					

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 52

	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

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):
KESTREL, 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 52

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

Table 13-3.4 Any serious ocular adverse event at the study eye by BCVA (SAF), binary analysis, week 52

	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

	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 (%)	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

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):
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 52

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

Table 13-3.6 Any serious ocular adverse event at the study eye by diabetes type (SAF), binary analysis, week 52

	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.

	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 (%)	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

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):
KESTREL, KITE: logit(proportion) = treatment [by diabetes type].
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 52

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

Table 13-3.8 Any serious ocular adverse event at the study eye by duration of DME (SAF), binary analysis, week 52

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

Table 13-3.9 Any serious ocular adverse event at the study eye by DME type (SAF), binary analysis, week 52

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

Table 13-3.10 Any serious ocular adverse event at the study eye by CSFT (SAF), binary analysis, week 52

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 52

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

Table 13-3.12 Any serious ocular adverse event at the study eye by exposure (SAF), binary analysis, week 52

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

Table 13-4.1 Any serious ocular adverse event at the fellow eye (SAF), binary analysis, week 52

	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.					

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 52

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

Table 13-4.3 Any serious ocular adverse event at the fellow eye by gender (SAF), binary analysis, week 52

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

Table 13-4.4 Any serious ocular adverse event at the fellow eye by BCVA (SAF), binary analysis, week 52

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 52

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 52

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

Table 13-4.7 Any serious ocular adverse event at the fellow eye by HbA1c (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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

Table 13-4.12 Any serious ocular adverse event at the fellow eye by exposure (SAF), binary analysis, week 52

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

Table 13-5.1 Any serious non-ocular adverse event (SAF), binary analysis, week 52

	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					

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 52

	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

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 52

	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

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 52

	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

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 13-5.5 Any serious non-ocular adverse event by region (SAF), binary analysis, week 52

	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

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 13-5.6 Any serious non-ocular adverse event by diabetes type (SAF), binary analysis, week 52

	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

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 52

	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

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 52

	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

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 13-5.9 Any serious non-ocular adverse event by DME type (SAF), binary analysis, week 52

	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

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 52

	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

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 52

	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

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 (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any serious non-ocular adverse event by exposure (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 (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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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 52

	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					

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 52

	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

	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 (%)	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

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 14-1.3 Any severe adverse event by gender (SAF), binary analysis, week 52

	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

	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 (%)	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

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 52

	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 *

	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 (%)	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

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 52

	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

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):
KITE: logit(proportion) = treatment [by region].
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 52

	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

	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 (%)	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

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):
KITE: logit(proportion) = treatment [by diabetes type].

Table 14-1.7 Any severe adverse event by HbA1c (SAF), binary analysis, week 52

	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

	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 (%)	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

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 52

	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

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 52

	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

	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 (%)	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

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 52

	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

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 52

	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

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 (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any severe adverse event by exposure (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 (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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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 52

	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					

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 52

	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

	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 (%)	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

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):
KITE: logit(proportion) = treatment [by age].

Table 14-2.3 Any severe ocular adverse event by gender (SAF), binary analysis, week 52

	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

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):
KESTREL, KITE: logit(proportion) = treatment [by gender].

Table 14-2.4 Any severe ocular adverse event by BCVA (SAF), binary analysis, week 52

	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

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 52

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

Table 14-2.6 Any severe ocular adverse event by diabetes type (SAF), binary analysis, week 52

	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.

	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 (%)	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

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):
KESTREL, KITE: logit(proportion) = treatment [by diabetes type].
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 52

	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

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 52

	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

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):
KESTREL, KITE: logit(proportion) = treatment [by duration of DME].

Table 14-2.9 Any severe ocular adverse event by DME type (SAF), binary analysis, week 52

	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

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):
KESTREL: logit(proportion) = treatment [by DME type].

Table 14-2.10 Any severe ocular adverse event by CSFT (SAF), binary analysis, week 52

	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

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):
KESTREL, KITE: logit(proportion) = treatment [by CSFT].

Table 14-2.11 Any severe ocular adverse event by status of SRF (SAF), binary analysis, week 52

	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

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):
KITE: logit(proportion) = treatment [by status of SRF].

Table 14-2.12 Any severe ocular adverse event by exposure (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any severe ocular adverse event by exposure (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 (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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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 14-3.1 Any severe ocular adverse event at the study eye (SAF), binary analysis, week 52

	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 *					

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 52

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

Table 14-3.3 Any severe ocular adverse event at the study eye by gender (SAF), binary analysis, week 52

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

Table 14-3.4 Any severe ocular adverse event at the study eye by BCVA (SAF), binary analysis, week 52

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

Table 14-3.5 Any severe ocular adverse event at the study eye by region (SAF), binary analysis, week 52

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

Table 14-3.6 Any severe ocular adverse event at the study eye by diabetes type (SAF), binary analysis, week 52

	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.

	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 (%)	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

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):
KESTREL, KITE: logit(proportion) = treatment [by diabetes type].
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 52

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

Table 14-3.8 Any severe ocular adverse event at the study eye by duration of DME (SAF), binary analysis, week 52

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

Table 14-3.9 Any severe ocular adverse event at the study eye by DME type (SAF), binary analysis, week 52

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

Table 14-3.10 Any severe ocular adverse event at the study eye by CSFT (SAF), binary analysis, week 52

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

Table 14-3.11 Any severe ocular adverse event at the study eye by status of SRF (SAF), binary analysis, week 52

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

Table 14-3.12 Any severe ocular adverse event at the study eye by exposure (SAF), binary analysis, week 52

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

Table 14-4.1 Any severe ocular adverse event at the fellow eye (SAF), binary analysis, week 52

	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 (%) p_H=0.663	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

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 52

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

Table 14-4.3 Any severe ocular adverse event at the fellow eye by gender (SAF), binary analysis, week 52

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 52

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

Table 14-4.5 Any severe ocular adverse event at the fellow eye by region (SAF), binary analysis, week 52

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 52

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

Table 14-4.7 Any severe ocular adverse event at the fellow eye by HbA1c (SAF), binary analysis, week 52

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

Table 14-4.8 Any severe ocular adverse event at the fellow eye by duration of DME (SAF), binary analysis, week 52

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

Table 14-4.9 Any severe ocular adverse event at the fellow eye by DME type (SAF), binary analysis, week 52

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

Table 14-4.10 Any severe ocular adverse event at the fellow eye by CSFT (SAF), binary analysis, week 52

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 52

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

Table 14-4.12 Any severe ocular adverse event at the fellow eye by exposure (SAF), binary analysis, week 52

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

Table 14-5.1 Any severe non-ocular adverse event (SAF), binary analysis, week 52

	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					

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 14-5.2 Any severe non-ocular adverse event by age (SAF), binary analysis, week 52

	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

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 14-5.3 Any severe non-ocular adverse event by gender (SAF), binary analysis, week 52

	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

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 14-5.4 Any severe non-ocular adverse event by BCVA (SAF), binary analysis, week 52

	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

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 52

	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

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):
KITE: logit(proportion) = treatment [by region].
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 52

	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

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):
KITE: logit(proportion) = treatment [by diabetes type].

Table 14-5.7 Any severe non-ocular adverse event by HbA1c (SAF), binary analysis, week 52

	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

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 14-5.8 Any severe non-ocular adverse event by duration of DME (SAF), binary analysis, week 52

	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

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 14-5.9 Any severe non-ocular adverse event by DME type (SAF), binary analysis, week 52

	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

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 52

	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

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 52

	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

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 (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any severe non-ocular adverse event by exposure (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 (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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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 52

	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					

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 15-1.2 Any adverse event leading to study drug discontinuation by age (SAF), binary analysis, week 52

	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

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 15-1.3 Any adverse event leading to study drug discontinuation by gender (SAF), binary analysis, week 52

	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

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 52

	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

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 15-1.5 Any adverse event leading to study drug discontinuation by region (SAF), binary analysis, week 52

	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

	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	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
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

	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 (%)	6 (12.5)	3 (5.3)	N.E.	2.57 [0.73; 8.98] 0.129	0.09 [-0.02; 0.20] 0.112

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):
KESTREL, KITE: logit(proportion) = treatment [by region].
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 52

	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.

	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 (%)	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

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):
KESTREL, KITE: logit(proportion) = treatment [by diabetes type].
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 52

	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

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 52

	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

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):
KESTREL, KITE: 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 52

	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

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):
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 52

	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

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):
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 52

	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

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 15-1.12 Any adverse event leading to study drug discontinuation by exposure (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any adverse event leading to study drug discontinuation by exposure (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 (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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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: logit(proportion) = treatment [by exposure].

Table 15-2.1 Any ocular adverse event leading to study drug discontinuation (SAF), binary analysis, week 52

	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					

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 52

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

Table 15-2.3 Any ocular adverse event leading to study drug discontinuation by gender (SAF), binary analysis, week 52

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 52

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 52

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 52

	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

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):
KESTREL, KITE: logit(proportion) = treatment [by diabetes type].
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 52

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 52

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 52

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

Table 15-2.10 Any ocular adverse event leading to study drug discontinuation by CSFT (SAF), binary analysis, week 52

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 52

	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

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):
KESTREL, KITE: logit(proportion) = treatment [by status of SRF].
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 (SAF), binary analysis, week 52

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

Table 15-3.1 Any ocular adverse event at the study eye leading to study drug discontinuation (SAF), binary analysis, week 52

	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					

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 52

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

Table 15-3.3 Any ocular adverse event at the study eye leading to study drug discontinuation by gender (SAF), binary analysis, week 52

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 52

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 52

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 52

	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

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):
KESTREL, KITE: logit(proportion) = treatment [by diabetes type].
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 52

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 52

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 52

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

Table 15-3.10 Any ocular adverse event at the study eye leading to study drug discontinuation by CSFT (SAF), binary analysis, week 52

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 52

	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

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):
KESTREL, KITE: logit(proportion) = treatment [by status of SRF].
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 (SAF), binary analysis, week 52

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

Table 15-4.1 Any ocular adverse event at the fellow eye leading to study drug discontinuation (SAF), binary analysis, week 52

	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.					

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 (SAF), binary analysis, week 52

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 52

	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					

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 15-5.2 Any non-ocular adverse event leading to study drug discontinuation by age (SAF), binary analysis, week 52

	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

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):
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 52

	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

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):
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 52

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

Table 15-5.5 Any non-ocular adverse event leading to study drug discontinuation by region (SAF), binary analysis, week 52

	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

	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	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 (%)	4 (2.0)	6 (2.9)	N.E.	0.71 [0.21; 2.37] 0.570	-0.01 [-0.04; 0.02] 0.541

	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):
KESTREL, KITE: logit(proportion) = treatment [by region].
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 52

	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

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):
KESTREL, KITE: logit(proportion) = treatment [by diabetes type].
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 52

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

Table 15-5.8 Any non-ocular adverse event leading to study drug discontinuation by duration of DME (SAF), binary analysis, week 52

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

Table 15-5.9 Any non-ocular adverse event leading to study drug discontinuation by DME type (SAF), binary analysis, week 52

	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

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 52

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

Table 15-5.11 Any non-ocular adverse event leading to study drug discontinuation by status of SRF (SAF), binary analysis, week 52

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

Table 15-5.12 Any non-ocular adverse event leading to study drug discontinuation by exposure (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any non-ocular adverse event leading to study drug discontinuation by exposure (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 (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
.....

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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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, KITE: logit(proportion) = treatment [by exposure].

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 52

	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 52					
Eye disorders					
KESTREL, n (%)	91 (48.1)	82 (43.9)	1.19 [0.79; 1.78] 0.403	1.10 [0.88; 1.37] 0.404	0.04 [-0.06; 0.14] 0.403
KITE, n (%)	72 (40.2)	68 (37.6)	1.12 [0.73; 1.71] 0.606	1.07 [0.83; 1.39] 0.606	0.03 [-0.07; 0.13] 0.605
Pooled Analysis, n (%) p_H=0.838	163 (44.3)	150 (40.8)	1.15 [0.86; 1.55] 0.339	1.09 [0.92; 1.28] 0.337	0.03 [-0.04; 0.11] 0.336
Conjunctival haemorrhage					
KESTREL, n (%)	17 (9.0)	21 (11.2)	0.78 [0.40; 1.53] 0.473	0.80 [0.44; 1.47] 0.473	-0.02 [-0.08; 0.04] 0.472
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=0.968	25 (6.8)	31 (8.4)	0.79 [0.44; 1.41] 0.427	0.80 [0.49; 1.33] 0.395	-0.02 [-0.05; 0.02] 0.394
Diabetic retinal oedema					
KESTREL, n (%)	10 (5.3)	11 (5.9)	0.89 [0.37; 2.16] 0.803	0.90 [0.39; 2.07] 0.803	-0.01 [-0.05; 0.04] 0.803
KITE, n (%)	16 (8.9)	16 (8.8)	1.01 [0.49; 2.09] 0.974	1.01 [0.52; 1.96] 0.974	0.00 [-0.06; 0.06] 0.974
Pooled Analysis, n (%) p_H=0.831	26 (7.1)	27 (7.3)	0.95 [0.54; 1.69] 0.861	0.97 [0.58; 1.62] 0.894	-0.00 [-0.04; 0.03] 0.894
Cataract					
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

	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 (%)	7 (3.9)	12 (6.6)	0.57 [0.22; 1.49] 0.254	0.59 [0.24; 1.46] 0.255	-0.03 [-0.07; 0.02] 0.247
Pooled Analysis, n (%) p_H=0.398	19 (5.2)	24 (6.5)	0.76 [0.40; 1.42] 0.386	0.79 [0.44; 1.42] 0.430	-0.01 [-0.05; 0.02] 0.430
Dry eye					
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 (%)	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=0.947	14 (3.8)	11 (3.0)	1.28 [0.55; 2.96] 0.567	1.28 [0.59; 2.77] 0.536	0.01 [-0.02; 0.03] 0.535
Vitreous floaters					
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 (%)	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=0.195	13 (3.5)	10 (2.7)	0.98 [0.37; 2.62] 0.965	1.29 [0.57; 2.91] 0.532	0.01 [-0.02; 0.03] 0.532
Vitreous detachment					
KESTREL, n (%)	11 (5.8)	5 (2.7)	2.25 [0.77; 6.60] 0.140	2.18 [0.77; 6.14] 0.142	0.03 [-0.01; 0.07] 0.129
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.	11 (3.0)	6 (1.6)	N.E.	1.76 [0.68; 4.53] 0.237	0.01 [-0.01; 0.03] 0.223
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)	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 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=0.631	11 (3.0)	9 (2.4)	1.23 [0.50; 3.01] 0.655	1.22 [0.51; 2.91] 0.650	0.01 [-0.02; 0.03] 0.650
Eye pain					
KESTREL, n (%)	4 (2.1)	5 (2.7)	0.79 [0.21; 2.98] 0.724	0.79 [0.22; 2.90] 0.724	-0.01 [-0.04; 0.03] 0.724
KITE, n (%)	6 (3.4)	3 (1.7)	2.06 [0.51; 8.36] 0.313	2.02 [0.51; 7.96] 0.314	0.02 [-0.02; 0.05] 0.303
Pooled Analysis, n (%) p_H=0.330	10 (2.7)	8 (2.2)	1.26 [0.48; 3.31] 0.638	1.25 [0.50; 3.13] 0.633	0.01 [-0.02; 0.03] 0.633
Infections and infestations					
KESTREL, n (%)	68 (36.0)	50 (26.7)	1.54 [0.99; 2.39] 0.054	1.35 [0.99; 1.82] 0.056	0.09 [-0.00; 0.19] 0.052
KITE, n (%)	46 (25.7)	54 (29.8)	0.81 [0.51; 1.29] 0.381	0.86 [0.62; 1.20] 0.382	-0.04 [-0.13; 0.05] 0.380
Pooled Analysis, n (%) p_H=0.050 *	114 (31.0)	104 (28.3)	1.13 [0.82; 1.55] 0.464	1.10 [0.88; 1.37] 0.423	0.03 [-0.04; 0.09] 0.423
Nasopharyngitis					
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 (%)	11 (6.1)	12 (6.6)	0.92 [0.40; 2.15] 0.851	0.93 [0.42; 2.05] 0.851	-0.00 [-0.06; 0.05] 0.851
Pooled Analysis, n (%) p_H=0.612	27 (7.3)	25 (6.8)	1.07 [0.61; 1.89] 0.811	1.08 [0.64; 1.82] 0.777	0.01 [-0.03; 0.04] 0.776
Urinary tract infection					
KESTREL, n (%)	15 (7.9)	7 (3.7)	2.22 [0.88; 5.57] 0.090	2.12 [0.88; 5.08] 0.092	0.04 [-0.01; 0.09] 0.081
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.	15 (4.1)	10 (2.7)	N.E.	1.47 [0.68; 3.16] 0.324	0.01 [-0.01; 0.04] 0.315

	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**
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 (%)	6 (3.4)	3 (1.7)	2.06 [0.51; 8.36] 0.313	2.02 [0.51; 7.96] 0.314	0.02 [-0.02; 0.05] 0.303
Pooled Analysis, n (%) p_H=0.609	11 (3.0)	7 (1.9)	1.59 [0.61; 4.18] 0.346	1.57 [0.62; 4.01] 0.340	0.01 [-0.01; 0.03] 0.339
Influenza					
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 (%)	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=0.497	10 (2.7)	7 (1.9)	1.44 [0.53; 3.87] 0.474	1.43 [0.55; 3.72] 0.463	0.01 [-0.01; 0.03] 0.462
Upper respiratory tract infection					
KESTREL, 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 (%)	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=0.985	10 (2.7)	4 (1.1)	2.54 [0.79; 8.18] 0.118	2.50 [0.79; 7.90] 0.106	0.02 [-0.00; 0.04] 0.105
Metabolism and nutrition disorders					
KESTREL, n (%)	35 (18.5)	18 (9.6)	2.13 [1.16; 3.92] 0.015 *	1.92 [1.13; 3.27] 0.016 *	0.09 [0.02; 0.16] 0.012 *
KITE, n (%)	17 (9.5)	19 (10.5)	0.89 [0.45; 1.78] 0.752	0.90 [0.49; 1.68] 0.752	-0.01 [-0.07; 0.05] 0.752
Pooled Analysis, n (%) p_H=0.064	52 (14.1)	37 (10.1)	1.39 [0.88; 2.21] 0.156	1.40 [0.94; 2.09] 0.091	0.04 [-0.01; 0.09] 0.091

	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**
Vascular disorders					
KESTREL, n (%)	24 (12.7)	22 (11.8)	1.09 [0.59; 2.02] 0.782	1.08 [0.63; 1.86] 0.782	0.01 [-0.06; 0.08] 0.782
KITE, n (%)	24 (13.4)	18 (9.9)	1.40 [0.73; 2.68] 0.308	1.35 [0.76; 2.40] 0.309	0.03 [-0.03; 0.10] 0.306
Pooled Analysis, n (%) p_H=0.583	48 (13.0)	40 (10.9)	1.23 [0.79; 1.93] 0.358	1.20 [0.81; 1.78] 0.365	0.02 [-0.03; 0.07] 0.364
Hypertension					
KESTREL, n (%)	17 (9.0)	16 (8.6)	1.06 [0.52; 2.16] 0.881	1.05 [0.55; 2.02] 0.881	0.00 [-0.05; 0.06] 0.881
KITE, n (%)	13 (7.3)	10 (5.5)	1.34 [0.57; 3.14] 0.502	1.31 [0.59; 2.92] 0.502	0.02 [-0.03; 0.07] 0.500
Pooled Analysis, n (%) p_H=0.676	30 (8.2)	26 (7.1)	1.19 [0.68; 2.06] 0.545	1.15 [0.70; 1.91] 0.583	0.01 [-0.03; 0.05] 0.582
Gastrointestinal disorders					
KESTREL, n (%)	27 (14.3)	19 (10.2)	1.47 [0.79; 2.75] 0.224	1.41 [0.81; 2.44] 0.225	0.04 [-0.02; 0.11] 0.221
KITE, n (%)	17 (9.5)	21 (11.6)	0.80 [0.41; 1.57] 0.516	0.82 [0.45; 1.50] 0.517	-0.02 [-0.08; 0.04] 0.515
Pooled Analysis, n (%) p_H=0.193	44 (12.0)	40 (10.9)	1.09 [0.69; 1.73] 0.707	1.10 [0.73; 1.65] 0.646	0.01 [-0.04; 0.06] 0.646
Diarrhoea					
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 (%)	3 (1.7)	6 (3.3)	0.50 [0.12; 2.02] 0.328	0.51 [0.13; 1.99] 0.329	-0.02 [-0.05; 0.02] 0.318
Pooled Analysis, n (%) p_H=0.254	9 (2.4)	10 (2.7)	0.87 [0.34; 2.25] 0.779	0.90 [0.37; 2.19] 0.816	-0.00 [-0.03; 0.02] 0.816

	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**
Investigations					
KESTREL, n (%)	20 (10.6)	19 (10.2)	1.05 [0.54; 2.03] 0.893	1.04 [0.57; 1.89] 0.893	0.00 [-0.06; 0.07] 0.893
KITE, n (%)	19 (10.6)	24 (13.3)	0.78 [0.41; 1.47] 0.440	0.80 [0.45; 1.41] 0.440	-0.03 [-0.09; 0.04] 0.438
Pooled Analysis, n (%) p_H=0.527	39 (10.6)	43 (11.7)	0.90 [0.57; 1.43] 0.669	0.91 [0.60; 1.37] 0.642	-0.01 [-0.06; 0.03] 0.642
Renal and urinary disorders					
KESTREL, n (%)	14 (7.4)	17 (9.1)	0.80 [0.38; 1.67] 0.554	0.81 [0.41; 1.60] 0.554	-0.02 [-0.07; 0.04] 0.553
KITE, n (%)	10 (5.6)	23 (12.7)	0.41 [0.19; 0.88] 0.023 *	0.44 [0.22; 0.90] 0.024 *	-0.07 [-0.13; -0.01] 0.018 *
Pooled Analysis, n (%) p_H=0.215	24 (6.5)	40 (10.9)	0.57 [0.34; 0.98] 0.042 *	0.60 [0.37; 0.98] 0.037 *	-0.04 [-0.08; -0.00] 0.036 *
Nervous system disorders					
KESTREL, n (%)	17 (9.0)	19 (10.2)	0.87 [0.44; 1.74] 0.701	0.89 [0.48; 1.65] 0.701	-0.01 [-0.07; 0.05] 0.701
KITE, n (%)	16 (8.9)	20 (11.0)	0.79 [0.40; 1.58] 0.505	0.81 [0.43; 1.51] 0.505	-0.02 [-0.08; 0.04] 0.504
Pooled Analysis, n (%) p_H=0.840	33 (9.0)	39 (10.6)	0.83 [0.51; 1.36] 0.460	0.85 [0.54; 1.31] 0.458	-0.02 [-0.06; 0.03] 0.457
Headache					
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

	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 (%)	15 (7.9)	24 (12.8)	0.59 [0.30; 1.16] 0.123	0.62 [0.34; 1.14] 0.124	-0.05 [-0.11; 0.01] 0.119
KITE, n (%)	14 (7.8)	12 (6.6)	1.19 [0.54; 2.66] 0.663	1.18 [0.56; 2.48] 0.663	0.01 [-0.04; 0.07] 0.662
Pooled Analysis, n (%) p_H=0.183	29 (7.9)	36 (9.8)	0.83 [0.49; 1.40] 0.487	0.80 [0.50; 1.28] 0.359	-0.02 [-0.06; 0.02] 0.359
General disorders and administration site conditions					
KESTREL, n (%)	16 (8.5)	14 (7.5)	1.14 [0.54; 2.41] 0.726	1.13 [0.57; 2.25] 0.726	0.01 [-0.04; 0.06] 0.726
KITE, n (%)	19 (10.6)	15 (8.3)	1.31 [0.65; 2.68] 0.451	1.28 [0.67; 2.44] 0.452	0.02 [-0.04; 0.08] 0.450
Pooled Analysis, n (%) p_H=0.790	35 (9.5)	29 (7.9)	1.22 [0.73; 2.05] 0.443	1.21 [0.75; 1.93] 0.431	0.02 [-0.02; 0.06] 0.430
Pyrexia					
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 (%)	6 (3.4)	3 (1.7)	2.06 [0.51; 8.36] 0.313	2.02 [0.51; 7.96] 0.314	0.02 [-0.02; 0.05] 0.303
Pooled Analysis, n (%) p_H=0.722	12 (3.3)	5 (1.4)	2.51 [0.86; 7.32] 0.093	2.40 [0.85; 6.76] 0.086	0.02 [-0.00; 0.04] 0.085
Musculoskeletal and connective tissue disorders					
KESTREL, n (%)	19 (10.1)	12 (6.4)	1.63 [0.77; 3.46] 0.203	1.57 [0.78; 3.14] 0.205	0.04 [-0.02; 0.09] 0.199
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=0.306	35 (9.5)	29 (7.9)	1.25 [0.74; 2.10] 0.402	1.21 [0.75; 1.93] 0.432	0.02 [-0.02; 0.06] 0.431

	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**
Respiratory, thoracic and mediastinal disorders					
KESTREL, n (%)	22 (11.6)	18 (9.6)	1.24 [0.64; 2.39] 0.527	1.21 [0.67; 2.18] 0.527	0.02 [-0.04; 0.08] 0.526
KITE, n (%)	10 (5.6)	16 (8.8)	0.61 [0.27; 1.38] 0.237	0.63 [0.29; 1.35] 0.238	-0.03 [-0.09; 0.02] 0.232
Pooled Analysis, n (%) p_H=0.188	32 (8.7)	34 (9.2)	0.87 [0.52; 1.48] 0.617	0.94 [0.59; 1.49] 0.790	-0.01 [-0.05; 0.04] 0.789
Cough					
KESTREL, n (%)	8 (4.2)	8 (4.3)	0.99 [0.36; 2.69] 0.983	0.99 [0.38; 2.58] 0.983	-0.00 [-0.04; 0.04] 0.983
KITE, n (%)	3 (1.7)	5 (2.8)	0.60 [0.14; 2.55] 0.489	0.61 [0.15; 2.50] 0.489	-0.01 [-0.04; 0.02] 0.484
Pooled Analysis, n (%) p_H=0.578	11 (3.0)	13 (3.5)	0.77 [0.32; 1.85] 0.566	0.84 [0.38; 1.86] 0.672	-0.01 [-0.03; 0.02] 0.671
Cardiac disorders					
KESTREL, n (%)	12 (6.3)	14 (7.5)	0.84 [0.38; 1.86] 0.664	0.85 [0.40; 1.78] 0.664	-0.01 [-0.06; 0.04] 0.664
KITE, n (%)	6 (3.4)	11 (6.1)	0.54 [0.19; 1.48] 0.229	0.55 [0.21; 1.46] 0.231	-0.03 [-0.07; 0.02] 0.221
Pooled Analysis, n (%) p_H=0.499	18 (4.9)	25 (6.8)	0.67 [0.35; 1.28] 0.228	0.72 [0.40; 1.29] 0.268	-0.02 [-0.05; 0.01] 0.267
Blood and lymphatic system disorders					
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
KITE, n (%)	5 (2.8)	11 (6.1)	0.44 [0.15; 1.31] 0.140	0.46 [0.16; 1.30] 0.142	-0.03 [-0.08; 0.01] 0.129
Pooled Analysis, n (%) p_H=0.341	14 (3.8)	21 (5.7)	0.63 [0.31; 1.28] 0.203	0.67 [0.34; 1.29] 0.225	-0.02 [-0.05; 0.01] 0.224

	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**
Anaemia					
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)	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=0.508	11 (3.0)	14 (3.8)	0.75 [0.33; 1.71] 0.498	0.78 [0.36; 1.71] 0.540	-0.01 [-0.03; 0.02] 0.540
Skin and subcutaneous tissue disorders					
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 (%)	8 (4.5)	9 (5.0)	0.89 [0.34; 2.37] 0.822	0.90 [0.35; 2.28] 0.822	-0.01 [-0.05; 0.04] 0.822
Pooled Analysis, n (%) p_H=0.276	21 (5.7)	16 (4.3)	1.31 [0.67; 2.59] 0.431	1.31 [0.70; 2.48] 0.401	0.01 [-0.02; 0.05] 0.400
Psychiatric disorders					
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 (%)	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=0.771	14 (3.8)	12 (3.3)	1.14 [0.51; 2.55] 0.744	1.16 [0.55; 2.48] 0.694	0.01 [-0.02; 0.03] 0.694
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
KESTREL, n (%)	6 (3.2)	7 (3.7)	0.84 [0.28; 2.56] 0.763	0.85 [0.29; 2.48] 0.763	-0.01 [-0.04; 0.03] 0.763
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 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=0.642	11 (3.0)	11 (3.0)	1.03 [0.43; 2.45] 0.945	1.00 [0.44; 2.27] 0.997	-0.00 [-0.02; 0.02] 0.997

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 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.634				
< 65 years, n (%)	7 (6.7)	9 (9.7)	0.67 [0.24; 1.89] 0.452	0.70 [0.27; 1.79] 0.452	-0.03 [-0.11; 0.05] 0.453
≥ 65 years, n (%)	7 (8.2)	8 (8.5)	0.96 [0.33; 2.78] 0.947	0.97 [0.37; 2.56] 0.947	-0.00 [-0.08; 0.08] 0.947
KITE					
Interaction Test:	p = 0.128				
< 65 years, n (%)	8 (8.0)	12 (11.8)	0.65 [0.25; 1.67] 0.373	0.68 [0.29; 1.59] 0.374	-0.04 [-0.12; 0.04] 0.369
≥ 65 years, n (%)	2 (2.5)	11 (13.9)	0.16 [0.03; 0.75] 0.020 *	0.18 [0.04; 0.79] 0.023 *	-0.11 [-0.20; -0.03] 0.008 *
Pooled Analysis					
Interaction Test:	p = 0.510				
< 65 years, n (%)	15 (7.4)	21 (10.8)	0.67 [0.33; 1.35] 0.260	0.69 [0.36; 1.29] 0.243	-0.03 [-0.09; 0.02] 0.242

	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 (%)	9 (5.5)	19 (11.0)	0.47 [0.20; 1.06] 0.070	0.50 [0.24; 1.08] 0.069	-0.05 [-0.11; 0.00] 0.067

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 16-1.3 Any adverse event by SOC, PT and gender (SAF), binary analysis, week 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: p_H=**0.215**					
KESTREL					
Interaction Test:	p = 0.575				
Male, n (%)	10 (9.1)	12 (9.5)	0.95 [0.39; 2.29] 0.909	0.95 [0.43; 2.12] 0.909	-0.00 [-0.08; 0.07] 0.909
Female, n (%)	4 (5.1)	5 (8.2)	0.60 [0.15; 2.33] 0.458	0.62 [0.17; 2.20] 0.458	-0.03 [-0.12; 0.05] 0.465
KITE					
Interaction Test:	p = 0.148				
Male, n (%)	9 (7.5)	14 (12.2)	0.58 [0.24; 1.41] 0.232	0.62 [0.28; 1.37] 0.234	-0.05 [-0.12; 0.03] 0.229
Female, n (%)	1 (1.7)	9 (13.6)	0.11 [0.01; 0.89] 0.039 *	0.12 [0.02; 0.95] 0.045 *	-0.12 [-0.21; -0.03] 0.009 *
Pooled Analysis					
Interaction Test:	p = 0.142				
Male, n (%)	19 (8.3)	26 (10.8)	0.75 [0.40; 1.40] 0.365	0.76 [0.44; 1.34] 0.348	-0.03 [-0.08; 0.03] 0.346

	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 (%)	5 (3.6)	14 (11.0)	0.30 [0.10; 0.86] 0.026 *	0.32 [0.11; 0.91] 0.022 *	-0.07 [-0.14; -0.01] 0.022 *

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 16-1.4 Any adverse event by SOC, PT and BCVA (SAF), binary analysis, week 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: $\mathbf{p_H=0.215}$					
KESTREL					
Interaction Test:	p = 0.532				
≤ 65 letters, n (%)	5 (6.8)	7 (10.9)	0.59 [0.18; 1.96] 0.389	0.62 [0.21; 1.85] 0.390	-0.04 [-0.14; 0.05] 0.391
> 65 letters, n (%)	9 (7.8)	10 (8.1)	0.96 [0.38; 2.45] 0.931	0.96 [0.41; 2.28] 0.931	-0.00 [-0.07; 0.07] 0.931
KITE					
Interaction Test:	p = 0.414				
≤ 65 letters, n (%)	2 (3.1)	11 (12.1)	0.23 [0.05; 1.08] 0.063	0.25 [0.06; 1.11] 0.069	-0.09 [-0.17; -0.01] 0.025 *
> 65 letters, n (%)	8 (7.0)	12 (13.3)	0.49 [0.19; 1.26] 0.138	0.53 [0.22; 1.23] 0.139	-0.06 [-0.15; 0.02] 0.143
Pooled Analysis					
Interaction Test:	p = 0.389				
≤ 65 letters, n (%)	7 (5.0)	18 (11.6)	0.42 [0.17; 1.04] 0.060	0.42 [0.17; 1.00] 0.041 *	-0.07 [-0.13; -0.01] 0.034 *

	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 (%)	17 (7.4)	22 (10.3)	0.68 [0.35; 1.33] 0.261	0.71 [0.39; 1.29] 0.259	-0.03 [-0.08; 0.02] 0.263

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 16-1.5 Any adverse event by SOC, PT and region (SAF), binary analysis, week 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.817				
Region of the Americas, n (%)	9 (10.0)	11 (13.3)	0.73 [0.29; 1.86] 0.505	0.75 [0.33; 1.73] 0.505	-0.03 [-0.13; 0.06] 0.505
European Region, n (%)	4 (5.8)	4 (5.3)	1.09 [0.26; 4.55] 0.903	1.09 [0.28; 4.18] 0.903	0.00 [-0.07; 0.08] 0.904
Western Pacific Region, n (%)	1 (3.3)	2 (6.9)	0.47 [0.04; 5.43] 0.542	0.48 [0.05; 5.05] 0.544	-0.04 [-0.15; 0.08] 0.534

	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:	p = 0.028 *				
South-East Asia Region and Eastern Mediterranean Region, n (%)	3 (11.5)	3 (14.3)	0.78 [0.14; 4.35] 0.779	0.81 [0.18; 3.60] 0.779	-0.03 [-0.22; 0.17] 0.781
European Region, n (%)	3 (2.2)	17 (12.9)	0.15 [0.04; 0.54] 0.003 *	0.17 [0.05; 0.58] 0.004 *	-0.11 [-0.17; -0.04] <.001 *
Western Pacific Region, 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
Pooled Analysis					
Interaction Test:	p = 0.371				
Region of the Americas, n (%)	9 (10.0)	11 (13.3)	0.53 [0.16; 1.78] 0.303	0.75 [0.33; 1.73] 0.505	-0.03 [-0.13; 0.06] 0.505
South-East Asia Region and Eastern Mediterranean Region, n (%)	3 (11.5)	3 (14.3)	1.09 [0.16; 7.22] 0.930	0.81 [0.18; 3.60] 0.781	-0.03 [-0.22; 0.17] 0.781
European Region, n (%)	7 (3.4)	21 (10.1)	0.37 [0.14; 0.95] 0.039 *	0.34 [0.15; 0.78] 0.007 *	-0.07 [-0.12; -0.02] 0.006 *
Western Pacific Region, n (%)	5 (10.4)	5 (8.8)	1.33 [0.35; 4.97] 0.676	1.34 [0.43; 4.13] 0.618	0.03 [-0.09; 0.14] 0.626

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 16-1.6 Any adverse event by SOC, PT and diabetes type (SAF), binary analysis, week 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	N.E.				
Type 1, 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 (%)	13 (7.3)	17 (9.4)	0.76 [0.36; 1.63] 0.486	0.78 [0.39; 1.56] 0.486	-0.02 [-0.08; 0.04] 0.484
KITE					
Interaction Test:	p = 0.411				
Type 1, n (%)	1 (5.3)	2 (28.6)	0.14 [0.01; 1.86] 0.136	0.18 [0.02; 1.73] 0.139	-0.23 [-0.58; 0.12] 0.191
Type 2, n (%)	9 (5.6)	21 (12.1)	0.43 [0.19; 0.98] 0.044 *	0.47 [0.22; 0.99] 0.046 *	-0.06 [-0.12; -0.00] 0.036 *
Pooled Analysis					
Interaction Test:	p = 0.736				
Type 1, n (%)	2 (6.5)	2 (15.4)	0.40 [0.05; 3.23] 0.391	0.44 [0.09; 2.17] 0.315	-0.09 [-0.31; 0.13] 0.401

	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 (%)	22 (6.5)	38 (10.7)	0.58 [0.33; 1.01] 0.056	0.61 [0.37; 1.01] 0.052	-0.04 [-0.08; -0.00] 0.050 *

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):
Renal and urinary disorders / KESTREL: logit(proportion) = treatment [by diabetes type].

Table 16-1.7 Any adverse event by SOC, PT and HbA1c (SAF), binary analysis, week 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: p_H=**0.215**					
KESTREL					
Interaction Test:	p = 0.153				
< 7.5 %, n (%)	5 (6.6)	13 (12.1)	0.51 [0.17; 1.49] 0.219	0.54 [0.20; 1.46] 0.224	-0.06 [-0.14; 0.03] 0.190
≥ 7.5 %, n (%)	9 (8.0)	4 (5.0)	1.66 [0.49; 5.59] 0.413	1.61 [0.51; 5.04] 0.416	0.03 [-0.04; 0.10] 0.391
KITE					
Interaction Test:	p = 0.290				
< 7.5 %, n (%)	6 (7.3)	11 (11.5)	0.61 [0.22; 1.73] 0.352	0.64 [0.25; 1.65] 0.355	-0.04 [-0.13; 0.04] 0.340
≥ 7.5 %, n (%)	4 (4.1)	12 (14.1)	0.26 [0.08; 0.85] 0.025 *	0.29 [0.10; 0.87] 0.027 *	-0.10 [-0.18; -0.02] 0.020 *
Pooled Analysis					
Interaction Test:	p = 0.853				
< 7.5 %, n (%)	11 (7.0)	24 (11.8)	0.56 [0.27; 1.19] 0.131	0.59 [0.30; 1.17] 0.123	-0.05 [-0.11; 0.01] 0.110

	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 (%)	13 (6.2)	16 (9.7)	0.62 [0.29; 1.34] 0.226	0.64 [0.31; 1.33] 0.226	-0.03 [-0.09; 0.02] 0.234

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 16-1.8 Any adverse event by SOC, PT and duration of DME (SAF), binary analysis, week 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.271				
≤ 3 months, n (%)	8 (6.7)	12 (10.9)	0.58 [0.23; 1.49] 0.258	0.61 [0.26; 1.44] 0.260	-0.04 [-0.12; 0.03] 0.257
> 3 - < 12 months, n (%)	2 (6.7)	4 (10.3)	0.63 [0.11; 3.66] 0.602	0.65 [0.13; 3.32] 0.604	-0.04 [-0.17; 0.09] 0.590
≥ 12 months, n (%)	4 (10.3)	1 (2.6)	4.23 [0.45; 39.70] 0.207	3.90 [0.46; 33.30] 0.214	0.08 [-0.03; 0.18] 0.166
KITE					
Interaction Test:	p = 0.327				
≤ 3 months, n (%)	3 (3.5)	14 (15.2)	0.20 [0.06; 0.74] 0.015 *	0.23 [0.07; 0.78] 0.018 *	-0.12 [-0.20; -0.03] 0.006 *
> 3 - < 12 months, n (%)	4 (7.8)	5 (10.2)	0.75 [0.19; 2.97] 0.681	0.77 [0.22; 2.70] 0.681	-0.02 [-0.14; 0.09] 0.680

	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**
≥ 12 months, n (%)	3 (7.0)	4 (10.0)	0.68 [0.14; 3.22] 0.622	0.70 [0.17; 2.93] 0.623	-0.03 [-0.15; 0.09] 0.622
Pooled Analysis					
Interaction Test:	p = 0.153				
≤ 3 months, n (%)	11 (5.4)	26 (12.9)	0.37 [0.17; 0.78] 0.009 *	0.41 [0.21; 0.82] 0.009 *	-0.07 [-0.13; -0.02] 0.008 *
> 3 - < 12 months, n (%)	6 (7.4)	9 (10.2)	0.76 [0.26; 2.26] 0.624	0.72 [0.27; 1.95] 0.518	-0.03 [-0.11; 0.06] 0.512
≥ 12 months, n (%)	7 (8.5)	5 (6.4)	1.40 [0.42; 4.63] 0.583	1.33 [0.44; 4.00] 0.615	0.02 [-0.06; 0.10] 0.614

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 16-1.9 Any adverse event by SOC, PT and DME type (SAF), binary analysis, week 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.926				
focal, n (%)	2 (3.4)	2 (4.2)	0.81 [0.11; 5.95] 0.834	0.81 [0.12; 5.56] 0.833	-0.01 [-0.08; 0.07] 0.835
diffuse, n (%)	12 (9.4)	14 (10.4)	0.89 [0.40; 2.02] 0.788	0.90 [0.44; 1.88] 0.788	-0.01 [-0.08; 0.06] 0.787
KITE					
Interaction Test:	p = 0.540				
focal, n (%)	4 (6.3)	7 (10.6)	0.57 [0.16; 2.06] 0.392	0.60 [0.18; 1.95] 0.394	-0.04 [-0.14; 0.05] 0.383
diffuse, n (%)	6 (5.2)	15 (13.8)	0.34 [0.13; 0.92] 0.034 *	0.38 [0.15; 0.94] 0.037 *	-0.09 [-0.16; -0.01] 0.028 *
Pooled Analysis					
Interaction Test:	p = 0.887				
focal, n (%)	6 (4.9)	9 (7.9)	0.64 [0.22; 1.88] 0.416	0.65 [0.24; 1.77] 0.399	-0.03 [-0.09; 0.04] 0.398

	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 (%)	18 (7.4)	29 (11.9)	0.59 [0.31; 1.09] 0.092	0.63 [0.36; 1.09] 0.096	-0.04 [-0.10; 0.01] 0.096

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 16-1.10 Any adverse event by SOC, PT and CSFT (SAF), binary analysis, week 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.553				
< 450 µm, n (%)	7 (6.5)	5 (5.2)	1.27 [0.39; 4.16] 0.688	1.26 [0.41; 3.83] 0.688	0.01 [-0.05; 0.08] 0.686
≥ 450 - < 650 µm, n (%)	5 (7.1)	9 (12.7)	0.53 [0.17; 1.67] 0.278	0.56 [0.20; 1.60] 0.281	-0.06 [-0.15; 0.04] 0.269
≥ 650 µm, n (%)	2 (16.7)	3 (15.0)	1.13 [0.16; 7.98] 0.900	1.11 [0.22; 5.73] 0.900	0.02 [-0.25; 0.28] 0.901
KITE					
Interaction Test:	N.E.				
< 450 µm, n (%)	7 (8.2)	9 (11.0)	0.73 [0.26; 2.06] 0.549	0.75 [0.29; 1.92] 0.549	-0.03 [-0.12; 0.06] 0.548
≥ 450 - < 650 µm, n (%)	3 (4.1)	10 (12.7)	0.29 [0.08; 1.10] 0.070	0.32 [0.09; 1.12] 0.074	-0.09 [-0.17; -0.00] 0.050 *

	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**
≥ 650 µm, n (%)	0 (0.0)	3 (15.8)	N.E.	0.14 [0.01; 2.47] 0.178	-0.16 [-0.32; 0.01] 0.059
Pooled Analysis					
Interaction Test:	p = 0.355				
< 450 µm, n (%)	14 (7.3)	14 (7.9)	0.90 [0.41; 1.96] 0.795	0.94 [0.46; 1.91] 0.854	-0.01 [-0.06; 0.05] 0.853
≥ 450 - < 650 µm, n (%)	8 (5.6)	19 (12.7)	0.41 [0.17; 0.98] 0.045 *	0.44 [0.20; 0.97] 0.035 *	-0.07 [-0.14; -0.01] 0.032 *
≥ 650 µm, n (%)	2 (6.3)	6 (15.4)	0.38 [0.07; 2.04] 0.259	0.51 [0.14; 1.89] 0.307	-0.08 [-0.23; 0.06] 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
*: $p < 0.05$
.....

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):
Renal and urinary disorders / KITE: logit(proportion) = treatment [by CSFT].

Table 16-1.11 Any adverse event by SOC, PT and status of SRF (SAF), binary analysis, week 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.889				
presence, n (%)	7 (11.3)	8 (13.1)	0.84 [0.29; 2.49] 0.757	0.86 [0.33; 2.23] 0.757	-0.02 [-0.13; 0.10] 0.757
absence, n (%)	7 (5.5)	9 (7.1)	0.76 [0.27; 2.10] 0.595	0.77 [0.30; 2.01] 0.595	-0.02 [-0.08; 0.04] 0.594
KITE					
Interaction Test:	p = 0.956				
presence, 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 (%)	7 (5.7)	15 (13.2)	0.40 [0.16; 1.02] 0.054	0.43 [0.18; 1.02] 0.056	-0.07 [-0.15; -0.00] 0.049 *
Pooled Analysis					
Interaction Test:	p = 0.708				
presence, n (%)	10 (8.5)	16 (12.5)	0.66 [0.28; 1.52] 0.324	0.67 [0.31; 1.42] 0.287	-0.04 [-0.12; 0.03] 0.279

	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 (%)	14 (5.6)	24 (10.0)	0.53 [0.27; 1.06] 0.073	0.56 [0.30; 1.05] 0.066	-0.04 [-0.09; 0.00] 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
*: $p < 0.05$
.....

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 16-1.12 Any adverse event by SOC, PT and exposure (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and exposure (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	71 / 71	75 / 75			
Exposed, N'/N	118 / 118	112 / 112			
KITE, N'/N	179 / 179	181 / 181			
Non-exposed, N'/N	85 / 85	90 / 90			
Exposed, N'/N	94 / 94	91 / 91			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Non-exposed, N'/N	156 / 156	165 / 165			
Exposed, N'/N	212 / 212	203 / 203			
Any adverse event by SOC and PT, week 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.143				
Non-exposed, n (%)	9 (12.7)	7 (9.3)	1.41 [0.50; 4.01] 0.520	1.36 [0.53; 3.45] 0.520	0.03 [-0.07; 0.14] 0.519
Exposed, n (%)	5 (4.2)	10 (8.9)	0.45 [0.15; 1.36] 0.159	0.47 [0.17; 1.35] 0.161	-0.05 [-0.11; 0.02] 0.152
KITE					
Interaction Test:	p = 0.781				
Non-exposed, n (%)	6 (7.1)	13 (14.4)	0.45 [0.16; 1.24] 0.124	0.49 [0.19; 1.23] 0.127	-0.07 [-0.16; 0.02] 0.111
Exposed, n (%)	4 (4.3)	10 (11.0)	0.36 [0.11; 1.19] 0.095	0.39 [0.13; 1.19] 0.098	-0.07 [-0.14; 0.01] 0.083
Pooled Analysis					
Interaction Test:	p = 0.194				
Non-exposed, n (%)	15 (9.6)	20 (12.1)	0.80 [0.39; 1.64] 0.542	0.79 [0.42; 1.50] 0.473	-0.03 [-0.09; 0.04] 0.472

	Treatment Groups		Comparison		
Any adverse event by SOC, PT and exposure (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed, n (%)	9 (4.2)	20 (9.9)	0.39 [0.17; 0.89] 0.025 *	0.43 [0.20; 0.92] 0.026 *	-0.06 [-0.11; -0.01] 0.026 *

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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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 16-2.1 Any ocular adverse event by SOC and PT (SAF), binary analysis, week 52

	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 52					
Eye disorders					
KESTREL, n (%)	91 (48.1)	82 (43.9)	1.19 [0.79; 1.78] 0.403	1.10 [0.88; 1.37] 0.404	0.04 [-0.06; 0.14] 0.403
KITE, n (%)	72 (40.2)	68 (37.6)	1.12 [0.73; 1.71] 0.606	1.07 [0.83; 1.39] 0.606	0.03 [-0.07; 0.13] 0.605
Pooled Analysis, n (%) p_H=0.838	163 (44.3)	150 (40.8)	1.15 [0.86; 1.55] 0.339	1.09 [0.92; 1.28] 0.337	0.03 [-0.04; 0.11] 0.336
Conjunctival haemorrhage					
KESTREL, n (%)	17 (9.0)	21 (11.2)	0.78 [0.40; 1.53] 0.473	0.80 [0.44; 1.47] 0.473	-0.02 [-0.08; 0.04] 0.472
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=0.968	25 (6.8)	31 (8.4)	0.79 [0.44; 1.41] 0.427	0.80 [0.49; 1.33] 0.395	-0.02 [-0.05; 0.02] 0.394
Diabetic retinal oedema					
KESTREL, n (%)	10 (5.3)	11 (5.9)	0.89 [0.37; 2.16] 0.803	0.90 [0.39; 2.07] 0.803	-0.01 [-0.05; 0.04] 0.803
KITE, n (%)	16 (8.9)	16 (8.8)	1.01 [0.49; 2.09] 0.974	1.01 [0.52; 1.96] 0.974	0.00 [-0.06; 0.06] 0.974
Pooled Analysis, n (%) p_H=0.831	26 (7.1)	27 (7.3)	0.95 [0.54; 1.69] 0.861	0.97 [0.58; 1.62] 0.894	-0.00 [-0.04; 0.03] 0.894
Cataract					
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

	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 (%)	7 (3.9)	12 (6.6)	0.57 [0.22; 1.49] 0.254	0.59 [0.24; 1.46] 0.255	-0.03 [-0.07; 0.02] 0.247
Pooled Analysis, n (%) p_H=0.398	19 (5.2)	24 (6.5)	0.76 [0.40; 1.42] 0.386	0.79 [0.44; 1.42] 0.430	-0.01 [-0.05; 0.02] 0.430
Dry eye					
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 (%)	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=0.947	14 (3.8)	11 (3.0)	1.28 [0.55; 2.96] 0.567	1.28 [0.59; 2.77] 0.536	0.01 [-0.02; 0.03] 0.535
Vitreous floaters					
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 (%)	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=0.195	13 (3.5)	10 (2.7)	0.98 [0.37; 2.62] 0.965	1.29 [0.57; 2.91] 0.532	0.01 [-0.02; 0.03] 0.532
Vitreous detachment					
KESTREL, n (%)	11 (5.8)	5 (2.7)	2.25 [0.77; 6.60] 0.140	2.18 [0.77; 6.14] 0.142	0.03 [-0.01; 0.07] 0.129
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.	11 (3.0)	6 (1.6)	N.E.	1.76 [0.68; 4.53] 0.237	0.01 [-0.01; 0.03] 0.223
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)	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 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=0.631	11 (3.0)	9 (2.4)	1.23 [0.50; 3.01] 0.655	1.22 [0.51; 2.91] 0.650	0.01 [-0.02; 0.03] 0.650
Eye pain					
KESTREL, n (%)	4 (2.1)	5 (2.7)	0.79 [0.21; 2.98] 0.724	0.79 [0.22; 2.90] 0.724	-0.01 [-0.04; 0.03] 0.724
KITE, n (%)	6 (3.4)	3 (1.7)	2.06 [0.51; 8.36] 0.313	2.02 [0.51; 7.96] 0.314	0.02 [-0.02; 0.05] 0.303
Pooled Analysis, n (%) p_H=0.330	10 (2.7)	8 (2.2)	1.26 [0.48; 3.31] 0.638	1.25 [0.50; 3.13] 0.633	0.01 [-0.02; 0.03] 0.633
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 (%)	10 (5.6)	5 (2.8)	2.08 [0.70; 6.22] 0.189	2.02 [0.71; 5.80] 0.190	0.03 [-0.01; 0.07] 0.180
Pooled Analysis, n (%) p_H=0.748	18 (4.9)	10 (2.7)	1.83 [0.83; 4.02] 0.135	1.80 [0.84; 3.85] 0.123	0.02 [-0.01; 0.05] 0.122

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 16-2.2 Any ocular adverse event by SOC, PT and age (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 16-2.12 Any ocular adverse event by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

	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 52					
Eye disorders					
KESTREL, n (%)	67 (35.4)	66 (35.3)	1.01 [0.66; 1.54] 0.975	1.00 [0.76; 1.32] 0.975	0.00 [-0.10; 0.10] 0.975
KITE, n (%)	45 (25.1)	47 (26.0)	0.96 [0.60; 1.54] 0.857	0.97 [0.68; 1.38] 0.857	-0.01 [-0.10; 0.08] 0.857
Pooled Analysis, n (%) p_H=0.877	112 (30.4)	113 (30.7)	0.98 [0.72; 1.35] 0.912	0.99 [0.80; 1.23] 0.923	-0.00 [-0.07; 0.06] 0.923
Conjunctival haemorrhage					
KESTREL, n (%)	14 (7.4)	18 (9.6)	0.75 [0.36; 1.56] 0.442	0.77 [0.39; 1.50] 0.443	-0.02 [-0.08; 0.03] 0.441
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=0.500	21 (5.7)	24 (6.5)	0.94 [0.49; 1.82] 0.854	0.87 [0.50; 1.53] 0.632	-0.01 [-0.04; 0.03] 0.632
Cataract					
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 (%)	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=0.529	13 (3.5)	14 (3.8)	0.87 [0.39; 1.93] 0.729	0.93 [0.44; 1.94] 0.839	-0.00 [-0.03; 0.02] 0.839
Dry eye					
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

	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 (%)	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=0.586	12 (3.3)	10 (2.7)	1.30 [0.53; 3.22] 0.564	1.20 [0.53; 2.75] 0.660	0.01 [-0.02; 0.03] 0.659
Vitreous floaters					
KESTREL, n (%)	10 (5.3)	4 (2.1)	2.56 [0.79; 8.30] 0.118	2.47 [0.79; 7.75] 0.120	0.03 [-0.01; 0.07] 0.105
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=0.223	12 (3.3)	7 (1.9)	1.33 [0.46; 3.86] 0.604	1.71 [0.68; 4.29] 0.249	0.01 [-0.01; 0.04] 0.248
Infections and infestations					
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 (%)	9 (5.0)	4 (2.2)	2.34 [0.71; 7.75] 0.163	2.28 [0.71; 7.25] 0.165	0.03 [-0.01; 0.07] 0.152
Pooled Analysis, n (%) p_H=0.871	15 (4.1)	7 (1.9)	2.17 [0.86; 5.46] 0.101	2.15 [0.89; 5.20] 0.083	0.02 [-0.00; 0.05] 0.082

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 16-3.2 Any ocular adverse event at the study eye by SOC, PT and age (SAF), binary analysis, week 52

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

Table 16-3.3 Any ocular adverse event at the study eye by SOC, PT and gender (SAF), binary analysis, week 52

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

Table 16-3.4 Any ocular adverse event at the study eye by SOC, PT and BCVA (SAF), binary analysis, week 52

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

Table 16-3.5 Any ocular adverse event at the study eye by SOC, PT and region (SAF), binary analysis, week 52

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

Table 16-3.6 Any ocular adverse event at the study eye by SOC, PT and diabetes type (SAF), binary analysis, week 52

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

Table 16-3.7 Any ocular adverse event at the study eye by SOC, PT and HbA1c (SAF), binary analysis, week 52

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

Table 16-3.8 Any ocular adverse event at the study eye by SOC, PT and duration of DME (SAF), binary analysis, week 52

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

Table 16-3.9 Any ocular adverse event at the study eye by SOC, PT and DME type (SAF), binary analysis, week 52

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

Table 16-3.10 Any ocular adverse event at the study eye by SOC, PT and CSFT (SAF), binary analysis, week 52

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

Table 16-3.11 Any ocular adverse event at the study eye by SOC, PT and status of SRF (SAF), binary analysis, week 52

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

Table 16-3.12 Any ocular adverse event at the study eye by SOC, PT and exposure (SAF), binary analysis, week 52

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

Table 16-4.1 Any ocular adverse event at the fellow eye by SOC and PT (SAF), binary analysis, week 52

	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 52					
Eye disorders					
KESTREL, n (%)	56 (29.6)	48 (25.7)	1.22 [0.78; 1.92] 0.391	1.15 [0.83; 1.60] 0.392	0.04 [-0.05; 0.13] 0.390
KITE, n (%)	48 (26.8)	51 (28.2)	0.93 [0.59; 1.48] 0.772	0.95 [0.68; 1.33] 0.772	-0.01 [-0.11; 0.08] 0.772
Pooled Analysis, n (%) p_H=0.420	104 (28.3)	99 (26.9)	1.07 [0.77; 1.48] 0.682	1.05 [0.83; 1.33] 0.681	0.01 [-0.05; 0.08] 0.680
Diabetic retinal oedema					
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 (%)	14 (7.8)	14 (7.7)	1.01 [0.47; 2.19] 0.976	1.01 [0.50; 2.06] 0.976	0.00 [-0.05; 0.06] 0.976
Pooled Analysis, n (%) p_H=0.360	19 (5.2)	23 (6.3)	0.73 [0.37; 1.45] 0.372	0.83 [0.46; 1.49] 0.532	-0.01 [-0.04; 0.02] 0.532
Cataract					
KESTREL, n (%)	6 (3.2)	6 (3.2)	0.99 [0.31; 3.12] 0.985	0.99 [0.32; 3.01] 0.985	-0.00 [-0.04; 0.04] 0.985
KITE, n (%)	5 (2.8)	8 (4.4)	0.62 [0.20; 1.94] 0.412	0.63 [0.21; 1.89] 0.413	-0.02 [-0.05; 0.02] 0.407
Pooled Analysis, n (%) p_H=0.573	11 (3.0)	14 (3.8)	0.79 [0.35; 1.77] 0.563	0.79 [0.36; 1.71] 0.543	-0.01 [-0.03; 0.02] 0.543
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

	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**
KITE, n (%)	1 (0.6)	6 (3.3)	0.16 [0.02; 1.38] 0.096	0.17 [0.02; 1.39] 0.098	-0.03 [-0.06; 0.00] 0.056
Pooled Analysis, n (%) p_H=0.241	6 (1.6)	13 (3.5)	0.34 [0.10; 1.14] 0.081	0.46 [0.18; 1.20] 0.103	-0.02 [-0.04; 0.00] 0.102
Dry eye					
KESTREL, n (%)	3 (1.6)	3 (1.6)	0.99 [0.20; 4.96] 0.990	0.99 [0.20; 4.84] 0.990	-0.00 [-0.03; 0.03] 0.990
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=0.613	11 (3.0)	8 (2.2)	1.27 [0.47; 3.43] 0.637	1.38 [0.56; 3.39] 0.479	0.01 [-0.01; 0.03] 0.479

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 16-4.2 Any ocular adverse event at the fellow eye by SOC, PT and age (SAF), binary analysis, week 52

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

Table 16-4.3 Any ocular adverse event at the fellow eye by SOC, PT and gender (SAF), binary analysis, week 52

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

Table 16-4.4 Any ocular adverse event at the fellow eye by SOC, PT and BCVA (SAF), binary analysis, week 52

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

Table 16-4.5 Any ocular adverse event at the fellow eye by SOC, PT and region (SAF), binary analysis, week 52

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

Table 16-4.6 Any ocular adverse event at the fellow eye by SOC, PT and diabetes type (SAF), binary analysis, week 52

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

Table 16-4.7 Any ocular adverse event at the fellow eye by SOC, PT and HbA1c (SAF), binary analysis, week 52

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

Table 16-4.8 Any ocular adverse event at the fellow eye by SOC, PT and duration of DME (SAF), binary analysis, week 52

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

Table 16-4.9 Any ocular adverse event at the fellow eye by SOC, PT and DME type (SAF), binary analysis, week 52

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

Table 16-4.10 Any ocular adverse event at the fellow eye by SOC, PT and CSFT (SAF), binary analysis, week 52

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

Table 16-4.11 Any ocular adverse event at the fellow eye by SOC, PT and status of SRF (SAF), binary analysis, week 52

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

Table 16-4.12 Any ocular adverse event at the fellow eye by SOC, PT and exposure (SAF), binary analysis, week 52

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

Table 16-5.1 Any non-ocular adverse event by SOC and PT (SAF), binary analysis, week 52

	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 52					
Infections and infestations					
KESTREL, n (%)	61 (32.3)	45 (24.1)	1.50 [0.96; 2.37] 0.078	1.34 [0.97; 1.86] 0.079	0.08 [-0.01; 0.17] 0.075
KITE, n (%)	40 (22.3)	50 (27.6)	0.75 [0.47; 1.22] 0.248	0.81 [0.56; 1.16] 0.249	-0.05 [-0.14; 0.04] 0.246
Pooled Analysis, n (%) p_H=0.040 *	101 (27.4)	95 (25.8)	1.07 [0.77; 1.49] 0.678	1.06 [0.84; 1.35] 0.621	0.02 [-0.05; 0.08] 0.621
Nasopharyngitis					
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 (%)	11 (6.1)	12 (6.6)	0.92 [0.40; 2.15] 0.851	0.93 [0.42; 2.05] 0.851	-0.00 [-0.06; 0.05] 0.851
Pooled Analysis, n (%) p_H=0.612	27 (7.3)	25 (6.8)	1.07 [0.61; 1.89] 0.811	1.08 [0.64; 1.82] 0.777	0.01 [-0.03; 0.04] 0.776
Urinary tract infection					
KESTREL, n (%)	15 (7.9)	7 (3.7)	2.22 [0.88; 5.57] 0.090	2.12 [0.88; 5.08] 0.092	0.04 [-0.01; 0.09] 0.081
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.	15 (4.1)	10 (2.7)	N.E.	1.47 [0.68; 3.16] 0.324	0.01 [-0.01; 0.04] 0.315
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

	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 (%)	6 (3.4)	3 (1.7)	2.06 [0.51; 8.36] 0.313	2.02 [0.51; 7.96] 0.314	0.02 [-0.02; 0.05] 0.303
Pooled Analysis, n (%) p_H=0.609	11 (3.0)	7 (1.9)	1.59 [0.61; 4.18] 0.346	1.57 [0.62; 4.01] 0.340	0.01 [-0.01; 0.03] 0.339
Influenza					
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 (%)	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=0.497	10 (2.7)	7 (1.9)	1.44 [0.53; 3.87] 0.474	1.43 [0.55; 3.72] 0.463	0.01 [-0.01; 0.03] 0.462
Upper respiratory tract infection					
KESTREL, 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 (%)	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=0.985	10 (2.7)	4 (1.1)	2.54 [0.79; 8.18] 0.118	2.50 [0.79; 7.90] 0.106	0.02 [-0.00; 0.04] 0.105
Metabolism and nutrition disorders					
KESTREL, n (%)	35 (18.5)	18 (9.6)	2.13 [1.16; 3.92] 0.015 *	1.92 [1.13; 3.27] 0.016 *	0.09 [0.02; 0.16] 0.012 *
KITE, n (%)	17 (9.5)	19 (10.5)	0.89 [0.45; 1.78] 0.752	0.90 [0.49; 1.68] 0.752	-0.01 [-0.07; 0.05] 0.752
Pooled Analysis, n (%) p_H=0.064	52 (14.1)	37 (10.1)	1.39 [0.88; 2.21] 0.156	1.40 [0.94; 2.09] 0.091	0.04 [-0.01; 0.09] 0.091
Vascular disorders					
KESTREL, n (%)	24 (12.7)	22 (11.8)	1.09 [0.59; 2.02] 0.782	1.08 [0.63; 1.86] 0.782	0.01 [-0.06; 0.08] 0.782
KITE, n (%)	24 (13.4)	18 (9.9)	1.40 [0.73; 2.68] 0.308	1.35 [0.76; 2.40] 0.309	0.03 [-0.03; 0.10] 0.306

	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=0.583	48 (13.0)	40 (10.9)	1.23 [0.79; 1.93] 0.358	1.20 [0.81; 1.78] 0.365	0.02 [-0.03; 0.07] 0.364
Hypertension					
KESTREL, n (%)	17 (9.0)	16 (8.6)	1.06 [0.52; 2.16] 0.881	1.05 [0.55; 2.02] 0.881	0.00 [-0.05; 0.06] 0.881
KITE, n (%)	13 (7.3)	10 (5.5)	1.34 [0.57; 3.14] 0.502	1.31 [0.59; 2.92] 0.502	0.02 [-0.03; 0.07] 0.500
Pooled Analysis, n (%) p_H=0.676	30 (8.2)	26 (7.1)	1.19 [0.68; 2.06] 0.545	1.15 [0.70; 1.91] 0.583	0.01 [-0.03; 0.05] 0.582
Gastrointestinal disorders					
KESTREL, n (%)	27 (14.3)	19 (10.2)	1.47 [0.79; 2.75] 0.224	1.41 [0.81; 2.44] 0.225	0.04 [-0.02; 0.11] 0.221
KITE, n (%)	17 (9.5)	21 (11.6)	0.80 [0.41; 1.57] 0.516	0.82 [0.45; 1.50] 0.517	-0.02 [-0.08; 0.04] 0.515
Pooled Analysis, n (%) p_H=0.193	44 (12.0)	40 (10.9)	1.09 [0.69; 1.73] 0.707	1.10 [0.73; 1.65] 0.646	0.01 [-0.04; 0.06] 0.646
Diarrhoea					
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 (%)	3 (1.7)	6 (3.3)	0.50 [0.12; 2.02] 0.328	0.51 [0.13; 1.99] 0.329	-0.02 [-0.05; 0.02] 0.318
Pooled Analysis, n (%) p_H=0.254	9 (2.4)	10 (2.7)	0.87 [0.34; 2.25] 0.779	0.90 [0.37; 2.19] 0.816	-0.00 [-0.03; 0.02] 0.816
Renal and urinary disorders					
KESTREL, n (%)	14 (7.4)	17 (9.1)	0.80 [0.38; 1.67] 0.554	0.81 [0.41; 1.60] 0.554	-0.02 [-0.07; 0.04] 0.553
KITE, n (%)	10 (5.6)	23 (12.7)	0.41 [0.19; 0.88] 0.023 *	0.44 [0.22; 0.90] 0.024 *	-0.07 [-0.13; -0.01] 0.018 *
Pooled Analysis, n (%) p_H=0.215	24 (6.5)	40 (10.9)	0.57 [0.34; 0.98] 0.042 *	0.60 [0.37; 0.98] 0.037 *	-0.04 [-0.08; -0.00] 0.036 *

	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**
Investigations					
KESTREL, n (%)	15 (7.9)	17 (9.1)	0.86 [0.42; 1.78] 0.689	0.87 [0.45; 1.70] 0.689	-0.01 [-0.07; 0.04] 0.688
KITE, n (%)	18 (10.1)	21 (11.6)	0.85 [0.44; 1.66] 0.637	0.87 [0.48; 1.57] 0.637	-0.02 [-0.08; 0.05] 0.637
Pooled Analysis, n (%) p_H=0.981	33 (9.0)	38 (10.3)	0.86 [0.52; 1.40] 0.540	0.87 [0.56; 1.35] 0.537	-0.01 [-0.06; 0.03] 0.536
Nervous system disorders					
KESTREL, n (%)	17 (9.0)	18 (9.6)	0.93 [0.46; 1.86] 0.833	0.93 [0.50; 1.76] 0.833	-0.01 [-0.07; 0.05] 0.833
KITE, n (%)	16 (8.9)	19 (10.5)	0.84 [0.42; 1.68] 0.618	0.85 [0.45; 1.60] 0.618	-0.02 [-0.08; 0.05] 0.617
Pooled Analysis, n (%) p_H=0.838	33 (9.0)	37 (10.1)	0.88 [0.54; 1.45] 0.619	0.89 [0.57; 1.39] 0.616	-0.01 [-0.05; 0.03] 0.616
Headache					
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
General disorders and administration site conditions					
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 (%)	19 (10.6)	15 (8.3)	1.31 [0.65; 2.68] 0.451	1.28 [0.67; 2.44] 0.452	0.02 [-0.04; 0.08] 0.450
Pooled Analysis, n (%) p_H=0.910	35 (9.5)	28 (7.6)	1.27 [0.76; 2.15] 0.362	1.25 [0.78; 2.01] 0.354	0.02 [-0.02; 0.06] 0.354

	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**
Pyrexia					
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 (%)	6 (3.4)	3 (1.7)	2.06 [0.51; 8.36] 0.313	2.02 [0.51; 7.96] 0.314	0.02 [-0.02; 0.05] 0.303
Pooled Analysis, n (%) p_H=0.722	12 (3.3)	5 (1.4)	2.51 [0.86; 7.32] 0.093	2.40 [0.85; 6.76] 0.086	0.02 [-0.00; 0.04] 0.085
Musculoskeletal and connective tissue disorders					
KESTREL, n (%)	19 (10.1)	12 (6.4)	1.63 [0.77; 3.46] 0.203	1.57 [0.78; 3.14] 0.205	0.04 [-0.02; 0.09] 0.199
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=0.306	35 (9.5)	29 (7.9)	1.25 [0.74; 2.10] 0.402	1.21 [0.75; 1.93] 0.432	0.02 [-0.02; 0.06] 0.431
Respiratory, thoracic and mediastinal disorders					
KESTREL, n (%)	22 (11.6)	18 (9.6)	1.24 [0.64; 2.39] 0.527	1.21 [0.67; 2.18] 0.527	0.02 [-0.04; 0.08] 0.526
KITE, n (%)	10 (5.6)	16 (8.8)	0.61 [0.27; 1.38] 0.237	0.63 [0.29; 1.35] 0.238	-0.03 [-0.09; 0.02] 0.232
Pooled Analysis, n (%) p_H=0.188	32 (8.7)	34 (9.2)	0.87 [0.52; 1.48] 0.617	0.94 [0.59; 1.49] 0.790	-0.01 [-0.05; 0.04] 0.789
Cough					
KESTREL, n (%)	8 (4.2)	8 (4.3)	0.99 [0.36; 2.69] 0.983	0.99 [0.38; 2.58] 0.983	-0.00 [-0.04; 0.04] 0.983
KITE, n (%)	3 (1.7)	5 (2.8)	0.60 [0.14; 2.55] 0.489	0.61 [0.15; 2.50] 0.489	-0.01 [-0.04; 0.02] 0.484
Pooled Analysis, n (%) p_H=0.578	11 (3.0)	13 (3.5)	0.77 [0.32; 1.85] 0.566	0.84 [0.38; 1.86] 0.672	-0.01 [-0.03; 0.02] 0.671

	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**
Injury, poisoning and procedural complications					
KESTREL, n (%)	14 (7.4)	19 (10.2)	0.71 [0.34; 1.46] 0.347	0.73 [0.38; 1.41] 0.348	-0.03 [-0.08; 0.03] 0.345
KITE, n (%)	14 (7.8)	9 (5.0)	1.62 [0.68; 3.85] 0.273	1.57 [0.70; 3.54] 0.274	0.03 [-0.02; 0.08] 0.269
Pooled Analysis, n (%) p_H=0.149	28 (7.6)	28 (7.6)	1.06 [0.61; 1.86] 0.833	1.00 [0.60; 1.65] 0.995	-0.00 [-0.04; 0.04] 0.995
Cardiac disorders					
KESTREL, n (%)	12 (6.3)	14 (7.5)	0.84 [0.38; 1.86] 0.664	0.85 [0.40; 1.78] 0.664	-0.01 [-0.06; 0.04] 0.664
KITE, n (%)	6 (3.4)	11 (6.1)	0.54 [0.19; 1.48] 0.229	0.55 [0.21; 1.46] 0.231	-0.03 [-0.07; 0.02] 0.221
Pooled Analysis, n (%) p_H=0.499	18 (4.9)	25 (6.8)	0.67 [0.35; 1.28] 0.228	0.72 [0.40; 1.29] 0.268	-0.02 [-0.05; 0.01] 0.267
Blood and lymphatic system disorders					
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
KITE, n (%)	5 (2.8)	11 (6.1)	0.44 [0.15; 1.31] 0.140	0.46 [0.16; 1.30] 0.142	-0.03 [-0.08; 0.01] 0.129
Pooled Analysis, n (%) p_H=0.341	14 (3.8)	21 (5.7)	0.63 [0.31; 1.28] 0.203	0.67 [0.34; 1.29] 0.225	-0.02 [-0.05; 0.01] 0.224
Anaemia					
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)	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=0.508	11 (3.0)	14 (3.8)	0.75 [0.33; 1.71] 0.498	0.78 [0.36; 1.71] 0.540	-0.01 [-0.03; 0.02] 0.540

	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**
Skin and subcutaneous tissue disorders					
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 (%)	8 (4.5)	9 (5.0)	0.89 [0.34; 2.37] 0.822	0.90 [0.35; 2.28] 0.822	-0.01 [-0.05; 0.04] 0.822
Pooled Analysis, n (%) p_H=0.276	21 (5.7)	16 (4.3)	1.31 [0.67; 2.59] 0.431	1.31 [0.70; 2.48] 0.401	0.01 [-0.02; 0.05] 0.400
Psychiatric disorders					
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 (%)	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=0.771	14 (3.8)	12 (3.3)	1.14 [0.51; 2.55] 0.744	1.16 [0.55; 2.48] 0.694	0.01 [-0.02; 0.03] 0.694
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
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 (%)	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 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=0.507	10 (2.7)	11 (3.0)	0.94 [0.39; 2.27] 0.885	0.91 [0.39; 2.11] 0.823	-0.00 [-0.03; 0.02] 0.822

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 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.634				
< 65 years, n (%)	7 (6.7)	9 (9.7)	0.67 [0.24; 1.89] 0.452	0.70 [0.27; 1.79] 0.452	-0.03 [-0.11; 0.05] 0.453
≥ 65 years, n (%)	7 (8.2)	8 (8.5)	0.96 [0.33; 2.78] 0.947	0.97 [0.37; 2.56] 0.947	-0.00 [-0.08; 0.08] 0.947
KITE					
Interaction Test:	p = 0.128				
< 65 years, n (%)	8 (8.0)	12 (11.8)	0.65 [0.25; 1.67] 0.373	0.68 [0.29; 1.59] 0.374	-0.04 [-0.12; 0.04] 0.369
≥ 65 years, n (%)	2 (2.5)	11 (13.9)	0.16 [0.03; 0.75] 0.020 *	0.18 [0.04; 0.79] 0.023 *	-0.11 [-0.20; -0.03] 0.008 *
Pooled Analysis					
Interaction Test:	p = 0.510				
< 65 years, n (%)	15 (7.4)	21 (10.8)	0.67 [0.33; 1.35] 0.260	0.69 [0.36; 1.29] 0.243	-0.03 [-0.09; 0.02] 0.242

	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 (%)	9 (5.5)	19 (11.0)	0.47 [0.20; 1.06] 0.070	0.50 [0.24; 1.08] 0.069	-0.05 [-0.11; 0.00] 0.067

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 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.575				
Male, n (%)	10 (9.1)	12 (9.5)	0.95 [0.39; 2.29] 0.909	0.95 [0.43; 2.12] 0.909	-0.00 [-0.08; 0.07] 0.909
Female, n (%)	4 (5.1)	5 (8.2)	0.60 [0.15; 2.33] 0.458	0.62 [0.17; 2.20] 0.458	-0.03 [-0.12; 0.05] 0.465
KITE					
Interaction Test:	p = 0.148				
Male, n (%)	9 (7.5)	14 (12.2)	0.58 [0.24; 1.41] 0.232	0.62 [0.28; 1.37] 0.234	-0.05 [-0.12; 0.03] 0.229
Female, n (%)	1 (1.7)	9 (13.6)	0.11 [0.01; 0.89] 0.039 *	0.12 [0.02; 0.95] 0.045 *	-0.12 [-0.21; -0.03] 0.009 *
Pooled Analysis					
Interaction Test:	p = 0.142				
Male, n (%)	19 (8.3)	26 (10.8)	0.75 [0.40; 1.40] 0.365	0.76 [0.44; 1.34] 0.348	-0.03 [-0.08; 0.03] 0.346

	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 (%)	5 (3.6)	14 (11.0)	0.30 [0.10; 0.86] 0.026 *	0.32 [0.11; 0.91] 0.022 *	-0.07 [-0.14; -0.01] 0.022 *

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 16-5.4 Any non-ocular adverse event by SOC, PT and BCVA (SAF), binary analysis, week 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.532				
≤ 65 letters, n (%)	5 (6.8)	7 (10.9)	0.59 [0.18; 1.96] 0.389	0.62 [0.21; 1.85] 0.390	-0.04 [-0.14; 0.05] 0.391
> 65 letters, n (%)	9 (7.8)	10 (8.1)	0.96 [0.38; 2.45] 0.931	0.96 [0.41; 2.28] 0.931	-0.00 [-0.07; 0.07] 0.931
KITE					
Interaction Test:	p = 0.414				
≤ 65 letters, n (%)	2 (3.1)	11 (12.1)	0.23 [0.05; 1.08] 0.063	0.25 [0.06; 1.11] 0.069	-0.09 [-0.17; -0.01] 0.025 *
> 65 letters, n (%)	8 (7.0)	12 (13.3)	0.49 [0.19; 1.26] 0.138	0.53 [0.22; 1.23] 0.139	-0.06 [-0.15; 0.02] 0.143
Pooled Analysis					
Interaction Test:	p = 0.389				
≤ 65 letters, n (%)	7 (5.0)	18 (11.6)	0.42 [0.17; 1.04] 0.060	0.42 [0.17; 1.00] 0.041 *	-0.07 [-0.13; -0.01] 0.034 *

	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 (%)	17 (7.4)	22 (10.3)	0.68 [0.35; 1.33] 0.261	0.71 [0.39; 1.29] 0.259	-0.03 [-0.08; 0.02] 0.263

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 16-5.5 Any non-ocular adverse event by SOC, PT and region (SAF), binary analysis, week 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.817				
Region of the Americas, n (%)	9 (10.0)	11 (13.3)	0.73 [0.29; 1.86] 0.505	0.75 [0.33; 1.73] 0.505	-0.03 [-0.13; 0.06] 0.505
European Region, n (%)	4 (5.8)	4 (5.3)	1.09 [0.26; 4.55] 0.903	1.09 [0.28; 4.18] 0.903	0.00 [-0.07; 0.08] 0.904
Western Pacific Region, n (%)	1 (3.3)	2 (6.9)	0.47 [0.04; 5.43] 0.542	0.48 [0.05; 5.05] 0.544	-0.04 [-0.15; 0.08] 0.534

	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:	p = 0.028 *				
South-East Asia Region and Eastern Mediterranean Region, n (%)	3 (11.5)	3 (14.3)	0.78 [0.14; 4.35] 0.779	0.81 [0.18; 3.60] 0.779	-0.03 [-0.22; 0.17] 0.781
European Region, n (%)	3 (2.2)	17 (12.9)	0.15 [0.04; 0.54] 0.003 *	0.17 [0.05; 0.58] 0.004 *	-0.11 [-0.17; -0.04] <.001 *
Western Pacific Region, 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
Pooled Analysis					
Interaction Test:	p = 0.371				
Region of the Americas, n (%)	9 (10.0)	11 (13.3)	0.53 [0.16; 1.78] 0.303	0.75 [0.33; 1.73] 0.505	-0.03 [-0.13; 0.06] 0.505
South-East Asia Region and Eastern Mediterranean Region, n (%)	3 (11.5)	3 (14.3)	1.09 [0.16; 7.22] 0.930	0.81 [0.18; 3.60] 0.781	-0.03 [-0.22; 0.17] 0.781
European Region, n (%)	7 (3.4)	21 (10.1)	0.37 [0.14; 0.95] 0.039 *	0.34 [0.15; 0.78] 0.007 *	-0.07 [-0.12; -0.02] 0.006 *
Western Pacific Region, n (%)	5 (10.4)	5 (8.8)	1.33 [0.35; 4.97] 0.676	1.34 [0.43; 4.13] 0.618	0.03 [-0.09; 0.14] 0.626

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 16-5.6 Any non-ocular adverse event by SOC, PT and diabetes type (SAF), binary analysis, week 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: p_H=**0.215**					
KESTREL					
Interaction Test:	N.E.				
Type 1, 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 (%)	13 (7.3)	17 (9.4)	0.76 [0.36; 1.63] 0.486	0.78 [0.39; 1.56] 0.486	-0.02 [-0.08; 0.04] 0.484
KITE					
Interaction Test:	p = 0.411				
Type 1, n (%)	1 (5.3)	2 (28.6)	0.14 [0.01; 1.86] 0.136	0.18 [0.02; 1.73] 0.139	-0.23 [-0.58; 0.12] 0.191
Type 2, n (%)	9 (5.6)	21 (12.1)	0.43 [0.19; 0.98] 0.044 *	0.47 [0.22; 0.99] 0.046 *	-0.06 [-0.12; -0.00] 0.036 *
Pooled Analysis					
Interaction Test:	p = 0.736				
Type 1, n (%)	2 (6.5)	2 (15.4)	0.40 [0.05; 3.23] 0.391	0.44 [0.09; 2.17] 0.315	-0.09 [-0.31; 0.13] 0.401

	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 (%)	22 (6.5)	38 (10.7)	0.58 [0.33; 1.01] 0.056	0.61 [0.37; 1.01] 0.052	-0.04 [-0.08; -0.00] 0.050 *

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):
Renal and urinary disorders / KESTREL: logit(proportion) = treatment [by diabetes type].

Table 16-5.7 Any non-ocular adverse event by SOC, PT and HbA1c (SAF), binary analysis, week 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.153				
< 7.5 %, n (%)	5 (6.6)	13 (12.1)	0.51 [0.17; 1.49] 0.219	0.54 [0.20; 1.46] 0.224	-0.06 [-0.14; 0.03] 0.190
≥ 7.5 %, n (%)	9 (8.0)	4 (5.0)	1.66 [0.49; 5.59] 0.413	1.61 [0.51; 5.04] 0.416	0.03 [-0.04; 0.10] 0.391
KITE					
Interaction Test:	p = 0.290				
< 7.5 %, n (%)	6 (7.3)	11 (11.5)	0.61 [0.22; 1.73] 0.352	0.64 [0.25; 1.65] 0.355	-0.04 [-0.13; 0.04] 0.340
≥ 7.5 %, n (%)	4 (4.1)	12 (14.1)	0.26 [0.08; 0.85] 0.025 *	0.29 [0.10; 0.87] 0.027 *	-0.10 [-0.18; -0.02] 0.020 *
Pooled Analysis					
Interaction Test:	p = 0.853				
< 7.5 %, n (%)	11 (7.0)	24 (11.8)	0.56 [0.27; 1.19] 0.131	0.59 [0.30; 1.17] 0.123	-0.05 [-0.11; 0.01] 0.110

	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 (%)	13 (6.2)	16 (9.7)	0.62 [0.29; 1.34] 0.226	0.64 [0.31; 1.33] 0.226	-0.03 [-0.09; 0.02] 0.234

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 16-5.8 Any non-ocular adverse event by SOC, PT and duration of DME (SAF), binary analysis, week 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.271				
≤ 3 months, n (%)	8 (6.7)	12 (10.9)	0.58 [0.23; 1.49] 0.258	0.61 [0.26; 1.44] 0.260	-0.04 [-0.12; 0.03] 0.257
> 3 - < 12 months, n (%)	2 (6.7)	4 (10.3)	0.63 [0.11; 3.66] 0.602	0.65 [0.13; 3.32] 0.604	-0.04 [-0.17; 0.09] 0.590
≥ 12 months, n (%)	4 (10.3)	1 (2.6)	4.23 [0.45; 39.70] 0.207	3.90 [0.46; 33.30] 0.214	0.08 [-0.03; 0.18] 0.166
KITE					
Interaction Test:	p = 0.327				
≤ 3 months, n (%)	3 (3.5)	14 (15.2)	0.20 [0.06; 0.74] 0.015 *	0.23 [0.07; 0.78] 0.018 *	-0.12 [-0.20; -0.03] 0.006 *
> 3 - < 12 months, n (%)	4 (7.8)	5 (10.2)	0.75 [0.19; 2.97] 0.681	0.77 [0.22; 2.70] 0.681	-0.02 [-0.14; 0.09] 0.680

	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**
≥ 12 months, n (%)	3 (7.0)	4 (10.0)	0.68 [0.14; 3.22] 0.622	0.70 [0.17; 2.93] 0.623	-0.03 [-0.15; 0.09] 0.622
Pooled Analysis					
Interaction Test:	p = 0.153				
≤ 3 months, n (%)	11 (5.4)	26 (12.9)	0.37 [0.17; 0.78] 0.009 *	0.41 [0.21; 0.82] 0.009 *	-0.07 [-0.13; -0.02] 0.008 *
> 3 - < 12 months, n (%)	6 (7.4)	9 (10.2)	0.76 [0.26; 2.26] 0.624	0.72 [0.27; 1.95] 0.518	-0.03 [-0.11; 0.06] 0.512
≥ 12 months, n (%)	7 (8.5)	5 (6.4)	1.40 [0.42; 4.63] 0.583	1.33 [0.44; 4.00] 0.615	0.02 [-0.06; 0.10] 0.614

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 16-5.9 Any non-ocular adverse event by SOC, PT and DME type (SAF), binary analysis, week 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.926				
focal, n (%)	2 (3.4)	2 (4.2)	0.81 [0.11; 5.95] 0.834	0.81 [0.12; 5.56] 0.833	-0.01 [-0.08; 0.07] 0.835
diffuse, n (%)	12 (9.4)	14 (10.4)	0.89 [0.40; 2.02] 0.788	0.90 [0.44; 1.88] 0.788	-0.01 [-0.08; 0.06] 0.787
KITE					
Interaction Test:	p = 0.540				
focal, n (%)	4 (6.3)	7 (10.6)	0.57 [0.16; 2.06] 0.392	0.60 [0.18; 1.95] 0.394	-0.04 [-0.14; 0.05] 0.383
diffuse, n (%)	6 (5.2)	15 (13.8)	0.34 [0.13; 0.92] 0.034 *	0.38 [0.15; 0.94] 0.037 *	-0.09 [-0.16; -0.01] 0.028 *
Pooled Analysis					
Interaction Test:	p = 0.887				
focal, n (%)	6 (4.9)	9 (7.9)	0.64 [0.22; 1.88] 0.416	0.65 [0.24; 1.77] 0.399	-0.03 [-0.09; 0.04] 0.398

	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 (%)	18 (7.4)	29 (11.9)	0.59 [0.31; 1.09] 0.092	0.63 [0.36; 1.09] 0.096	-0.04 [-0.10; 0.01] 0.096

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 16-5.10 Any non-ocular adverse event by SOC, PT and CSFT (SAF), binary analysis, week 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.553				
< 450 µm, n (%)	7 (6.5)	5 (5.2)	1.27 [0.39; 4.16] 0.688	1.26 [0.41; 3.83] 0.688	0.01 [-0.05; 0.08] 0.686
≥ 450 - < 650 µm, n (%)	5 (7.1)	9 (12.7)	0.53 [0.17; 1.67] 0.278	0.56 [0.20; 1.60] 0.281	-0.06 [-0.15; 0.04] 0.269
≥ 650 µm, n (%)	2 (16.7)	3 (15.0)	1.13 [0.16; 7.98] 0.900	1.11 [0.22; 5.73] 0.900	0.02 [-0.25; 0.28] 0.901
KITE					
Interaction Test:	N.E.				
< 450 µm, n (%)	7 (8.2)	9 (11.0)	0.73 [0.26; 2.06] 0.549	0.75 [0.29; 1.92] 0.549	-0.03 [-0.12; 0.06] 0.548
≥ 450 - < 650 µm, n (%)	3 (4.1)	10 (12.7)	0.29 [0.08; 1.10] 0.070	0.32 [0.09; 1.12] 0.074	-0.09 [-0.17; -0.00] 0.050 *

	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**
≥ 650 µm, n (%)	0 (0.0)	3 (15.8)	N.E.	0.14 [0.01; 2.47] 0.178	-0.16 [-0.32; 0.01] 0.059
Pooled Analysis					
Interaction Test:	p = 0.355				
< 450 µm, n (%)	14 (7.3)	14 (7.9)	0.90 [0.41; 1.96] 0.795	0.94 [0.46; 1.91] 0.854	-0.01 [-0.06; 0.05] 0.853
≥ 450 - < 650 µm, n (%)	8 (5.6)	19 (12.7)	0.41 [0.17; 0.98] 0.045 *	0.44 [0.20; 0.97] 0.035 *	-0.07 [-0.14; -0.01] 0.032 *
≥ 650 µm, n (%)	2 (6.3)	6 (15.4)	0.38 [0.07; 2.04] 0.259	0.51 [0.14; 1.89] 0.307	-0.08 [-0.23; 0.06] 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
*: $p < 0.05$
.....

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):
Renal and urinary disorders / KITE: logit(proportion) = treatment [by CSFT].

Table 16-5.11 Any non-ocular adverse event by SOC, PT and status of SRF (SAF), binary analysis, week 52

	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 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.889				
presence, n (%)	7 (11.3)	8 (13.1)	0.84 [0.29; 2.49] 0.757	0.86 [0.33; 2.23] 0.757	-0.02 [-0.13; 0.10] 0.757
absence, n (%)	7 (5.5)	9 (7.1)	0.76 [0.27; 2.10] 0.595	0.77 [0.30; 2.01] 0.595	-0.02 [-0.08; 0.04] 0.594
KITE					
Interaction Test:	p = 0.956				
presence, 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 (%)	7 (5.7)	15 (13.2)	0.40 [0.16; 1.02] 0.054	0.43 [0.18; 1.02] 0.056	-0.07 [-0.15; -0.00] 0.049 *
Pooled Analysis					
Interaction Test:	p = 0.708				
presence, n (%)	10 (8.5)	16 (12.5)	0.66 [0.28; 1.52] 0.324	0.67 [0.31; 1.42] 0.287	-0.04 [-0.12; 0.03] 0.279

	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 (%)	14 (5.6)	24 (10.0)	0.53 [0.27; 1.06] 0.073	0.56 [0.30; 1.05] 0.066	-0.04 [-0.09; 0.00] 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
*: $p < 0.05$
.....

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 16-5.12 Any non-ocular adverse event by SOC, PT and exposure (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and exposure (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	71 / 71	75 / 75			
Exposed, N'/N	118 / 118	112 / 112			
KITE, N'/N	179 / 179	181 / 181			
Non-exposed, N'/N	85 / 85	90 / 90			
Exposed, N'/N	94 / 94	91 / 91			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Non-exposed, N'/N	156 / 156	165 / 165			
Exposed, N'/N	212 / 212	203 / 203			
Any non-ocular adverse event by SOC and PT, week 52					
Renal and urinary disorders					
Test of heterogeneity in main analysis: **p_H=0.215**					
KESTREL					
Interaction Test:	p = 0.143				
Non-exposed, n (%)	9 (12.7)	7 (9.3)	1.41 [0.50; 4.01] 0.520	1.36 [0.53; 3.45] 0.520	0.03 [-0.07; 0.14] 0.519
Exposed, n (%)	5 (4.2)	10 (8.9)	0.45 [0.15; 1.36] 0.159	0.47 [0.17; 1.35] 0.161	-0.05 [-0.11; 0.02] 0.152
KITE					
Interaction Test:	p = 0.781				
Non-exposed, n (%)	6 (7.1)	13 (14.4)	0.45 [0.16; 1.24] 0.124	0.49 [0.19; 1.23] 0.127	-0.07 [-0.16; 0.02] 0.111
Exposed, n (%)	4 (4.3)	10 (11.0)	0.36 [0.11; 1.19] 0.095	0.39 [0.13; 1.19] 0.098	-0.07 [-0.14; 0.01] 0.083
Pooled Analysis					
Interaction Test:	p = 0.194				
Non-exposed, n (%)	15 (9.6)	20 (12.1)	0.80 [0.39; 1.64] 0.542	0.79 [0.42; 1.50] 0.473	-0.03 [-0.09; 0.04] 0.472

	Treatment Groups		Comparison		
Any non-ocular adverse event by SOC, PT and exposure (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed, n (%)	9 (4.2)	20 (9.9)	0.39 [0.17; 0.89] 0.025 *	0.43 [0.20; 0.92] 0.026 *	-0.06 [-0.11; -0.01] 0.026 *

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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for RR obtained from Cochran-Mantel-Haenszel test (stratified by study).
RD (with CI and p-value) calculated via Mantel-Haenszel Estimator (stratified by study).

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 52

	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 52					
Cardiac disorders					
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 (%)	3 (1.7)	10 (5.5)	0.29 [0.08; 1.08] 0.065	0.30 [0.08; 1.08] 0.066	-0.04 [-0.08; -0.00] 0.048 *
Pooled Analysis, n (%) p_H=0.106	12 (3.3)	18 (4.9)	0.58 [0.26; 1.30] 0.186	0.67 [0.32; 1.36] 0.262	-0.02 [-0.04; 0.01] 0.262
Infections and infestations					
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 (%)	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=0.473	13 (3.5)	15 (4.1)	0.88 [0.41; 1.90] 0.748	0.87 [0.42; 1.80] 0.702	-0.01 [-0.03; 0.02] 0.702
Nervous system disorders					
KESTREL, n (%)	2 (1.1)	8 (4.3)	0.24 [0.05; 1.14] 0.073	0.25 [0.05; 1.15] 0.075	-0.03 [-0.06; 0.00] 0.052
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=0.159	7 (1.9)	13 (3.5)	0.48 [0.18; 1.33] 0.159	0.54 [0.22; 1.34] 0.174	-0.02 [-0.04; 0.01] 0.174

	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**
Vascular 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)	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=0.889	11 (3.0)	6 (1.6)	1.89 [0.66; 5.42] 0.234	1.83 [0.68; 4.89] 0.222	0.01 [-0.01; 0.04] 0.221
Renal and urinary disorders					
KESTREL, n (%)	4 (2.1)	6 (3.2)	0.65 [0.18; 2.35] 0.514	0.66 [0.19; 2.30] 0.514	-0.01 [-0.04; 0.02] 0.511
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=0.807	6 (1.6)	10 (2.7)	0.57 [0.20; 1.66] 0.304	0.60 [0.22; 1.63] 0.310	-0.01 [-0.03; 0.01] 0.309

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 17-1.2 Any serious adverse event by SOC, PT and age (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 17-1.12 Any serious adverse event by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

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

Table 17-2.2 Any serious ocular adverse event by SOC, PT and age (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 17-2.12 Any serious ocular adverse event by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 17-3.12 Any serious ocular adverse event at the study eye by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 17-4.12 Any serious ocular adverse event at the fellow eye by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

	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 52					
Cardiac disorders					
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 (%)	3 (1.7)	10 (5.5)	0.29 [0.08; 1.08] 0.065	0.30 [0.08; 1.08] 0.066	-0.04 [-0.08; -0.00] 0.048 *
Pooled Analysis, n (%) p_H=0.106	12 (3.3)	18 (4.9)	0.58 [0.26; 1.30] 0.186	0.67 [0.32; 1.36] 0.262	-0.02 [-0.04; 0.01] 0.262
Infections and infestations					
KESTREL, 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 (%)	5 (2.8)	8 (4.4)	0.62 [0.20; 1.94] 0.412	0.63 [0.21; 1.89] 0.413	-0.02 [-0.05; 0.02] 0.407
Pooled Analysis, n (%) p_H=0.328	12 (3.3)	13 (3.5)	0.94 [0.42; 2.12] 0.882	0.92 [0.43; 2.00] 0.840	-0.00 [-0.03; 0.02] 0.840
Nervous system disorders					
KESTREL, n (%)	2 (1.1)	8 (4.3)	0.24 [0.05; 1.14] 0.073	0.25 [0.05; 1.15] 0.075	-0.03 [-0.06; 0.00] 0.052
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=0.159	7 (1.9)	13 (3.5)	0.48 [0.18; 1.33] 0.159	0.54 [0.22; 1.34] 0.174	-0.02 [-0.04; 0.01] 0.174
Vascular 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

	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**
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=0.889	11 (3.0)	6 (1.6)	1.89 [0.66; 5.42] 0.234	1.83 [0.68; 4.89] 0.222	0.01 [-0.01; 0.04] 0.221
Renal and urinary disorders					
KESTREL, n (%)	4 (2.1)	6 (3.2)	0.65 [0.18; 2.35] 0.514	0.66 [0.19; 2.30] 0.514	-0.01 [-0.04; 0.02] 0.511
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=0.807	6 (1.6)	10 (2.7)	0.57 [0.20; 1.66] 0.304	0.60 [0.22; 1.63] 0.310	-0.01 [-0.03; 0.01] 0.309

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 17-5.2 Any serious non-ocular adverse event by SOC, PT and age (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 17-5.12 Any serious non-ocular adverse event by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

	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 52					
Eye disorders					
KESTREL, 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 (%)	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=0.114	8 (2.2)	12 (3.3)	0.87 [0.31; 2.44] 0.791	0.66 [0.28; 1.60] 0.359	-0.01 [-0.03; 0.01] 0.360
Cardiac 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 (%)	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

	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=0.502	11 (3.0)	7 (1.9)	1.44 [0.53; 3.94] 0.477	1.57 [0.61; 4.00] 0.344	0.01 [-0.01; 0.03] 0.343

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 18-1.12 Any severe adverse event by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

	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 52					
Eye disorders					
KESTREL, 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 (%)	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=0.114	8 (2.2)	12 (3.3)	0.87 [0.31; 2.44] 0.791	0.66 [0.28; 1.60] 0.359	-0.01 [-0.03; 0.01] 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.
RR and RD calculated directly (with Wald CI and p-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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 18-2.12 Any severe ocular adverse event by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

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

Table 18-3.2 Any severe ocular adverse event at the study eye by SOC, PT and age (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 18-3.12 Any severe ocular adverse event at the study eye by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

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

Table 18-4.2 Any severe ocular adverse event at the fellow eye by SOC, PT and age (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 18-4.12 Any severe ocular adverse event at the fellow eye by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

	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 52					
Cardiac 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 (%)	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=0.502	11 (3.0)	7 (1.9)	1.44 [0.53; 3.94] 0.477	1.57 [0.61; 4.00] 0.344	0.01 [-0.01; 0.03] 0.343

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 18-5.2 Any severe non-ocular adverse event by SOC, PT and age (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 18-5.12 Any severe non-ocular adverse event by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

	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)

	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
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)

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
.....

Table 19.2 Any ocular adverse event leading to study drug discontinuation by SOC and PT (SAF), binary analysis, week 52

	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)

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 52

	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)

N: Number of patients
N': Number of patients in the analysis
n (%): Number and percentage of patients with event
.....

Table 19.4 Any ocular adverse event at the fellow eye leading to study drug discontinuation by SOC and PT (SAF), binary analysis, week 52

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 52

	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)

	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
Confusional state, 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 52

	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 52					
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 (%)	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)	2 (0.5)	N.E.	0.60 [0.08; 4.51] 0.617	-0.00 [-0.01; 0.01] 0.565
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 (%)	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.	1 (0.3)	1 (0.3)	N.E.	1.00 [0.14; 7.04] 1.000	0.00 [-0.01; 0.01] 1.000
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 (%)	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)	2 (0.5)	N.E.	0.60 [0.08; 4.51] 0.617	-0.00 [-0.01; 0.01] 0.565

	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**
Intraocular inflammation					
KESTREL, n (%)	7 (3.7)	1 (0.5)	7.15 [0.87; 58.72] 0.067	6.93 [0.86; 55.74] 0.069	0.03 [0.00; 0.06] 0.032 *
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=0.209	11 (3.0)	4 (1.1)	3.17 [0.86; 11.67] 0.083	2.75 [0.88; 8.60] 0.068	0.02 [-0.00; 0.04] 0.067
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 (%)	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)	3 (1.7)	0.33 [0.03; 3.24] 0.343	0.34 [0.04; 3.21] 0.344	-0.01 [-0.03; 0.01] 0.318
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	3 (0.8)	N.E.	0.72 [0.14; 3.63] 0.686	-0.00 [-0.01; 0.01] 0.659
Retinal vascular occlusion severe					
KESTREL, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
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 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.	1 (0.3)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.474	0.00 [-0.00; 0.01] 0.315
Retinal vascular occlusion serious					
KESTREL, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
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.	1 (0.3)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.474	0.00 [-0.00; 0.01] 0.315

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 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	N.E.				
< 65 years, n (%)	3 (2.9)	0 (0.0)	N.E.	6.27 [0.33; 119.74] 0.223	0.03 [-0.00; 0.06] 0.079
≥ 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:	N.E.				
< 65 years, 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 (%)	2 (2.5)	3 (3.8)	0.66 [0.11; 4.05] 0.652	0.67 [0.11; 3.88] 0.652	-0.01 [-0.07; 0.04] 0.649
Pooled Analysis					
Interaction Test:	N.E.				
< 65 years, n (%)	5 (2.5)	0 (0.0)	N.E.	5.70 [0.69; 47.14] 0.067	0.02 [0.00; 0.05] 0.024 *

	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 (%)	6 (3.7)	4 (2.3)	1.77 [0.42; 7.46] 0.435	1.57 [0.46; 5.41] 0.471	0.01 [-0.02; 0.05] 0.475

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):
Intraocular inflammation / KESTREL, Intraocular inflammation / KITE: logit(proportion) = treatment [by age].
Intraocular inflammation / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by age].

Table 20-1.3 Any adverse events of special interest by gender (SAF), binary analysis, week 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	N.E.				
Male, n (%)	4 (3.6)	0 (0.0)	N.E.	10.30 [0.56; 189.14] 0.116	0.04 [0.00; 0.07] 0.042 *
Female, n (%)	3 (3.8)	1 (1.6)	2.37 [0.24; 23.35] 0.460	2.32 [0.25; 21.72] 0.462	0.02 [-0.03; 0.07] 0.423
KITE					
Interaction Test:	N.E.				
Male, n (%)	0 (0.0)	1 (0.9)	N.E.	0.32 [0.01; 7.77] 0.483	-0.01 [-0.03; 0.01] 0.315
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 = 0.622				
Male, n (%)	4 (1.7)	1 (0.4)	4.78 [0.50; 46.16] 0.176	2.65 [0.54; 12.94] 0.209	0.01 [-0.01; 0.03] 0.159

	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 (%)	7 (5.1)	3 (2.4)	2.49 [0.55; 11.30] 0.239	2.27 [0.60; 8.62] 0.217	0.03 [-0.02; 0.07] 0.209

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):
Intraocular inflammation / KESTREL, Intraocular inflammation / KITE: logit(proportion) = treatment [by gender].

Table 20-1.4 Any adverse events of special interest by BCVA (SAF), binary analysis, week 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	N.E.				
≤ 65 letters, n (%)	1 (1.4)	0 (0.0)	N.E.	2.60 [0.11; 62.73] 0.556	0.01 [-0.01; 0.04] 0.314
> 65 letters, n (%)	6 (5.2)	1 (0.8)	6.72 [0.80; 56.66] 0.080	6.42 [0.78; 52.49] 0.083	0.04 [0.00; 0.09] 0.048 *
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 = 0.350				
≤ 65 letters, n (%)	2 (1.4)	2 (1.3)	1.36 [0.16; 11.24] 0.778	1.16 [0.19; 7.14] 0.871	0.00 [-0.02; 0.03] 0.825

	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 (%)	9 (3.9)	2 (0.9)	4.52 [0.90; 22.75] 0.068	4.25 [0.95; 19.00] 0.039 *	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 + 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):
Intraocular inflammation / KESTREL: logit(proportion) = treatment [by BCVA].

Table 20-1.5 Any adverse events of special interest by region (SAF), binary analysis, week 52

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 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2, n (%)	7 (4.0)	1 (0.6)	7.41 [0.90; 60.86] 0.062	7.16 [0.89; 57.59] 0.064	0.03 [0.00; 0.06] 0.030 *
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 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 (%)	11 (3.3)	4 (1.1)	3.35 [0.91; 12.33] 0.070	2.91 [0.93; 9.13] 0.054	0.02 [-0.00; 0.04] 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):
Intraocular inflammation / KESTREL, Intraocular inflammation / KITE: logit(proportion) = treatment [by diabetes type].
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 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	N.E.				
< 7.5 %, n (%)	3 (3.9)	0 (0.0)	N.E.	9.82 [0.51; 187.35] 0.129	0.04 [-0.00; 0.08] 0.077
≥ 7.5 %, n (%)	4 (3.6)	1 (1.3)	2.93 [0.32; 26.67] 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 = 0.442				
< 7.5 %, n (%)	4 (2.5)	1 (0.5)	5.85 [0.60; 56.65] 0.127	3.86 [0.64; 23.32] 0.112	0.02 [-0.01; 0.05] 0.130

	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 (%)	7 (3.3)	3 (1.8)	2.11 [0.47; 9.54] 0.331	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
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):
Intraocular inflammation / KESTREL: logit(proportion) = treatment [by HbA1c].

Table 20-1.8 Any adverse events of special interest by duration of DME (SAF), binary analysis, week 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months, n (%)	4 (3.3)	1 (0.9)	3.76 [0.41; 34.15] 0.240	3.67 [0.42; 32.31] 0.242	0.02 [-0.01; 0.06] 0.195
> 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)	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 (%)	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

	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**
≥ 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
Pooled Analysis					
Interaction Test:	N.E.				
≤ 3 months, n (%)	7 (3.4)	3 (1.5)	2.51 [0.60; 10.52] 0.209	2.34 [0.61; 9.04] 0.203	0.02 [-0.01; 0.05] 0.199
> 3 - < 12 months, n (%)	2 (2.5)	1 (1.1)	N.E.	1.68 [0.31; 9.14] 0.542	0.01 [-0.03; 0.06] 0.495
≥ 12 months, 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):
Intraocular inflammation / KESTREL, Intraocular inflammation / KITE: logit(proportion) = treatment [by duration of DME].
Intraocular inflammation / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by duration of DME].

Table 20-1.9 Any adverse events of special interest by DME type (SAF), binary analysis, week 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.209**					
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 (%)	6 (4.7)	1 (0.7)	6.59 [0.78; 55.56] 0.083	6.33 [0.77; 51.86] 0.085	0.04 [0.00; 0.08] 0.049 *
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 = 0.812				
focal, n (%)	2 (1.6)	1 (0.9)	2.40 [0.19; 30.24] 0.497	1.55 [0.20; 11.93] 0.671	0.01 [-0.02; 0.04] 0.575

	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 (%)	9 (3.7)	3 (1.2)	3.36 [0.80; 14.11] 0.097	3.00 [0.83; 10.83] 0.077	0.02 [-0.00; 0.05] 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
*: $p < 0.05$
.....

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):
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 52

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

Table 20-1.11 Any adverse events of special interest by status of SRF (SAF), binary analysis, week 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	N.E.				
presence, 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 (%)	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 = 0.496				
presence, n (%)	1 (0.8)	1 (0.8)	1.26 [0.07; 22.16] 0.873	1.09 [0.15; 7.97] 0.936	0.00 [-0.02; 0.02] 0.953

	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 (%)	10 (4.0)	3 (1.3)	3.67 [0.88; 15.35] 0.074	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):
Intraocular inflammation / KESTREL, Intraocular inflammation / KITE: logit(proportion) = treatment [by status of SRF].

Table 20-1.12 Any adverse events of special interest by exposure (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any adverse events of special interest by exposure (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	71 / 71	75 / 75			
Exposed, N'/N	118 / 118	112 / 112			
KITE, N'/N	179 / 179	181 / 181			
Non-exposed, N'/N	85 / 85	90 / 90			
Exposed, N'/N	94 / 94	91 / 91			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Non-exposed, N'/N	156 / 156	165 / 165			
Exposed, N'/N	212 / 212	203 / 203			
Any adverse events of special interest, week 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed, n (%)	0 (0.0)	1 (1.3)	N.E.	0.35 [0.01; 8.50] 0.520	-0.01 [-0.04; 0.01] 0.314
Exposed, n (%)	7 (5.9)	0 (0.0)	N.E.	14.24 [0.82; 246.52] 0.068	0.06 [0.02; 0.10] 0.006 *
KITE					
Interaction Test:	p = 0.258				
Non-exposed, n (%)	3 (3.5)	1 (1.1)	3.26 [0.33; 31.93] 0.311	3.18 [0.34; 29.95] 0.313	0.02 [-0.02; 0.07] 0.290
Exposed, 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 = 0.536				
Non-exposed, n (%)	3 (1.9)	2 (1.2)	1.96 [0.29; 13.48] 0.492	1.48 [0.30; 7.41] 0.631	0.01 [-0.02; 0.03] 0.609

	Treatment Groups		Comparison		
Any adverse events of special interest by exposure (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed, n (%)	8 (3.8)	2 (1.0)	4.19 [0.80; 21.89] 0.090	3.26 [0.80; 13.31] 0.079	0.03 [-0.00; 0.06] 0.061

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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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 20-2.1 Any ocular adverse events of special interest by severity (SAF), binary analysis, week 52

	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 52					
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 (%)	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)	2 (0.5)	N.E.	0.60 [0.08; 4.51] 0.617	-0.00 [-0.01; 0.01] 0.565
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 (%)	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.	1 (0.3)	1 (0.3)	N.E.	1.00 [0.14; 7.04] 1.000	0.00 [-0.01; 0.01] 1.000
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 (%)	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)	2 (0.5)	N.E.	0.60 [0.08; 4.51] 0.617	-0.00 [-0.01; 0.01] 0.565
Intraocular inflammation					
KESTREL, n (%)	7 (3.7)	1 (0.5)	7.15 [0.87; 58.72] 0.067	6.93 [0.86; 55.74] 0.069	0.03 [0.00; 0.06] 0.032 *

	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**
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=0.209	11 (3.0)	4 (1.1)	3.17 [0.86; 11.67] 0.083	2.75 [0.88; 8.60] 0.068	0.02 [-0.00; 0.04] 0.067
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 (%)	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)	3 (1.7)	0.33 [0.03; 3.24] 0.343	0.34 [0.04; 3.21] 0.344	-0.01 [-0.03; 0.01] 0.318
Pooled Analysis, n (%) p_H=N.E.	2 (0.5)	3 (0.8)	N.E.	0.72 [0.14; 3.63] 0.686	-0.00 [-0.01; 0.01] 0.659
Retinal vascular occlusion severe					
KESTREL, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
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.	1 (0.3)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.474	0.00 [-0.00; 0.01] 0.315
Retinal vascular occlusion serious					
KESTREL, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.

	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**
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.	1 (0.3)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.474	0.00 [-0.00; 0.01] 0.315

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 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	N.E.				
< 65 years, n (%)	3 (2.9)	0 (0.0)	N.E.	6.27 [0.33; 119.74] 0.223	0.03 [-0.00; 0.06] 0.079
≥ 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:	N.E.				
< 65 years, 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 (%)	2 (2.5)	3 (3.8)	0.66 [0.11; 4.05] 0.652	0.67 [0.11; 3.88] 0.652	-0.01 [-0.07; 0.04] 0.649
Pooled Analysis					
Interaction Test:	N.E.				
< 65 years, n (%)	5 (2.5)	0 (0.0)	N.E.	5.70 [0.69; 47.14] 0.067	0.02 [0.00; 0.05] 0.024 *

	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 (%)	6 (3.7)	4 (2.3)	1.77 [0.42; 7.46] 0.435	1.57 [0.46; 5.41] 0.471	0.01 [-0.02; 0.05] 0.475

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):
Intraocular inflammation / KESTREL, Intraocular inflammation / KITE: logit(proportion) = treatment [by age].
Intraocular inflammation / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by age].

Table 20-2.3 Any ocular adverse events of special interest by gender (SAF), binary analysis, week 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	N.E.				
Male, n (%)	4 (3.6)	0 (0.0)	N.E.	10.30 [0.56; 189.14] 0.116	0.04 [0.00; 0.07] 0.042 *
Female, n (%)	3 (3.8)	1 (1.6)	2.37 [0.24; 23.35] 0.460	2.32 [0.25; 21.72] 0.462	0.02 [-0.03; 0.07] 0.423
KITE					
Interaction Test:	N.E.				
Male, n (%)	0 (0.0)	1 (0.9)	N.E.	0.32 [0.01; 7.77] 0.483	-0.01 [-0.03; 0.01] 0.315
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 = 0.622				
Male, n (%)	4 (1.7)	1 (0.4)	4.78 [0.50; 46.16] 0.176	2.65 [0.54; 12.94] 0.209	0.01 [-0.01; 0.03] 0.159

	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 (%)	7 (5.1)	3 (2.4)	2.49 [0.55; 11.30] 0.239	2.27 [0.60; 8.62] 0.217	0.03 [-0.02; 0.07] 0.209

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):
Intraocular inflammation / KESTREL, Intraocular inflammation / KITE: logit(proportion) = treatment [by gender].

Table 20-2.4 Any ocular adverse events of special interest by BCVA (SAF), binary analysis, week 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	N.E.				
≤ 65 letters, n (%)	1 (1.4)	0 (0.0)	N.E.	2.60 [0.11; 62.73] 0.556	0.01 [-0.01; 0.04] 0.314
> 65 letters, n (%)	6 (5.2)	1 (0.8)	6.72 [0.80; 56.66] 0.080	6.42 [0.78; 52.49] 0.083	0.04 [0.00; 0.09] 0.048 *
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 = 0.350				
≤ 65 letters, n (%)	2 (1.4)	2 (1.3)	1.36 [0.16; 11.24] 0.778	1.16 [0.19; 7.14] 0.871	0.00 [-0.02; 0.03] 0.825

	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 (%)	9 (3.9)	2 (0.9)	4.52 [0.90; 22.75] 0.068	4.25 [0.95; 19.00] 0.039 *	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 + 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):
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 52

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 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2, n (%)	7 (4.0)	1 (0.6)	7.41 [0.90; 60.86] 0.062	7.16 [0.89; 57.59] 0.064	0.03 [0.00; 0.06] 0.030 *
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 by diabetes type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Type 2, n (%)	11 (3.3)	4 (1.1)	3.35 [0.91; 12.33] 0.070	2.91 [0.93; 9.13] 0.054	0.02 [-0.00; 0.04] 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):
Intraocular inflammation / KESTREL, Intraocular inflammation / KITE: logit(proportion) = treatment [by diabetes type].
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 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	N.E.				
< 7.5 %, n (%)	3 (3.9)	0 (0.0)	N.E.	9.82 [0.51; 187.35] 0.129	0.04 [-0.00; 0.08] 0.077
≥ 7.5 %, n (%)	4 (3.6)	1 (1.3)	2.93 [0.32; 26.67] 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 = 0.442				
< 7.5 %, n (%)	4 (2.5)	1 (0.5)	5.85 [0.60; 56.65] 0.127	3.86 [0.64; 23.32] 0.112	0.02 [-0.01; 0.05] 0.130

	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 (%)	7 (3.3)	3 (1.8)	2.11 [0.47; 9.54] 0.331	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
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):
Intraocular inflammation / KESTREL: logit(proportion) = treatment [by HbA1c].

Table 20-2.8 Any ocular adverse events of special interest by duration of DME (SAF), binary analysis, week 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	N.E.				
≤ 3 months, n (%)	4 (3.3)	1 (0.9)	3.76 [0.41; 34.15] 0.240	3.67 [0.42; 32.31] 0.242	0.02 [-0.01; 0.06] 0.195
> 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)	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 (%)	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

	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**
≥ 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
Pooled Analysis					
Interaction Test:	N.E.				
≤ 3 months, n (%)	7 (3.4)	3 (1.5)	2.51 [0.60; 10.52] 0.209	2.34 [0.61; 9.04] 0.203	0.02 [-0.01; 0.05] 0.199
> 3 - < 12 months, n (%)	2 (2.5)	1 (1.1)	N.E.	1.68 [0.31; 9.14] 0.542	0.01 [-0.03; 0.06] 0.495
≥ 12 months, 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):
Intraocular inflammation / KESTREL, Intraocular inflammation / KITE: logit(proportion) = treatment [by duration of DME].
Intraocular inflammation / Pooled Analysis: logit(proportion) = treatment + study + treatment * study [by duration of DME].

Table 20-2.9 Any ocular adverse events of special interest by DME type (SAF), binary analysis, week 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.209**					
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 (%)	6 (4.7)	1 (0.7)	6.59 [0.78; 55.56] 0.083	6.33 [0.77; 51.86] 0.085	0.04 [0.00; 0.08] 0.049 *
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 = 0.812				
focal, n (%)	2 (1.6)	1 (0.9)	2.40 [0.19; 30.24] 0.497	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 by DME type (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
diffuse, n (%)	9 (3.7)	3 (1.2)	3.36 [0.80; 14.11] 0.097	3.00 [0.83; 10.83] 0.077	0.02 [-0.00; 0.05] 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
*: $p < 0.05$
.....

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):
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 52

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

Table 20-2.11 Any ocular adverse events of special interest by status of SRF (SAF), binary analysis, week 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	N.E.				
presence, 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 (%)	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 = 0.496				
presence, n (%)	1 (0.8)	1 (0.8)	1.26 [0.07; 22.16] 0.873	1.09 [0.15; 7.97] 0.936	0.00 [-0.02; 0.02] 0.953

	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 (%)	10 (4.0)	3 (1.3)	3.67 [0.88; 15.35] 0.074	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):
Intraocular inflammation / KESTREL, Intraocular inflammation / KITE: logit(proportion) = treatment [by status of SRF].

Table 20-2.12 Any ocular adverse events of special interest by exposure (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by exposure (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	71 / 71	75 / 75			
Exposed, N'/N	118 / 118	112 / 112			
KITE, N'/N	179 / 179	181 / 181			
Non-exposed, N'/N	85 / 85	90 / 90			
Exposed, N'/N	94 / 94	91 / 91			
Pooled Analysis, N'/N	368 / 368	368 / 368			
Non-exposed, N'/N	156 / 156	165 / 165			
Exposed, N'/N	212 / 212	203 / 203			
Any ocular adverse events of special interest, week 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.209**					
KESTREL					
Interaction Test:	N.E.				
Non-exposed, n (%)	0 (0.0)	1 (1.3)	N.E.	0.35 [0.01; 8.50] 0.520	-0.01 [-0.04; 0.01] 0.314
Exposed, n (%)	7 (5.9)	0 (0.0)	N.E.	14.24 [0.82; 246.52] 0.068	0.06 [0.02; 0.10] 0.006 *
KITE					
Interaction Test:	p = 0.258				
Non-exposed, n (%)	3 (3.5)	1 (1.1)	3.26 [0.33; 31.93] 0.311	3.18 [0.34; 29.95] 0.313	0.02 [-0.02; 0.07] 0.290
Exposed, 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 = 0.536				
Non-exposed, n (%)	3 (1.9)	2 (1.2)	1.96 [0.29; 13.48] 0.492	1.48 [0.30; 7.41] 0.631	0.01 [-0.02; 0.03] 0.609

	Treatment Groups		Comparison		
Any ocular adverse events of special interest by exposure (SAF)	**Brolucizumab**	**Aflibercept**	**OR [95% CI] p-value**	**RR [95% CI] p-value**	**RD [95% CI] p-value**
Exposed, n (%)	8 (3.8)	2 (1.0)	4.19 [0.80; 21.89] 0.090	3.26 [0.80; 13.31] 0.079	0.03 [-0.00; 0.06] 0.061

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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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 20-3.1 Any ocular adverse events of special interest at the study eye by severity (SAF), binary analysis, week 52

	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 52					
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 (%)	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)	2 (0.5)	N.E.	0.60 [0.08; 4.51] 0.617	-0.00 [-0.01; 0.01] 0.565
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 (%)	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.	1 (0.3)	1 (0.3)	N.E.	1.00 [0.14; 7.04] 1.000	0.00 [-0.01; 0.01] 1.000
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 (%)	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)	2 (0.5)	N.E.	0.60 [0.08; 4.51] 0.617	-0.00 [-0.01; 0.01] 0.565
Intraocular inflammation					
KESTREL, n (%)	7 (3.7)	1 (0.5)	7.15 [0.87; 58.72] 0.067	6.93 [0.86; 55.74] 0.069	0.03 [0.00; 0.06] 0.032 *

	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**
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=0.148	10 (2.7)	4 (1.1)	2.74 [0.72; 10.41] 0.138	2.50 [0.79; 7.94] 0.106	0.02 [-0.00; 0.04] 0.105
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 (%)	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)	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.	2 (0.5)	1 (0.3)	N.E.	1.67 [0.22; 12.61] 0.616	0.00 [-0.01; 0.01] 0.560
Retinal vascular occlusion severe					
KESTREL, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
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.	1 (0.3)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.474	0.00 [-0.00; 0.01] 0.315
Retinal vascular occlusion serious					
KESTREL, 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 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.	1 (0.3)	0 (0.0)	N.E.	3.03 [0.12; 73.97] 0.474	0.00 [-0.00; 0.01] 0.315

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 20-3.2 Any ocular adverse events of special interest at the study eye by age (SAF), binary analysis, week 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.148**					
KESTREL					
Interaction Test:	N.E.				
< 65 years, n (%)	3 (2.9)	0 (0.0)	N.E.	6.27 [0.33; 119.74] 0.223	0.03 [-0.00; 0.06] 0.079
≥ 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:	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 (%)	2 (2.5)	3 (3.8)	0.66 [0.11; 4.05] 0.652	0.67 [0.11; 3.88] 0.652	-0.01 [-0.07; 0.04] 0.649
Pooled Analysis					
Interaction Test:	N.E.				
< 65 years, n (%)	4 (2.0)	0 (0.0)	N.E.	4.71 [0.55; 40.50] 0.118	0.02 [0.00; 0.04] 0.045 *

	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 (%)	6 (3.7)	4 (2.3)	1.77 [0.42; 7.46] 0.435	1.57 [0.46; 5.41] 0.471	0.01 [-0.02; 0.05] 0.475

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):
Intraocular inflammation / KESTREL, Intraocular inflammation / KITE: logit(proportion) = treatment [by age].
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 52

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

Table 20-3.4 Any ocular adverse events of special interest at the study eye by BCVA (SAF), binary analysis, week 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.148**					
KESTREL					
Interaction Test:	N.E.				
≤ 65 letters, n (%)	1 (1.4)	0 (0.0)	N.E.	2.60 [0.11; 62.73] 0.556	0.01 [-0.01; 0.04] 0.314
> 65 letters, n (%)	6 (5.2)	1 (0.8)	6.72 [0.80; 56.66] 0.080	6.42 [0.78; 52.49] 0.083	0.04 [0.00; 0.09] 0.048 *
KITE					
Interaction Test:	p = 0.636				
≤ 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 (%)	2 (1.8)	1 (1.1)	1.59 [0.14; 17.81] 0.707	1.58 [0.15; 17.14] 0.707	0.01 [-0.03; 0.04] 0.697
Pooled Analysis					
Interaction Test:	p = 0.399				
≤ 65 letters, n (%)	2 (1.4)	2 (1.3)	1.29 [0.15; 10.79] 0.817	1.16 [0.19; 7.14] 0.871	0.00 [-0.02; 0.03] 0.825

	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 (%)	8 (3.5)	2 (0.9)	3.83 [0.74; 19.83] 0.110	3.82 [0.85; 17.25] 0.060	0.03 [-0.00; 0.05] 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 + 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):
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 52

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 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.148**					
KESTREL					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2, n (%)	7 (4.0)	1 (0.6)	7.41 [0.90; 60.86] 0.062	7.16 [0.89; 57.59] 0.064	0.03 [0.00; 0.06] 0.030 *
KITE					
Interaction Test:	N.E.				
Type 1, n (%)	0 (0.0)	0 (0.0)	N.E.	N.E.	N.E.
Type 2, n (%)	3 (1.9)	3 (1.7)	1.09 [0.22; 5.48] 0.917	1.09 [0.22; 5.31] 0.917	0.00 [-0.03; 0.03] 0.918
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 (%)	10 (3.0)	4 (1.1)	2.90 [0.76; 10.99] 0.118	2.64 [0.83; 8.42] 0.087	0.02 [-0.00; 0.04] 0.089

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):
Intraocular inflammation / KESTREL, Intraocular inflammation / KITE: logit(proportion) = treatment [by diabetes type].
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 52

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

Table 20-3.8 Any ocular adverse events of special interest at the study eye by duration of DME (SAF), binary analysis, week 52

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

Table 20-3.9 Any ocular adverse events of special interest at the study eye by DME type (SAF), binary analysis, week 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.148**					
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 (%)	6 (4.7)	1 (0.7)	6.59 [0.78; 55.56] 0.083	6.33 [0.77; 51.86] 0.085	0.04 [0.00; 0.08] 0.049 *
KITE					
Interaction Test:	N.E.				
focal, n (%)	0 (0.0)	1 (1.5)	N.E.	0.35 [0.01; 8.41] 0.517	-0.02 [-0.04; 0.01] 0.314
diffuse, n (%)	3 (2.6)	2 (1.8)	1.43 [0.23; 8.74] 0.697	1.42 [0.24; 8.35] 0.697	0.01 [-0.03; 0.05] 0.694
Pooled Analysis					
Interaction Test:	p = 0.514				
focal, n (%)	1 (0.8)	1 (0.9)	1.15 [0.06; 20.73] 0.925	0.92 [0.12; 6.86] 0.937	-0.00 [-0.02; 0.02] 0.954

	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 (%)	9 (3.7)	3 (1.2)	3.22 [0.76; 13.69] 0.114	3.00 [0.83; 10.83] 0.077	0.02 [-0.00; 0.05] 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
*: $p < 0.05$
.....

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):
Intraocular inflammation / KESTREL, Intraocular inflammation / KITE: 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 52

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 52

	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 52					
Intraocular inflammation					
Test of heterogeneity in main analysis: **p_H=0.148**					
KESTREL					
Interaction Test:	N.E.				
presence, 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 (%)	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 (%)	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 = 0.540				
presence, n (%)	1 (0.8)	1 (0.8)	1.20 [0.07; 21.24] 0.901	1.09 [0.15; 7.97] 0.936	0.00 [-0.02; 0.02] 0.953

	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 (%)	9 (3.6)	3 (1.3)	3.15 [0.73; 13.54] 0.123	2.88 [0.79; 10.44] 0.092	0.02 [-0.00; 0.05] 0.088

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):
Intraocular inflammation / KESTREL, Intraocular inflammation / KITE: logit(proportion) = treatment [by status of SRF].

Table 20-3.12 Any ocular adverse events of special interest at the study eye by exposure (SAF), binary analysis, week 52

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

Table 20-4.1 Any ocular adverse events of special interest at the fellow eye by severity (SAF), binary analysis, week 52

	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 52					
Intraocular inflammation					
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
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)	2 (1.1)	N.E.	0.20 [0.01; 4.18] 0.301	-0.01 [-0.03; 0.00] 0.155
Pooled Analysis, n (%) p_H=N.E.	0 (0.0)	2 (0.5)	N.E.	0.20 [0.01; 4.18] 0.251	-0.01 [-0.01; 0.00] 0.157
Retinal vascular occlusion severe					
KESTREL, 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**
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.					
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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 20-4.12 Any ocular adverse events of special interest at the fellow eye by exposure (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 20-5.12 Any non-ocular adverse events of special interest by exposure (SAF), binary analysis, week 52

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 52

	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					

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 52

	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

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 21-1.3 Any adverse event of potential relevance to intravitreal anti-VEGF injection by gender (SAF), binary analysis, week 52

	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

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 52

	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

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 21-1.5 Any adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF), binary analysis, week 52

	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

	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	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
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

	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 (%)	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

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 21-1.6 Any adverse event of potential relevance to intravitreal anti-VEGF injection by diabetes type (SAF), binary analysis, week 52

	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

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):
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 52

	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

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 21-1.8 Any adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF), binary analysis, week 52

	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

	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	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
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

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 52

	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

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 21-1.10 Any adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF), binary analysis, week 52

	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

	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	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
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

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 21-1.11 Any adverse event of potential relevance to intravitreal anti-VEGF injection by status of SRF (SAF), binary analysis, week 52

	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

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 21-1.12 Any adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (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 (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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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 52

	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					

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 21-2.2 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by age (SAF), binary analysis, week 52

	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

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 21-2.3 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by gender (SAF), binary analysis, week 52

	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

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 21-2.4 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by BCVA (SAF), binary analysis, week 52

	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

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 21-2.5 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by region (SAF), binary analysis, week 52

	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

	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	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
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

	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 (%)	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

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 52

	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

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):
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 52

	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

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 21-2.8 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by duration of DME (SAF), binary analysis, week 52

	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

	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	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
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

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 21-2.9 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by DME type (SAF), binary analysis, week 52

	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

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 21-2.10 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by CSFT (SAF), binary analysis, week 52

	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

	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	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
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

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 21-2.11 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by status of SRF (SAF), binary analysis, week 52

	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

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 21-2.12 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by exposure (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 (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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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 52

	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					

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 21-3.2 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by age (SAF), binary analysis, week 52

	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

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 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 52

	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

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 21-3.4 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by BCVA (SAF), binary analysis, week 52

	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

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 52

	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

	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**
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
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

	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	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

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 52

	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

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):
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 52

	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

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 21-3.8 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by duration of DME (SAF), binary analysis, week 52

	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

	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	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
≥ 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

	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	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

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 52

	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

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 52

	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

	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	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
≥ 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

	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	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

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 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 52

	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

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 21-3.12 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by exposure (SAF), binary analysis, week 52

	Treatment Groups		Comparison		
Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by exposure (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 (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 + treatment * exposure.
RR and RD calculated directly (with Wald CI and p-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 + treatment * exposure.
RR (with CI) calculated via Mantel-Haenszel Estimator (stratified by study), p-value for 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 52

	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.					

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 (SAF), binary analysis, week 52

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 52

	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.					

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 (SAF), binary analysis, week 52

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 52

	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.					

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 (SAF), binary analysis, week 52

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 52

	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.					

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 (SAF), binary analysis, week 52

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 52

	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.					

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 (SAF), binary analysis, week 52

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 52

	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.					

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 (SAF), binary analysis, week 52

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 52

	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.					

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 (SAF), binary analysis, week 52

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 52

	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.					

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 (SAF), binary analysis, week 52

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 52

	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.					

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 (SAF), binary analysis, week 52

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 52

	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.					

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 (SAF), binary analysis, week 52

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 52

	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.					

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 (SAF), binary analysis, week 52

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 52

	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.					

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 (SAF), binary analysis, week 52

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 52

	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 52					
Eye disorders					
KESTREL, n (%)	20 (10.6)	29 (15.5)	0.64 [0.35; 1.19] 0.158	0.68 [0.40; 1.16] 0.160	-0.05 [-0.12; 0.02] 0.155
KITE, n (%)	19 (10.6)	13 (7.2)	1.53 [0.73; 3.21] 0.255	1.48 [0.75; 2.90] 0.256	0.03 [-0.02; 0.09] 0.252
Pooled Analysis, n (%) p_H=0.076	39 (10.6)	42 (11.4)	0.99 [0.61; 1.59] 0.954	0.93 [0.61; 1.40] 0.716	-0.01 [-0.05; 0.04] 0.717
Conjunctival haemorrhage					
KESTREL, n (%)	10 (5.3)	16 (8.6)	0.60 [0.26; 1.35] 0.216	0.62 [0.29; 1.33] 0.217	-0.03 [-0.08; 0.02] 0.212
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

	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**
Pooled Analysis, n (%) p_H=0.147	17 (4.6)	20 (5.4)	1.03 [0.49; 2.15] 0.947	0.85 [0.45; 1.59] 0.603	-0.01 [-0.04; 0.02] 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
.....

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 24-1.12 Any adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

	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 52					
Eye disorders					
KESTREL, n (%)	20 (10.6)	29 (15.5)	0.64 [0.35; 1.19] 0.158	0.68 [0.40; 1.16] 0.160	-0.05 [-0.12; 0.02] 0.155
KITE, n (%)	19 (10.6)	13 (7.2)	1.53 [0.73; 3.21] 0.255	1.48 [0.75; 2.90] 0.256	0.03 [-0.02; 0.09] 0.252
Pooled Analysis, n (%) p_H=0.076	39 (10.6)	42 (11.4)	0.99 [0.61; 1.59] 0.954	0.93 [0.61; 1.40] 0.716	-0.01 [-0.05; 0.04] 0.717
Conjunctival haemorrhage					
KESTREL, n (%)	10 (5.3)	16 (8.6)	0.60 [0.26; 1.35] 0.216	0.62 [0.29; 1.33] 0.217	-0.03 [-0.08; 0.02] 0.212
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

	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**
Pooled Analysis, n (%) p_H=0.147	17 (4.6)	20 (5.4)	1.03 [0.49; 2.15] 0.947	0.85 [0.45; 1.59] 0.603	-0.01 [-0.04; 0.02] 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
.....

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 24-2.12 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

	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 52					
Eye disorders					
KESTREL, n (%)	20 (10.6)	29 (15.5)	0.64 [0.35; 1.19] 0.158	0.68 [0.40; 1.16] 0.160	-0.05 [-0.12; 0.02] 0.155
KITE, n (%)	19 (10.6)	13 (7.2)	1.53 [0.73; 3.21] 0.255	1.48 [0.75; 2.90] 0.256	0.03 [-0.02; 0.09] 0.252
Pooled Analysis, n (%) p_H=0.076	39 (10.6)	42 (11.4)	0.99 [0.61; 1.59] 0.954	0.93 [0.61; 1.40] 0.716	-0.01 [-0.05; 0.04] 0.717
Conjunctival haemorrhage					
KESTREL, n (%)	10 (5.3)	16 (8.6)	0.60 [0.26; 1.35] 0.216	0.62 [0.29; 1.33] 0.217	-0.03 [-0.08; 0.02] 0.212
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

	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**
Pooled Analysis, n (%) p_H=0.147	17 (4.6)	20 (5.4)	1.03 [0.49; 2.15] 0.947	0.85 [0.45; 1.59] 0.603	-0.01 [-0.04; 0.02] 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
.....

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 24-3.12 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 24-4.12 Any ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 24-5.12 Any non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 25-1.12 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 25-2.12 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 25-3.12 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 25-4.12 Any serious ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

Table 25-5.12 Any serious non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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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 52

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 52

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 52

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

Table 26-1.12 Any severe adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and exposure (SAF), binary analysis, week 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

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 52

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 52

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

Table 26-2.10 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and CSFT (SAF), binary analysis, week 52

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

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 52

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

Table 26-2.12 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and exposure (SAF), binary analysis, week 52

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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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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 52

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

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 52

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

Table 26-3.12 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the study eye by SOC, PT and exposure (SAF), binary analysis, week 52

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

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 52

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 52

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 52

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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 52

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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 52

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

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 52

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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 52

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Table 26-4.8 Any severe 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 52

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Table 26-4.9 Any severe 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 52

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

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 52

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

Table 26-4.11 Any severe 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 52

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Table 26-4.12 Any severe ocular adverse event of potential relevance to intravitreal anti-VEGF injection at the fellow eye by SOC, PT and exposure (SAF), binary analysis, week 52

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

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 52

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 52

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 52

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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 52

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

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 52

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

Table 26-5.6 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and diabetes type (SAF), binary analysis, week 52

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

Table 26-5.7 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and HbA1c (SAF), binary analysis, week 52

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

Table 26-5.8 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and duration of DME (SAF), binary analysis, week 52

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

Table 26-5.9 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and DME type (SAF), binary analysis, week 52

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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 52

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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 52

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Table 26-5.12 Any severe non-ocular adverse event of potential relevance to intravitreal anti-VEGF injection by SOC, PT and exposure (SAF), binary analysis, week 52

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

Brolucizumab/Beovu®

CRTH258B2301 (KESTREL) and CRTH258B2302 (KITE)

AMNOG Analysis

Figures

Date:	05th Jan 2022
Document status:	Draft
Author:	M. Schwager

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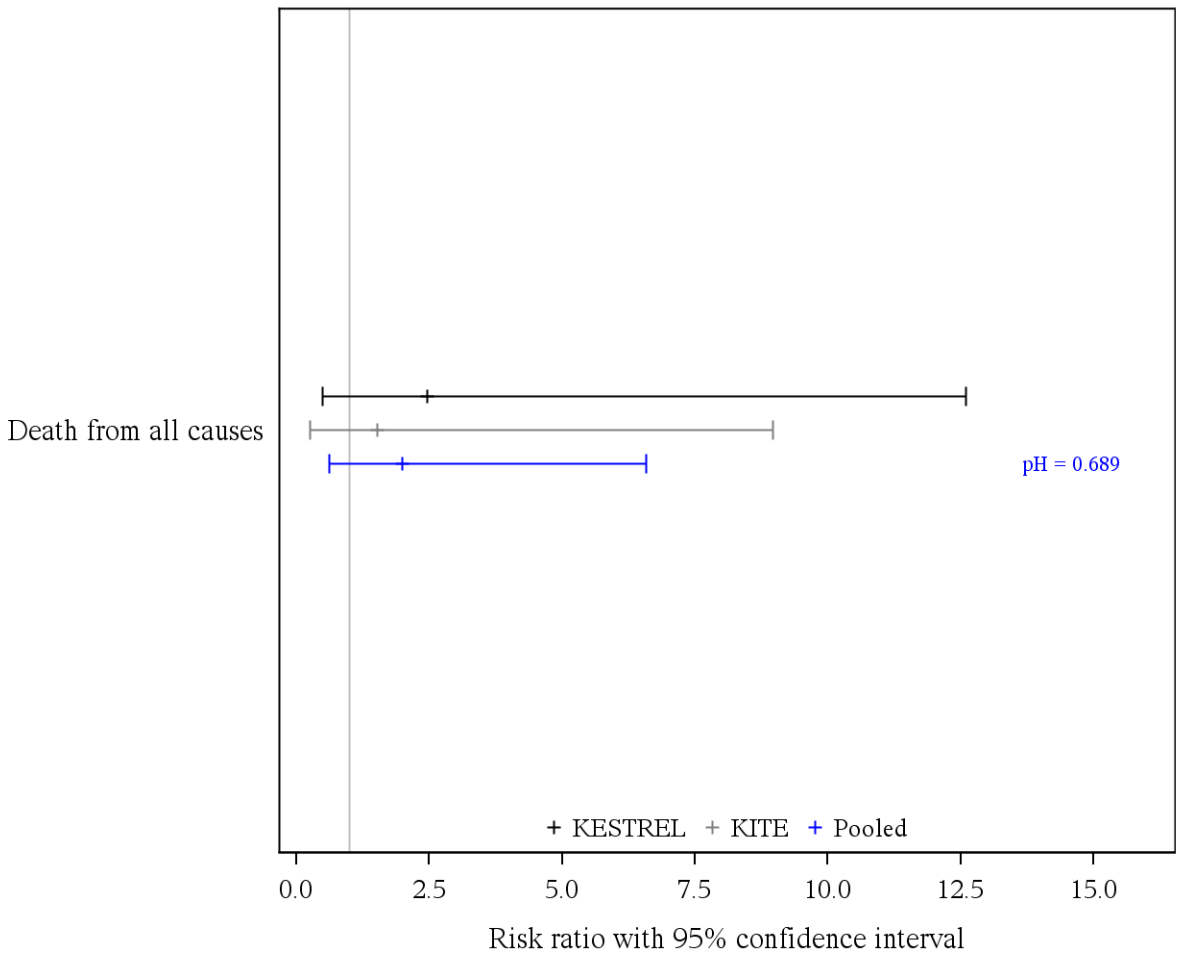
Figures

2 Mortality

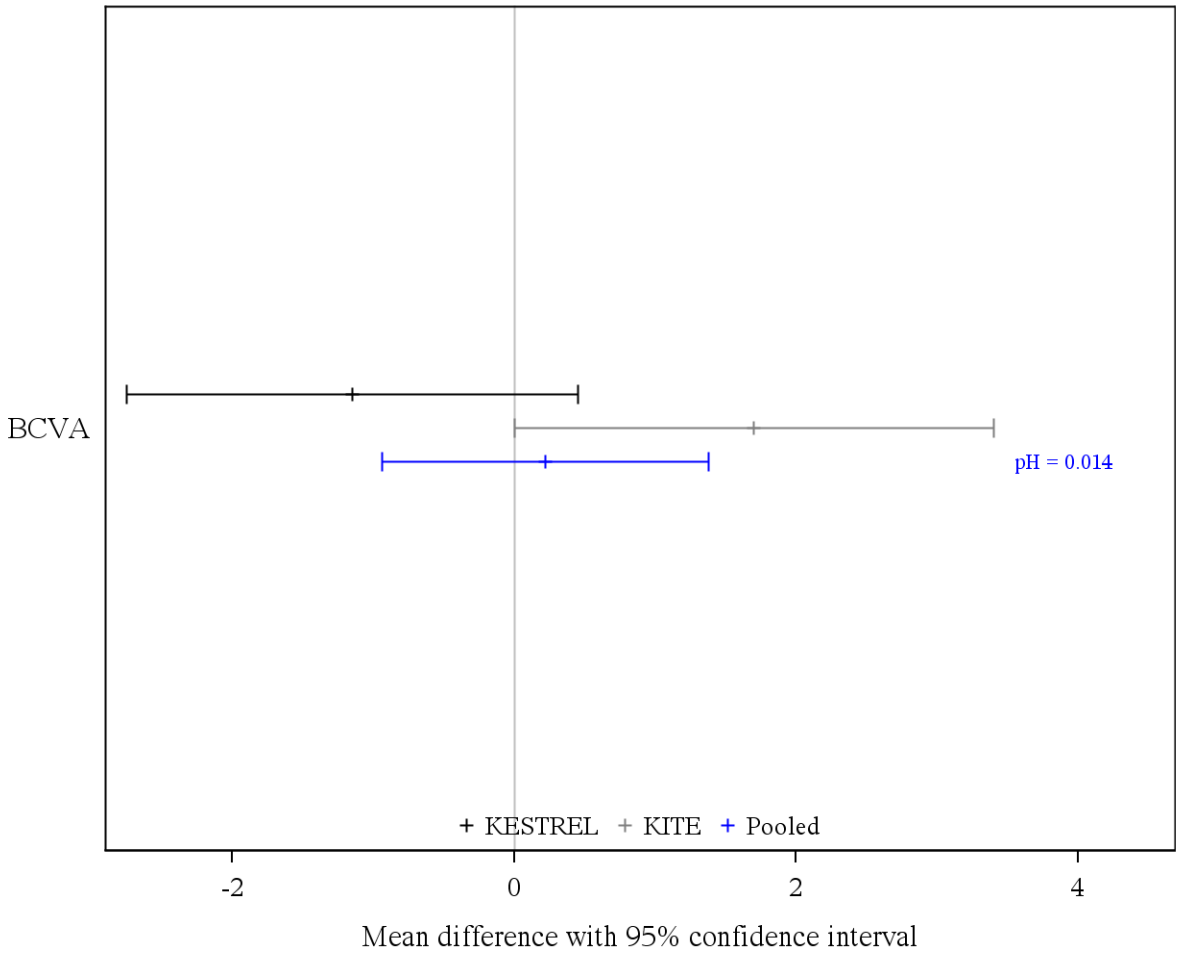
Figure 2.1 All-cause mortality (FAS), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

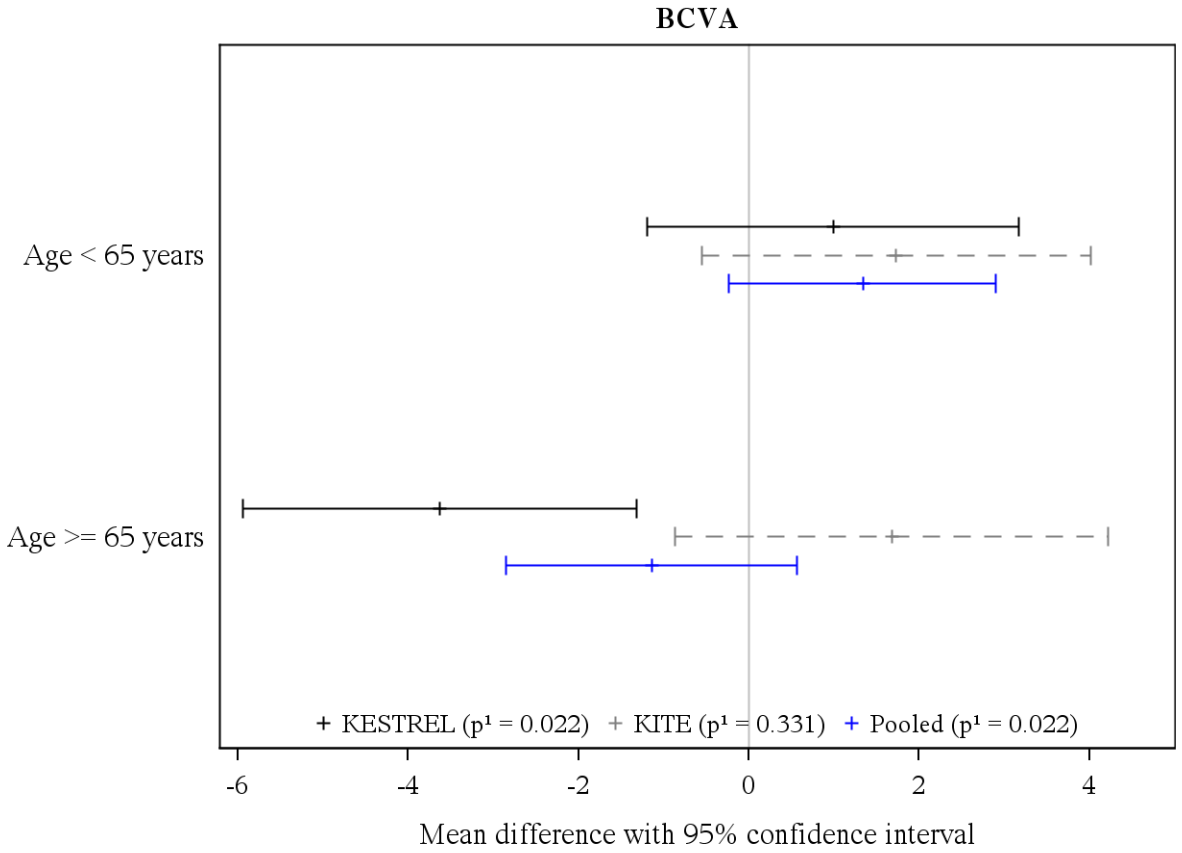
3 BCVA: Continuous analysis

Figure 3.1 BCVA (FAS), forest plot, week 52



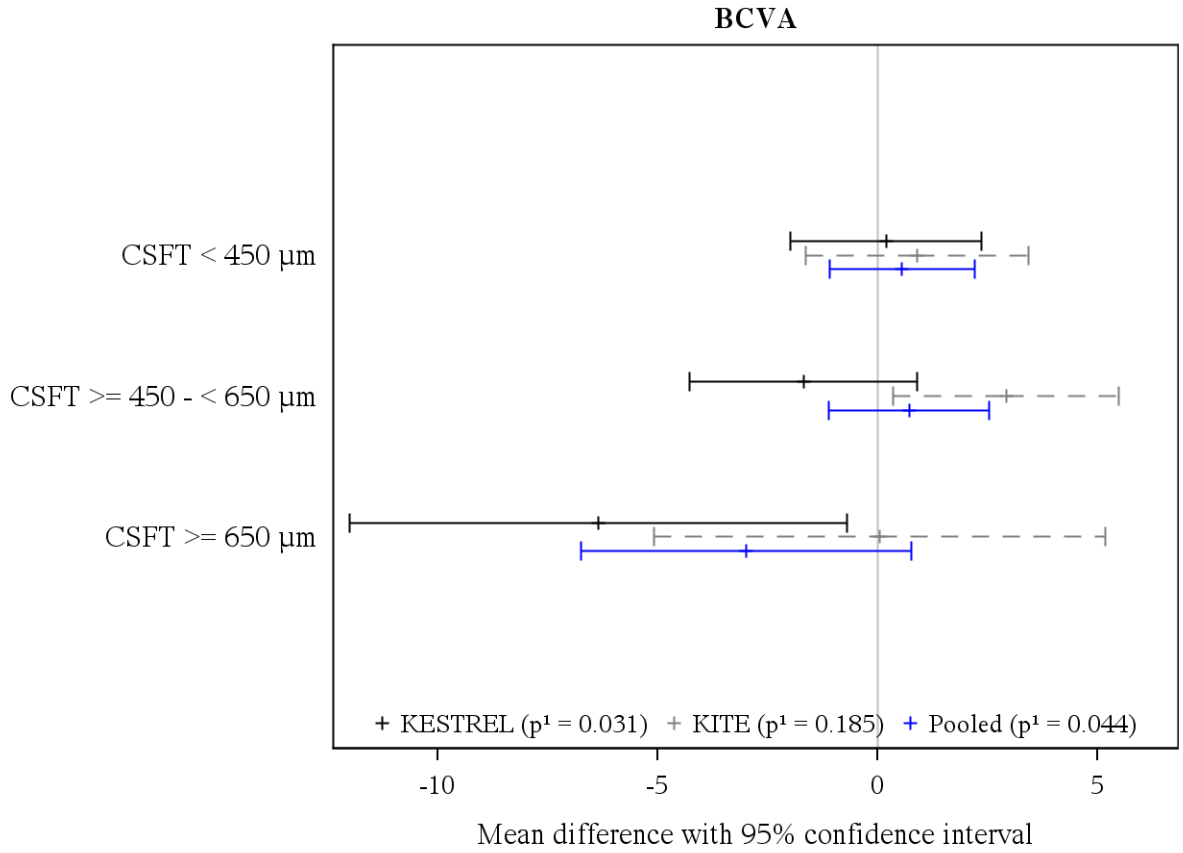
p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 3.2 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: $p_H = 0.014$

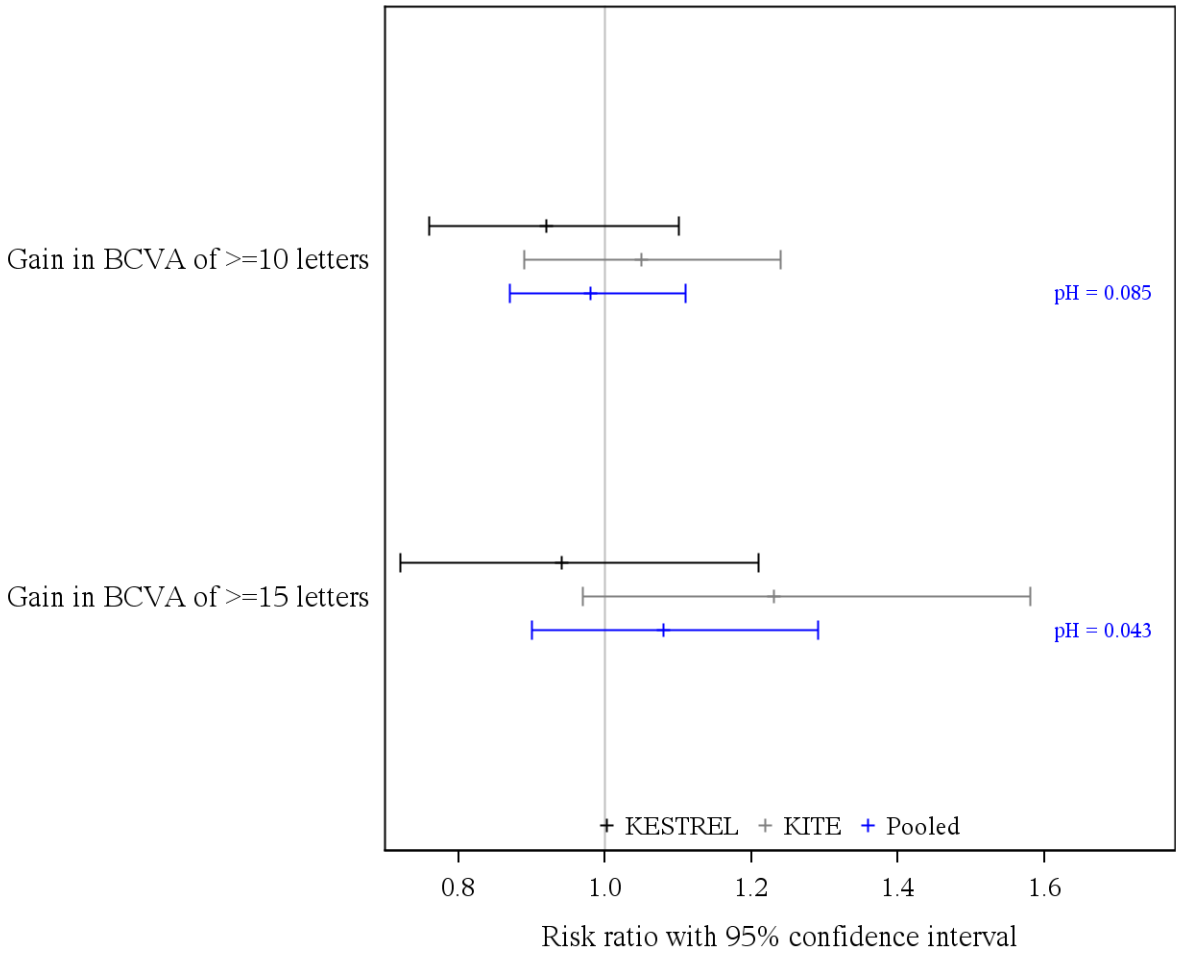
Figure 3.10 BCVA by CSFT (FAS), forest plot, week 52



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: $p_H = 0.014$

4 BCVA: Binary analysis (Gain)

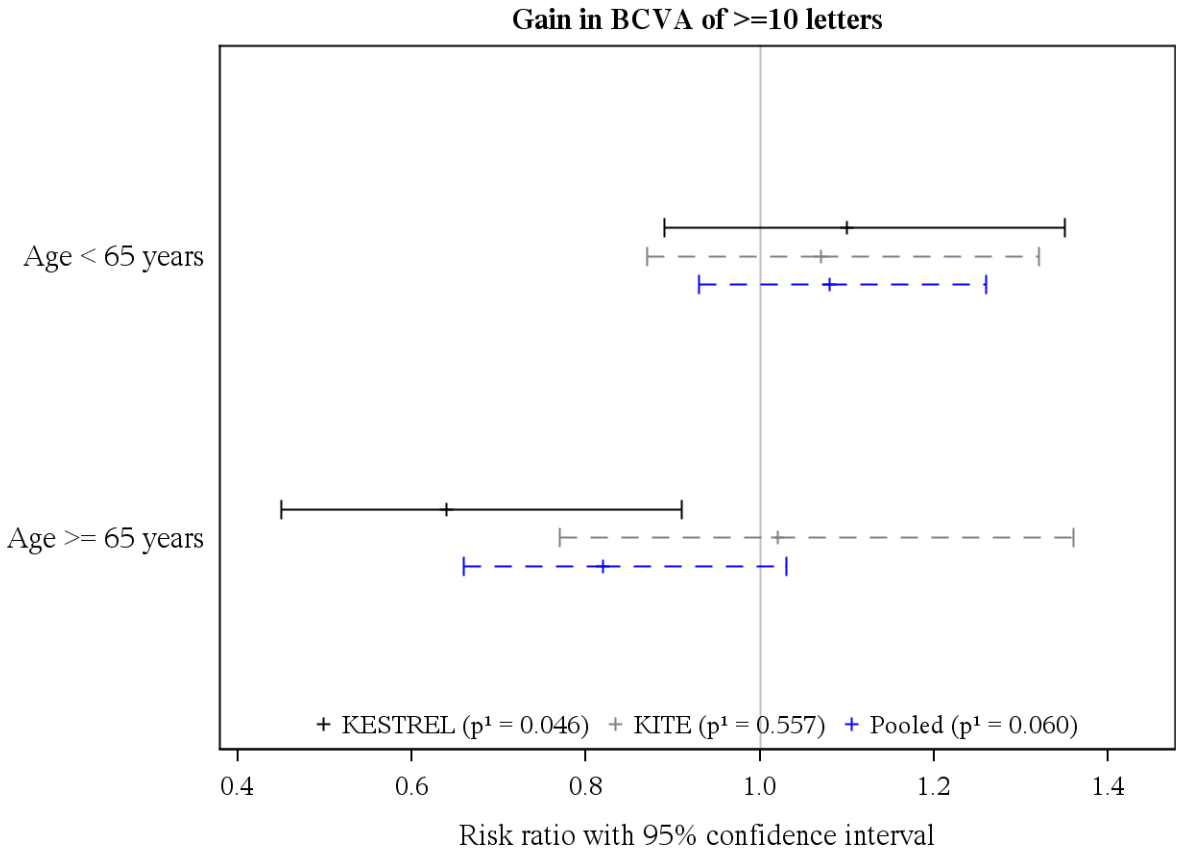
Figure 4.1 BCVA - Gain of 10 respectively 15 letters (FAS), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 4.2 BCVA - Gain of 10 respectively 15 letters by age (FAS), forest plot, week 52

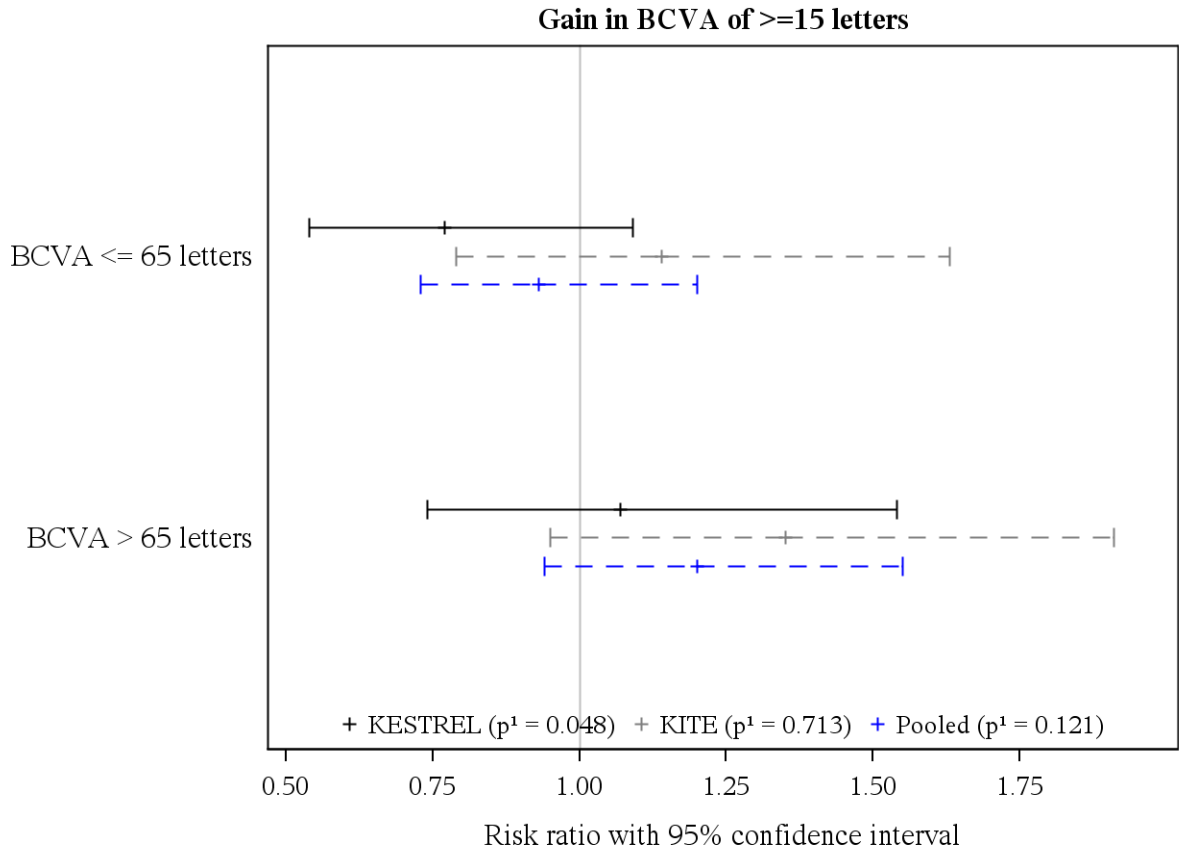
Figure 4.2.1 BCVA - Gain of 10 respectively 15 letters by age (FAS), forest plot, week 52, gain of >=10 letters



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 4.4 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), forest plot, week 52

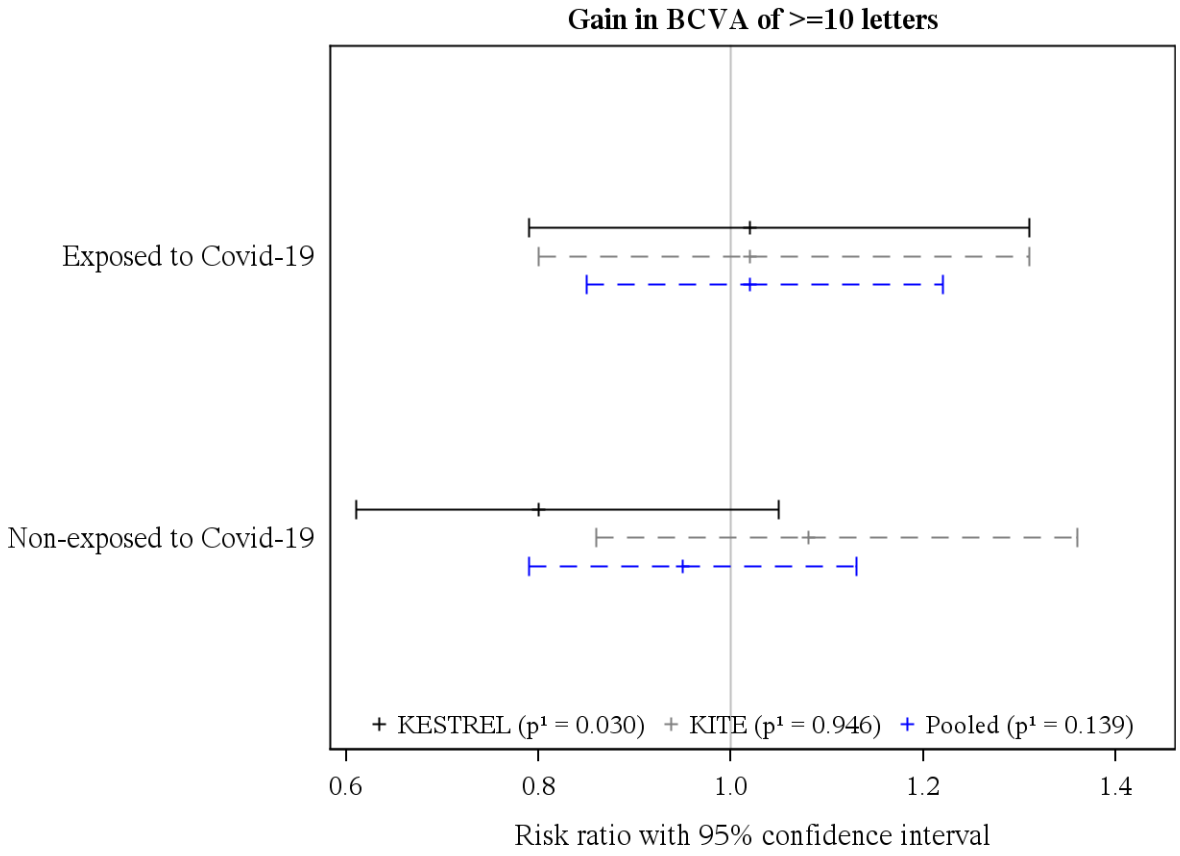
Figure 4.4.1 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), forest plot, week 52, gain of >=15 letters



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: $p_H = 0.043$

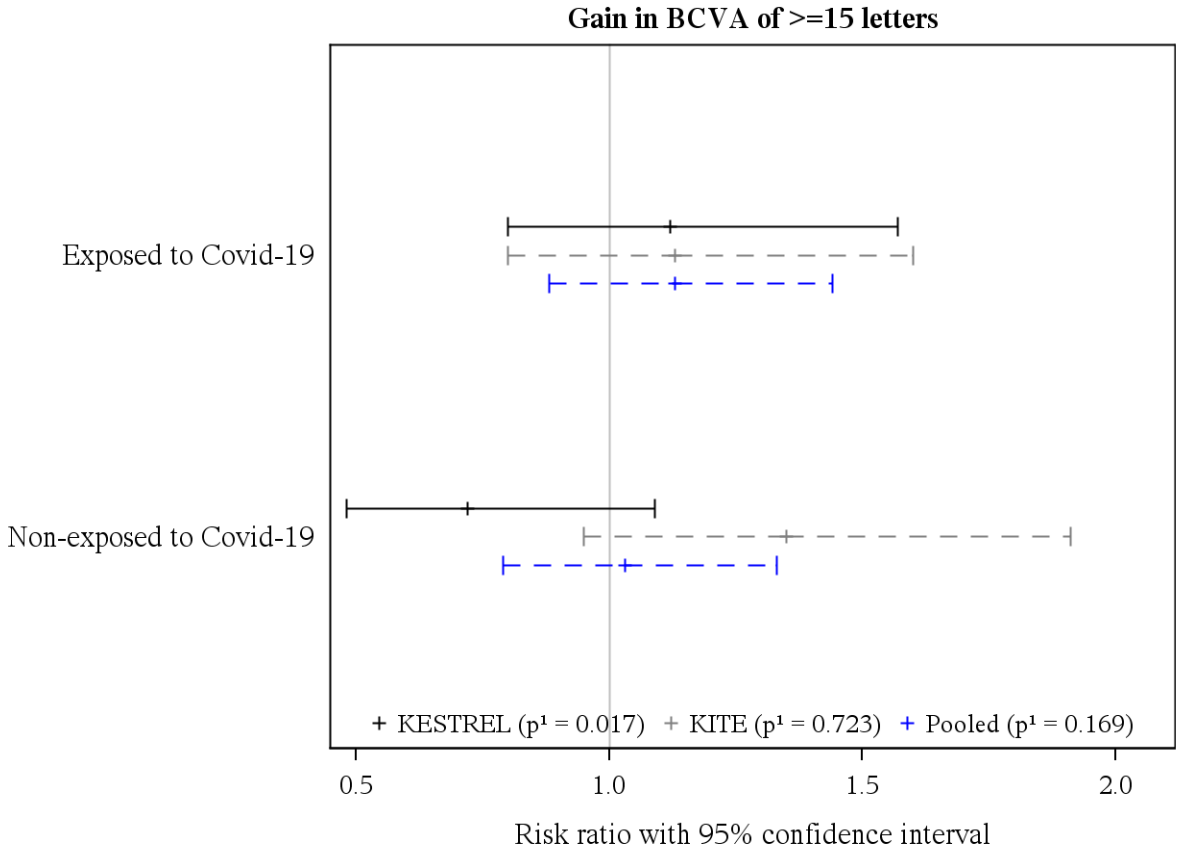
Figure 4.12 BCVA - Gain of 10 respectively 15 letters by exposure (FAS), forest plot, week 52

Figure 4.12.1 BCVA - Gain of 10 respectively 15 letters by exposure (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: $p_H = 0.085$

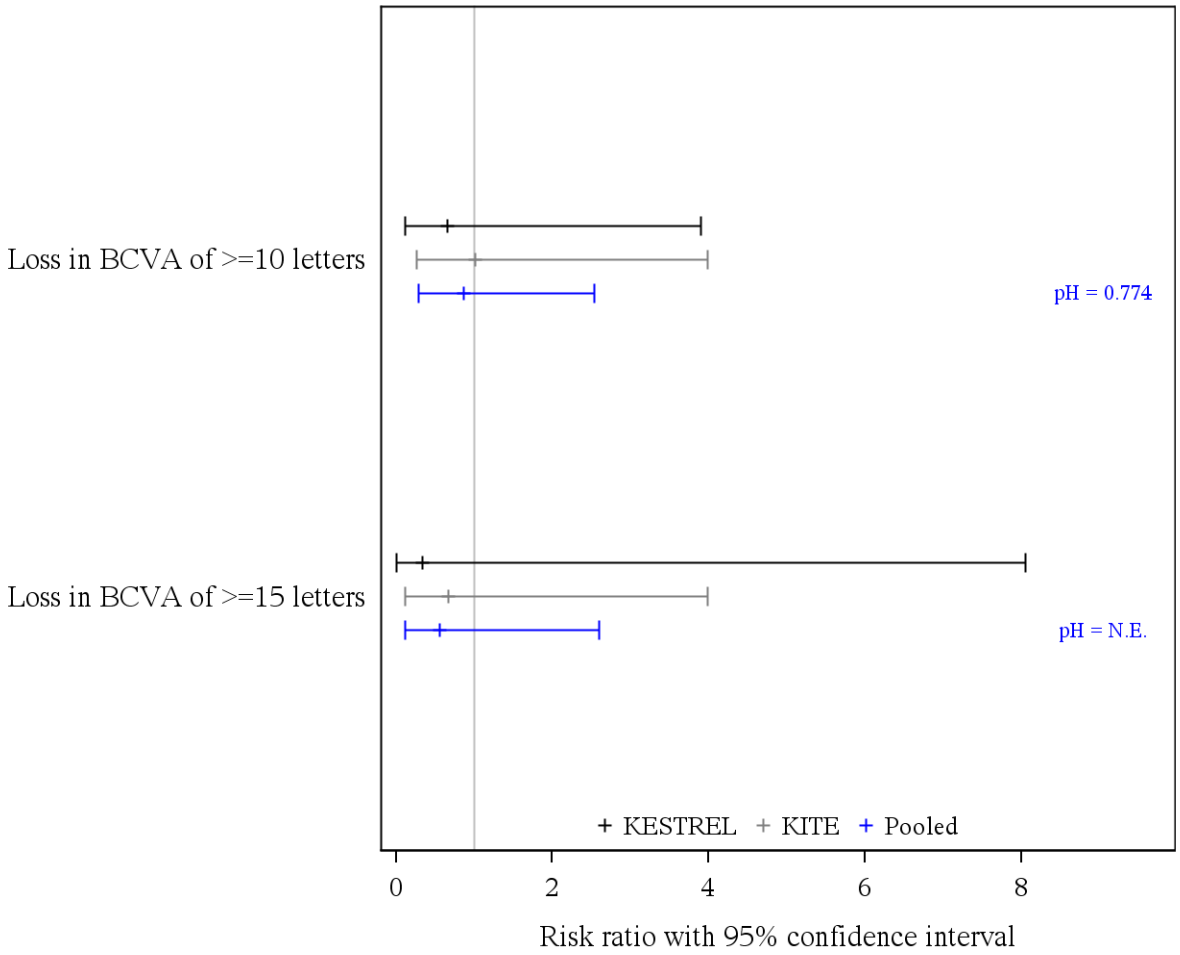
Figure 4.12.2 BCVA - Gain of 10 respectively 15 letters by exposure (FAS), forest plot, week 52, gain of >=15 letters



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: $p_H = 0.043$

5 BCVA: Binary analysis (Loss)

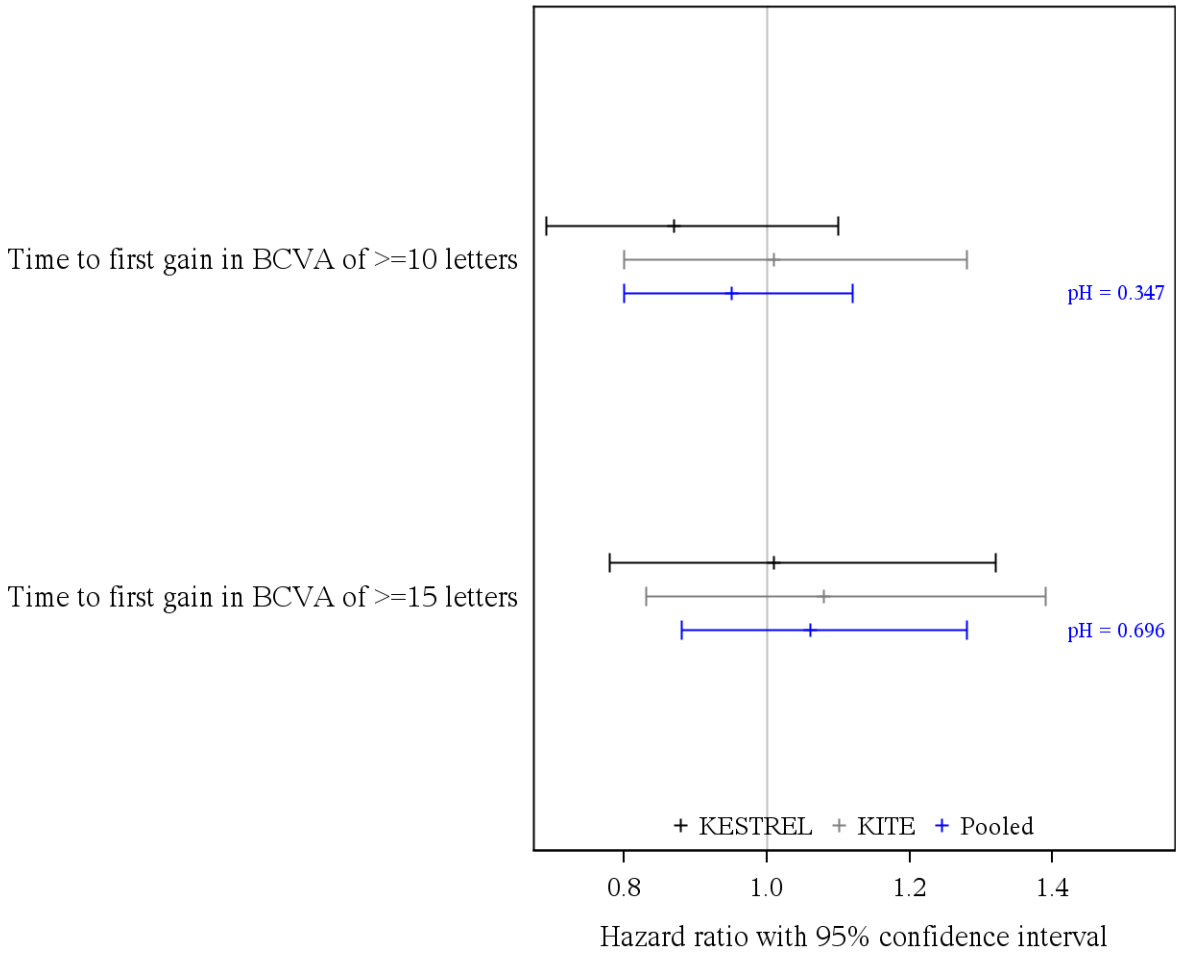
Figure 5.1 BCVA - Loss of 10 respectively 15 letters (FAS), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

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

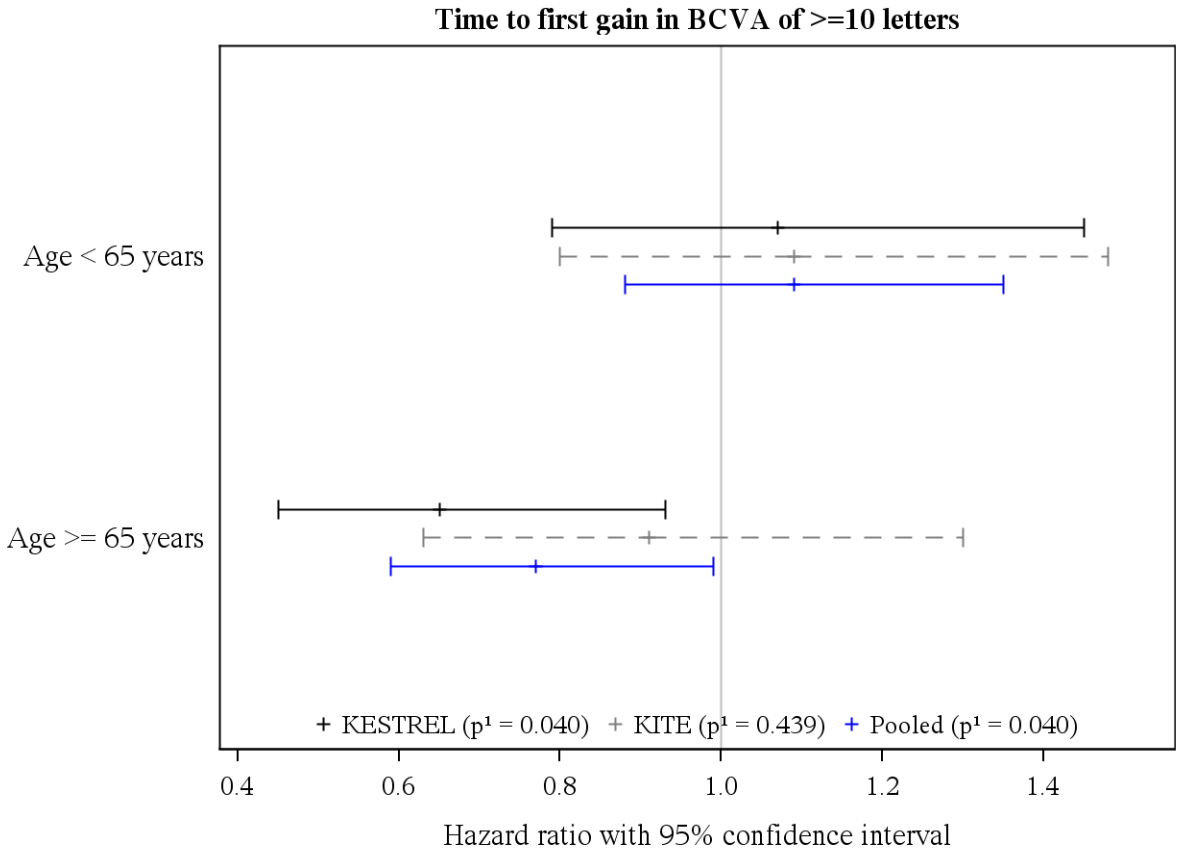
Figure 6.1.1 BCVA - Gain of 10 respectively 15 letters (FAS), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 6.2.1 BCVA - Gain of 10 respectively 15 letters by age (FAS), forest plot, week 52

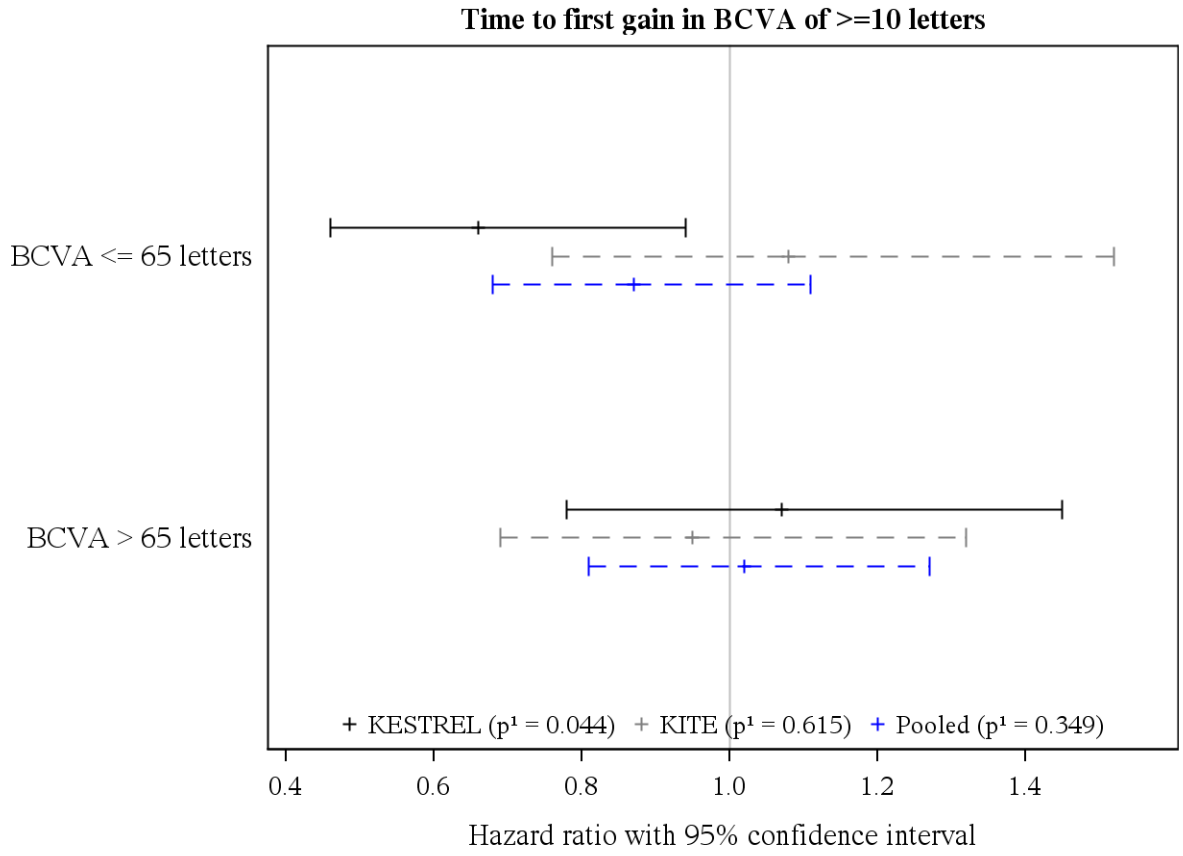
Figure 6.2.1.1 BCVA - Gain of 10 respectively 15 letters by age (FAS), forest plot, week 52, gain of >=10 letters



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 6.4.1 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), forest plot, week 52

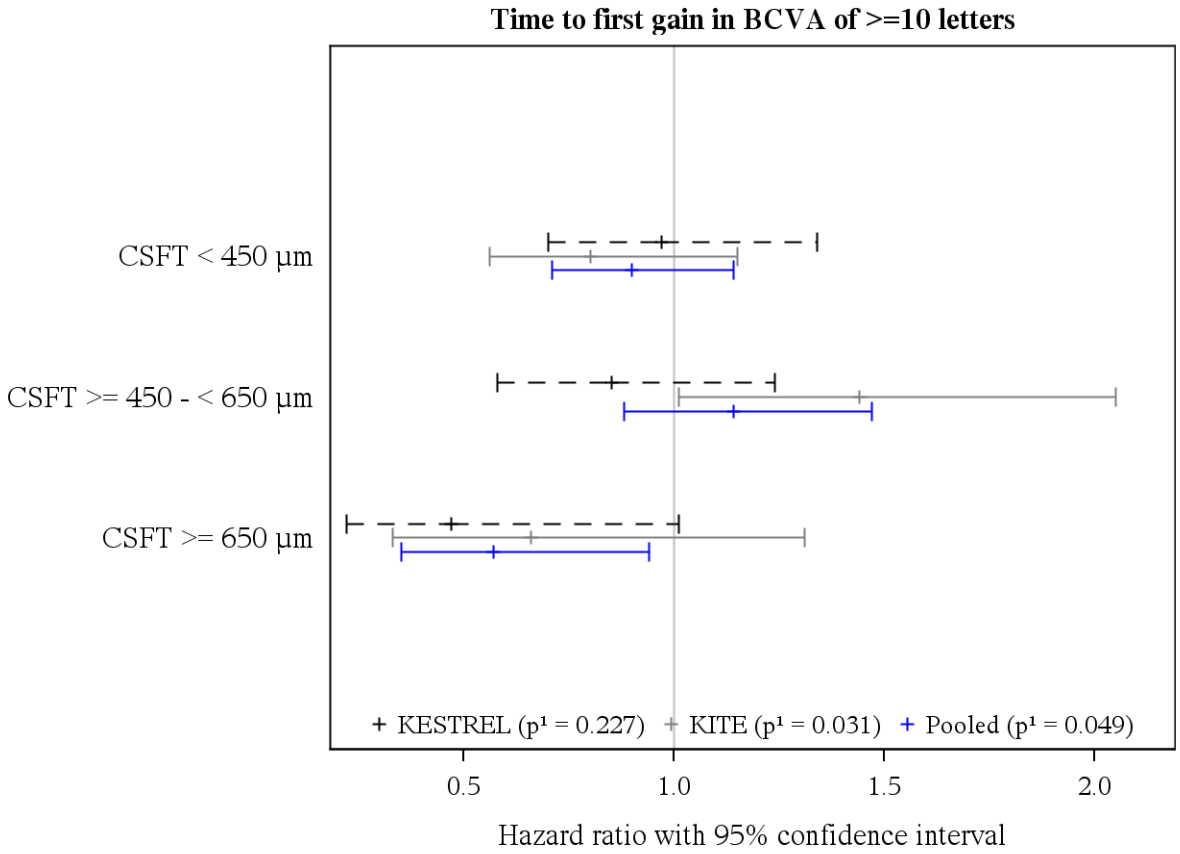
Figure 6.4.1.1 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), forest plot, week 52, gain of >=10 letters



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: $p_H = 0.347$

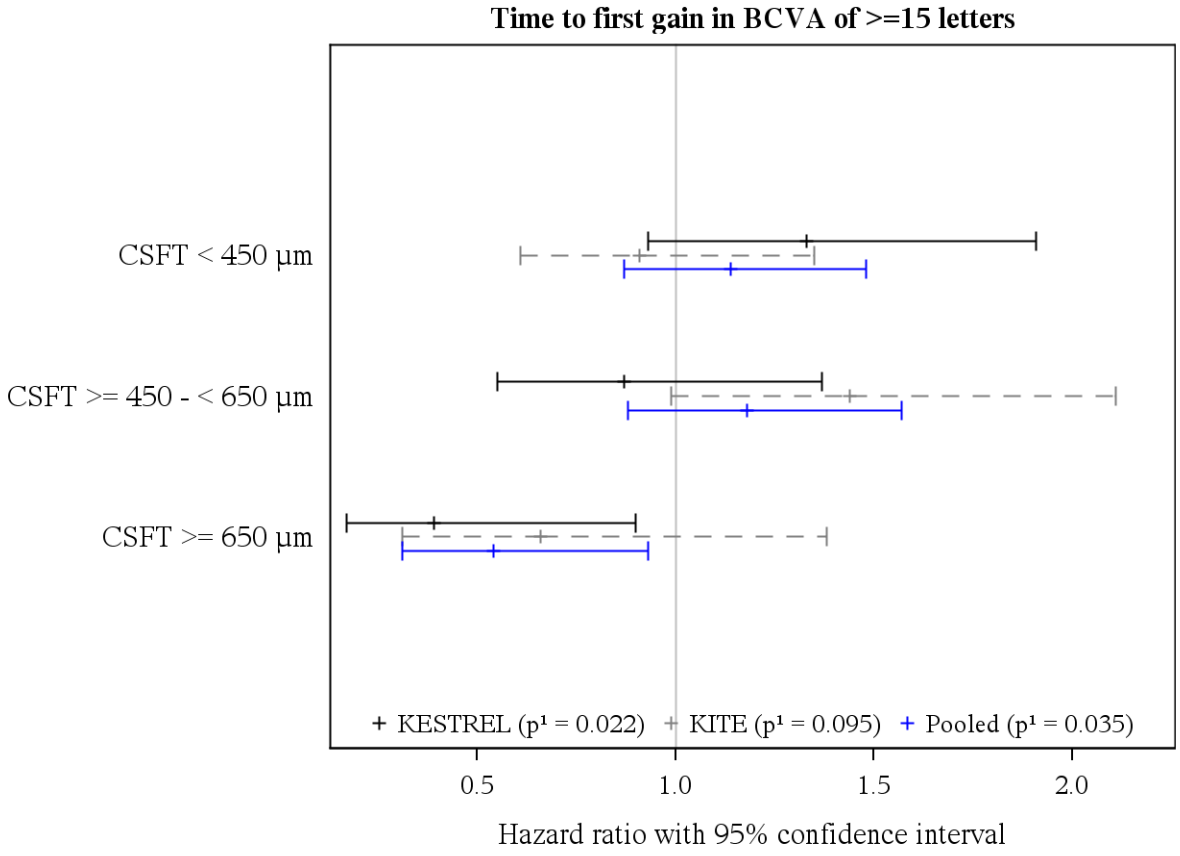
Figure 6.10.1 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), forest plot, week 52

Figure 6.10.1.1 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: $p_H = 0.347$

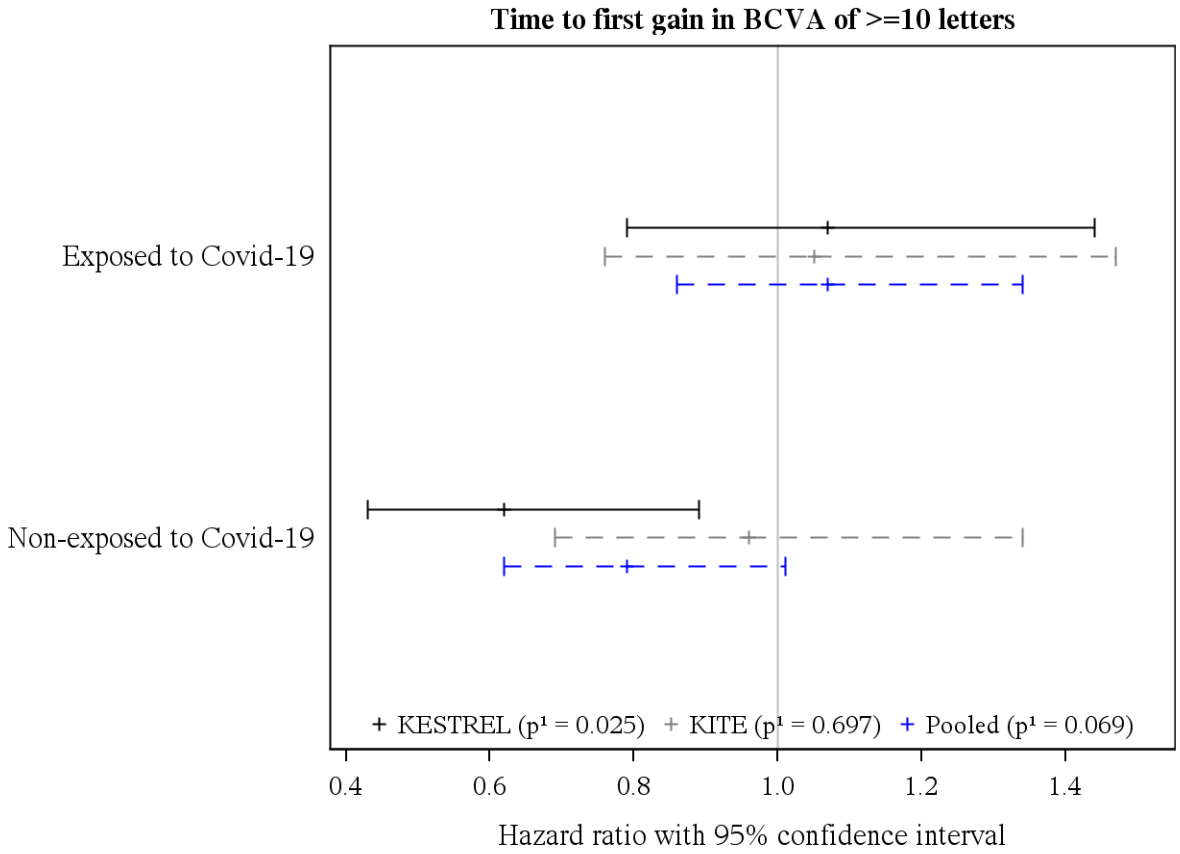
Figure 6.10.1.2 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), forest plot, week 52, gain of >=15 letters



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: $p_H = 0.696$

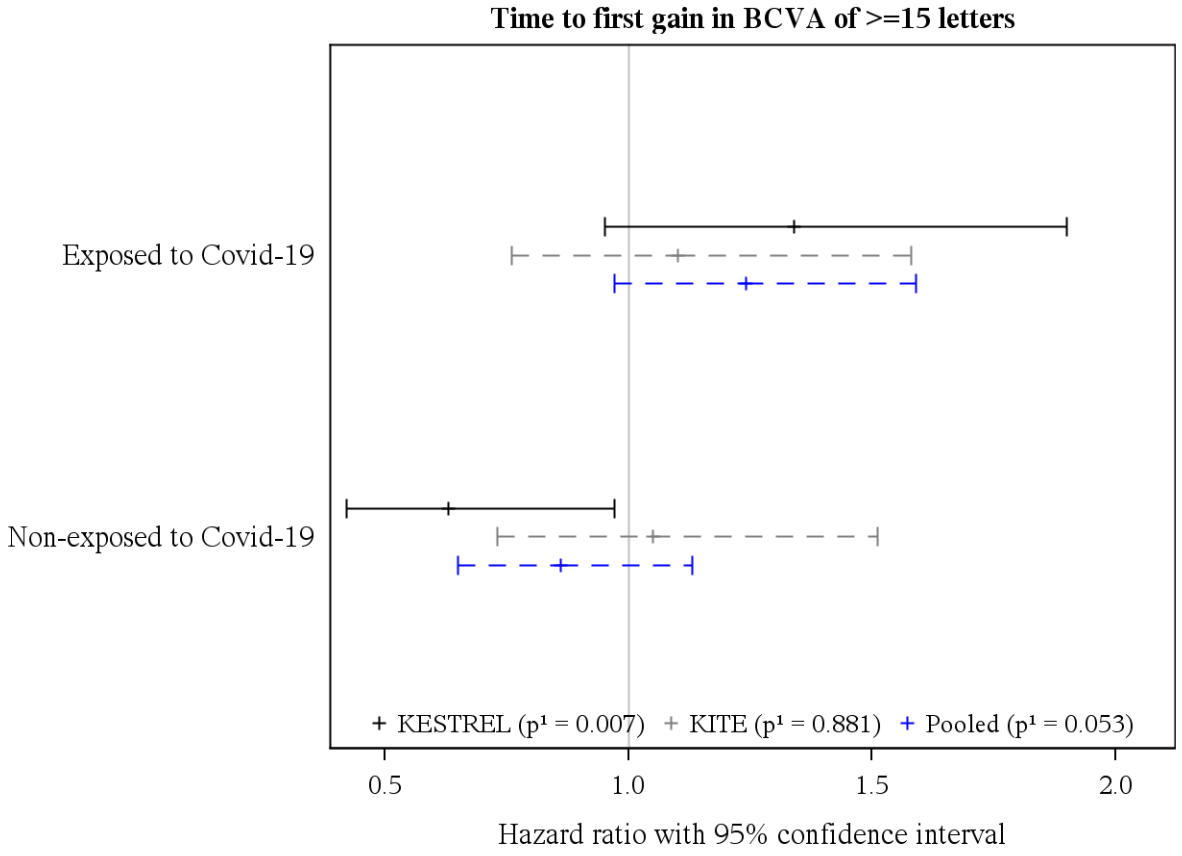
Figure 6.12.1 BCVA - Gain of 10 respectively 15 letters by exposure (FAS), forest plot, week 52

Figure 6.12.1.1 BCVA - Gain of 10 respectively 15 letters by exposure (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 6.12.1.2 BCVA - Gain of 10 respectively 15 letters by exposure (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 6.1.2 BCVA - Gain of 10 respectively 15 letters (FAS), Kaplan-Meier plot, week 52

Figure 6.1.2.1 BCVA - Gain of 10 respectively 15 letters (FAS), Kaplan-Meier plot, week 52, gain of >=10 letters

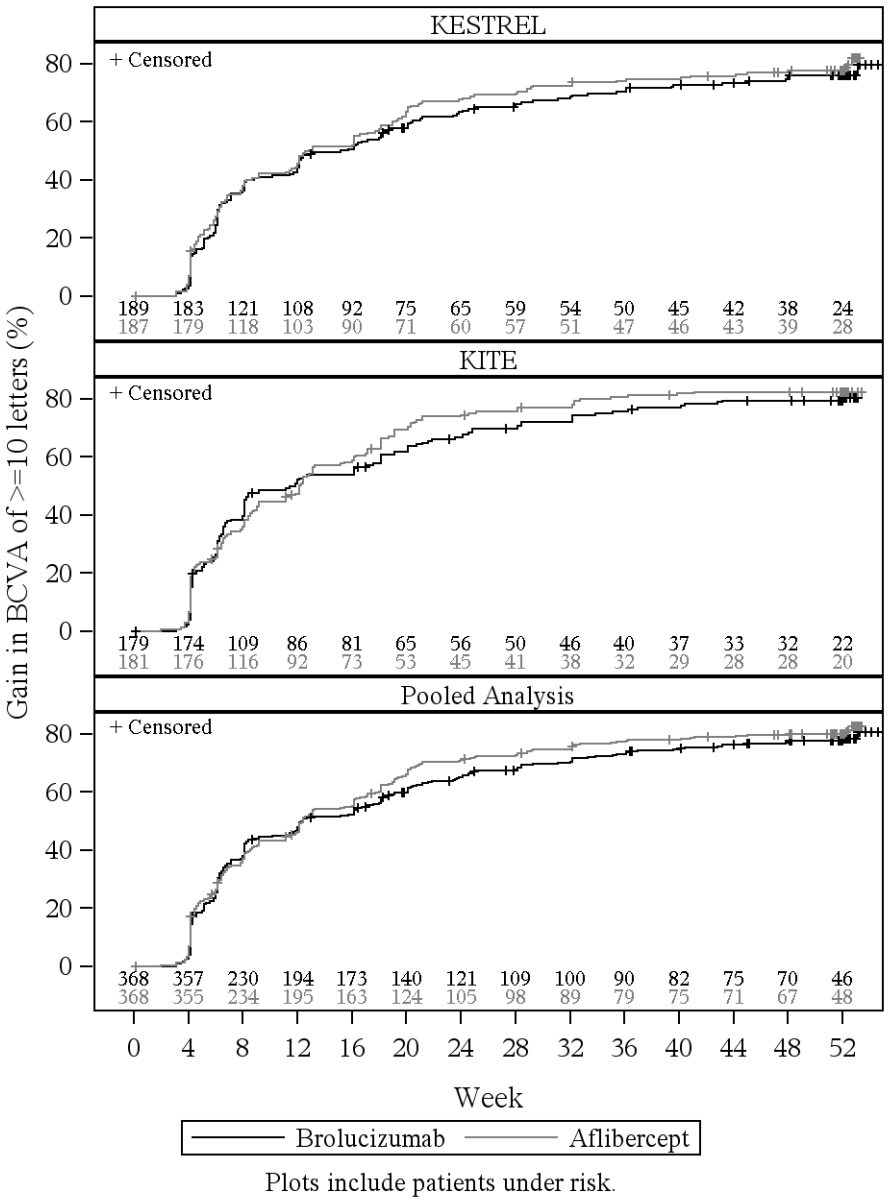
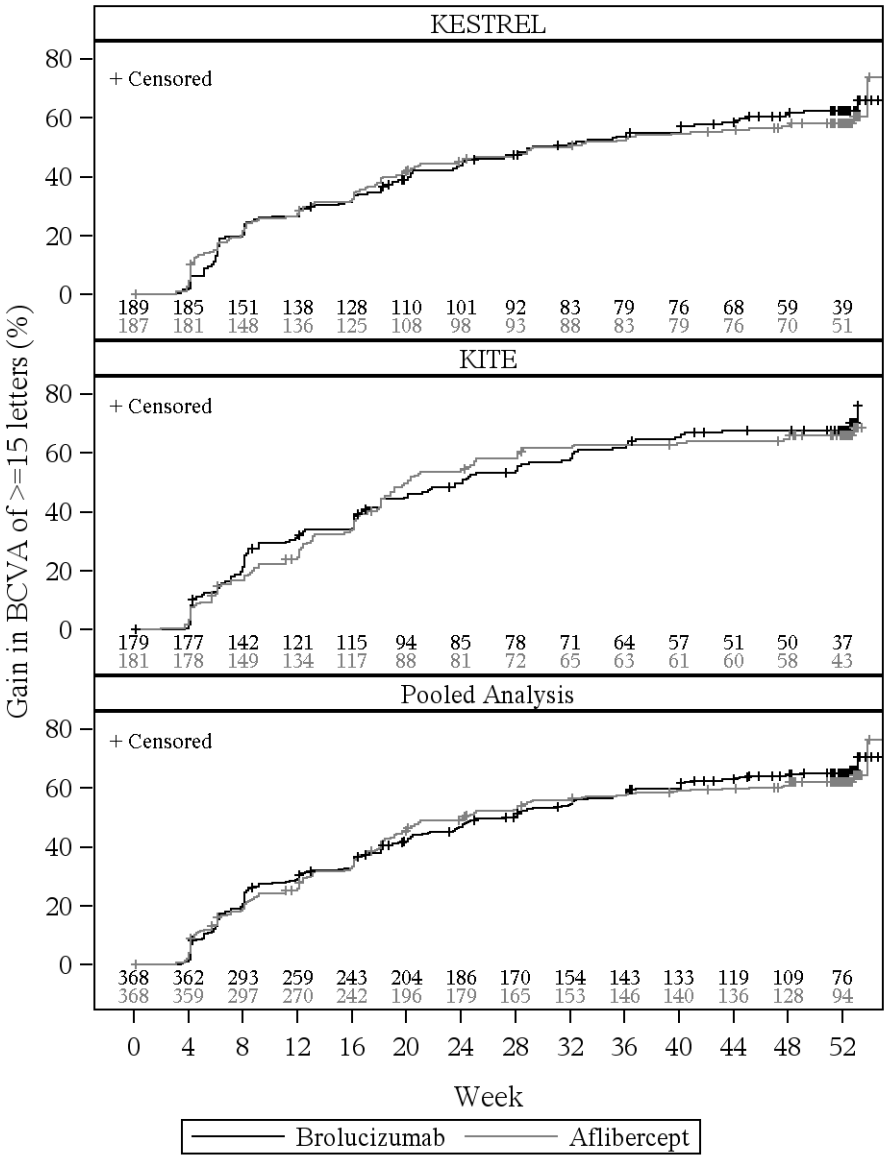


Figure 6.1.2.2 BCVA - Gain of 10 respectively 15 letters (FAS), Kaplan-Meier plot, week 52, gain of >=15 letters

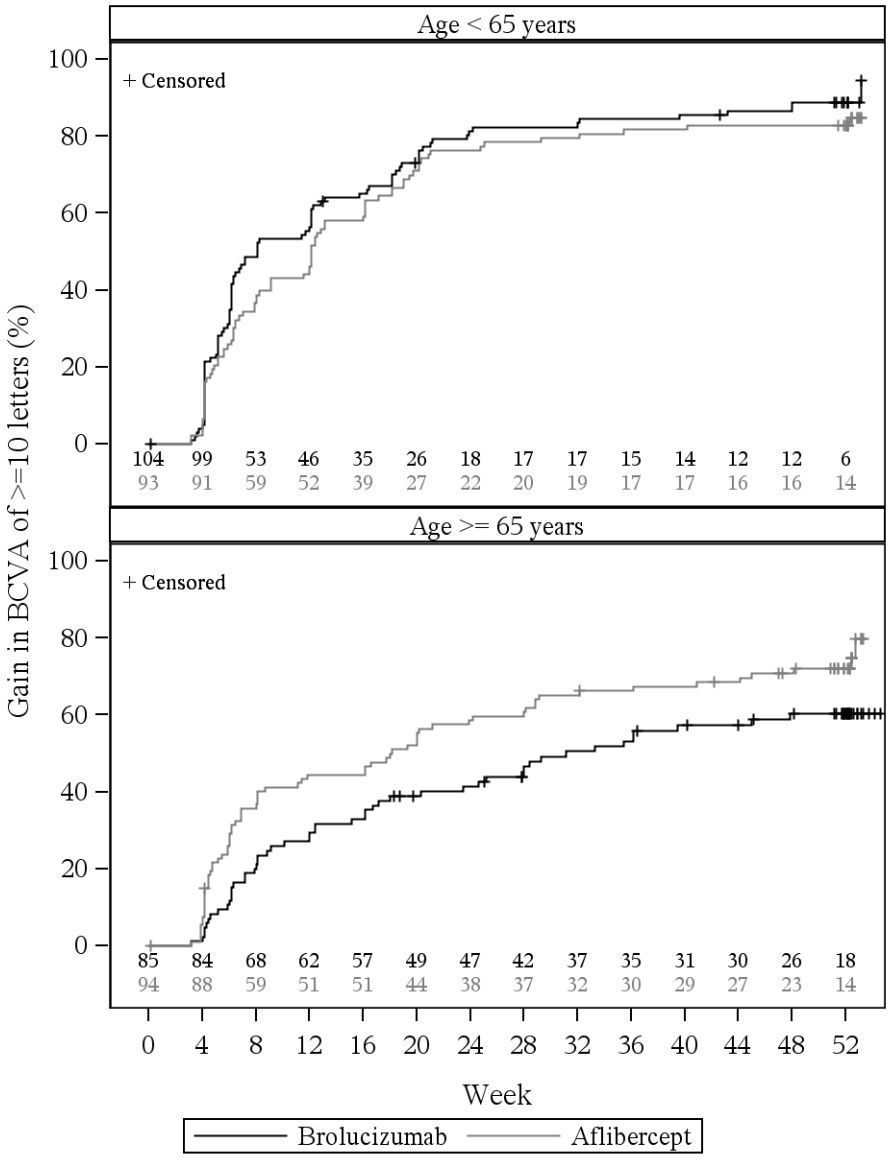


Plots include patients under risk.

Figure 6.2.2 BCVA - Gain of 10 respectively 15 letters by age (FAS), Kaplan-Meier plot, week 52

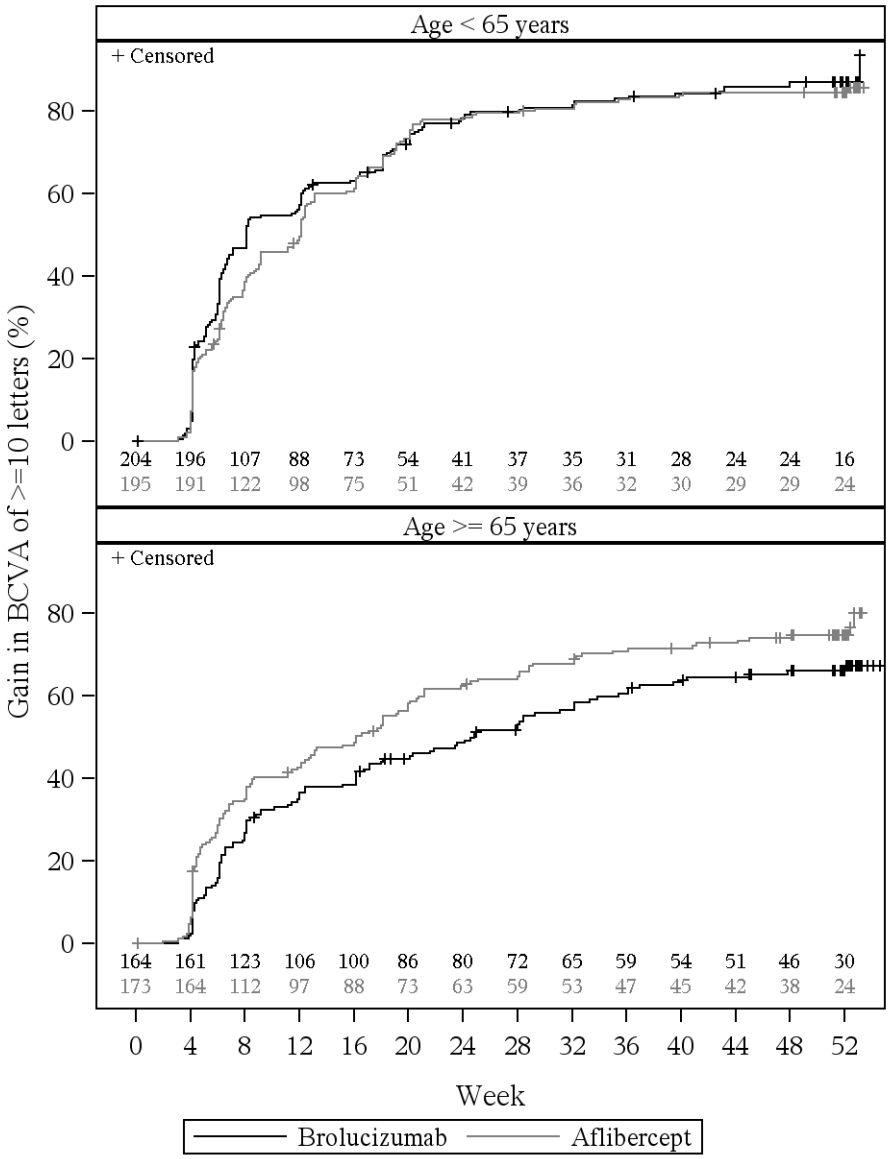
Figure 6.2.2.1 BCVA - Gain of 10 respectively 15 letters by age (FAS), Kaplan-Meier plot, week 52, gain of >=10 letters

Figure 6.2.2.1.1 BCVA - Gain of 10 respectively 15 letters by age (FAS), Kaplan-Meier plot, week 52, gain of >=10 letters for Kestrel



Plots include patients under risk.

Figure 6.2.2.1.3 BCVA - Gain of 10 respectively 15 letters by age (FAS), Kaplan-Meier plot, week 52, gain of >=10 letters for Pooled Analysis

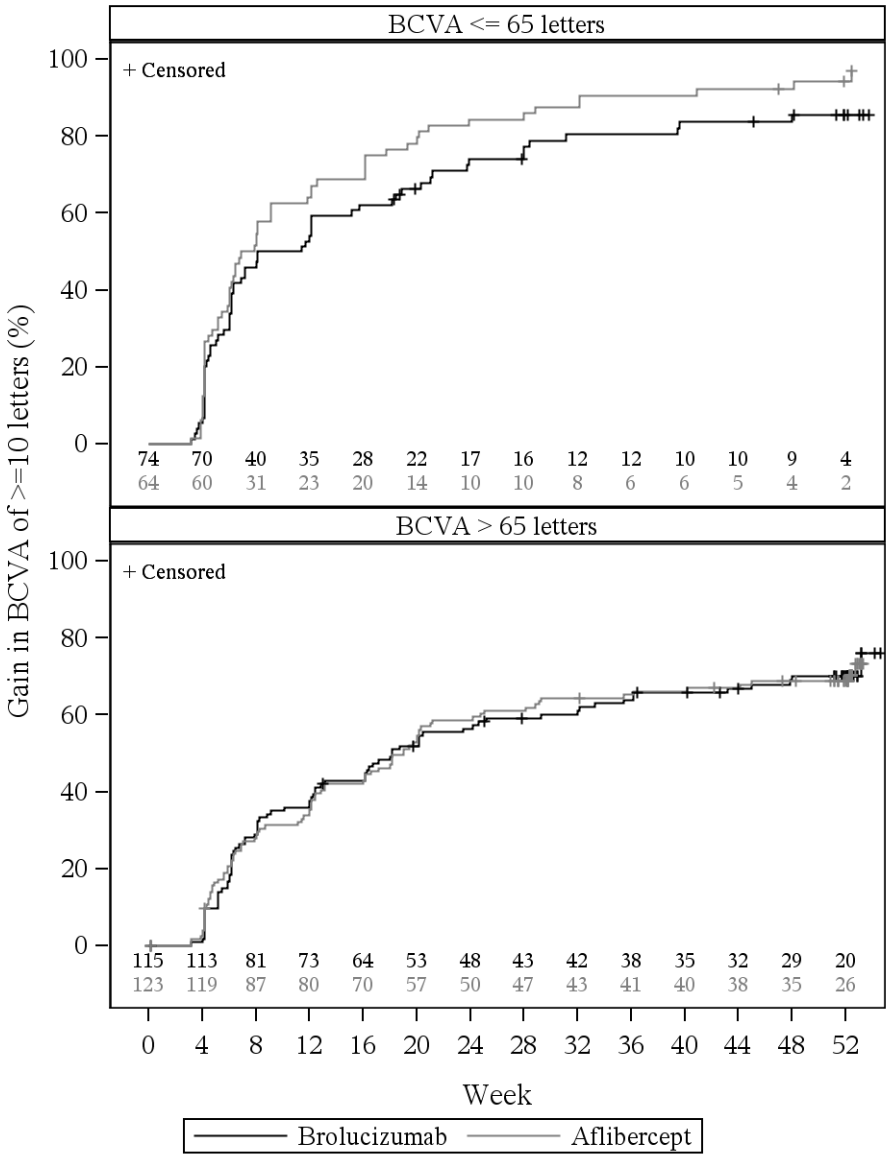


Plots include patients under risk.

Figure 6.4.2 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), Kaplan-Meier plot, week 52

Figure 6.4.2.1 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), Kaplan-Meier plot, week 52, gain of >=10 letters

Figure 6.4.2.1.1 BCVA - Gain of 10 respectively 15 letters by BCVA (FAS), Kaplan-Meier plot, week 52, gain of >=10 letters for Kestrel

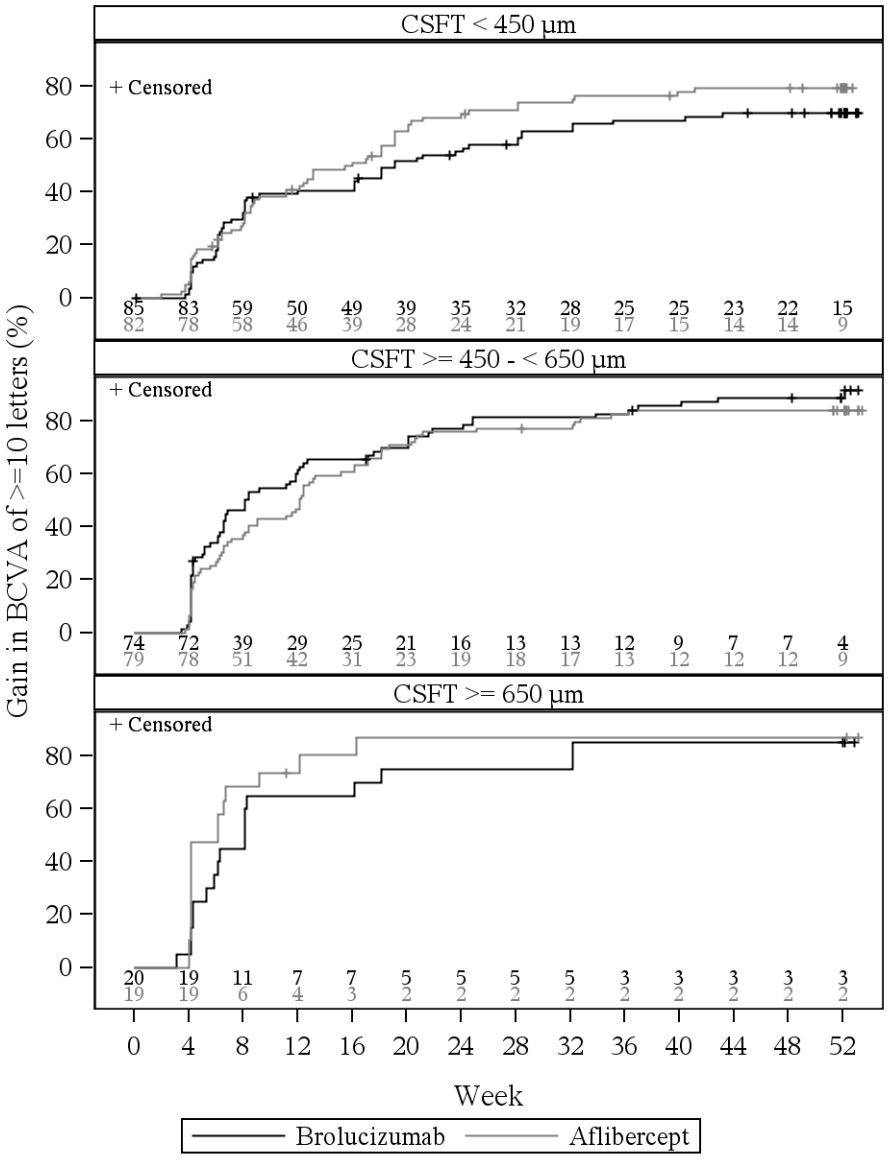


Plots include patients under risk.

Figure 6.10.2 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), Kaplan-Meier plot, week 52

Figure 6.10.2.1 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), Kaplan-Meier plot, week 52, gain of >=10 letters

Figure 6.10.2.1.2 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), Kaplan-Meier plot, week 52, gain of >=10 letters for Kite



Plots include patients under risk.

Figure 6.10.2.1.3 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), Kaplan-Meier plot, week 52, gain of >=10 letters for Pooled Analysis

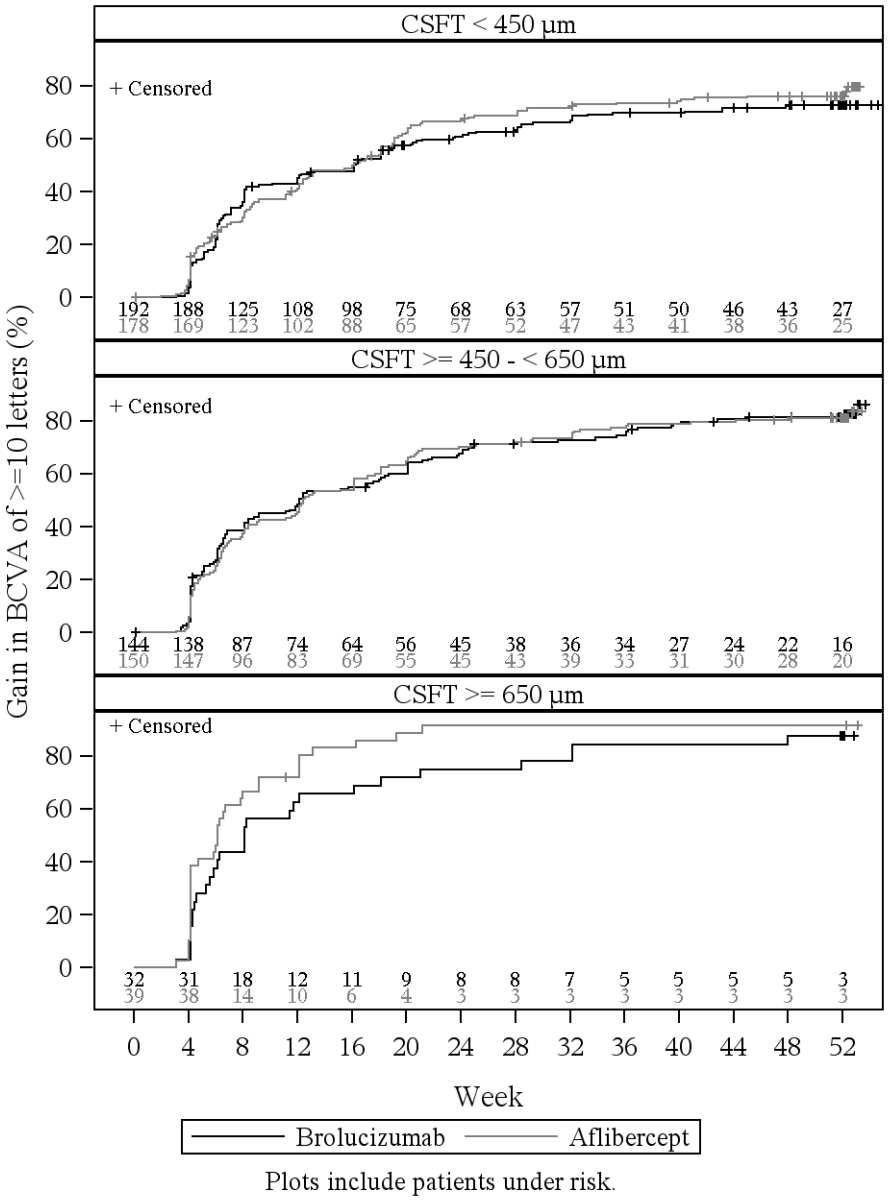
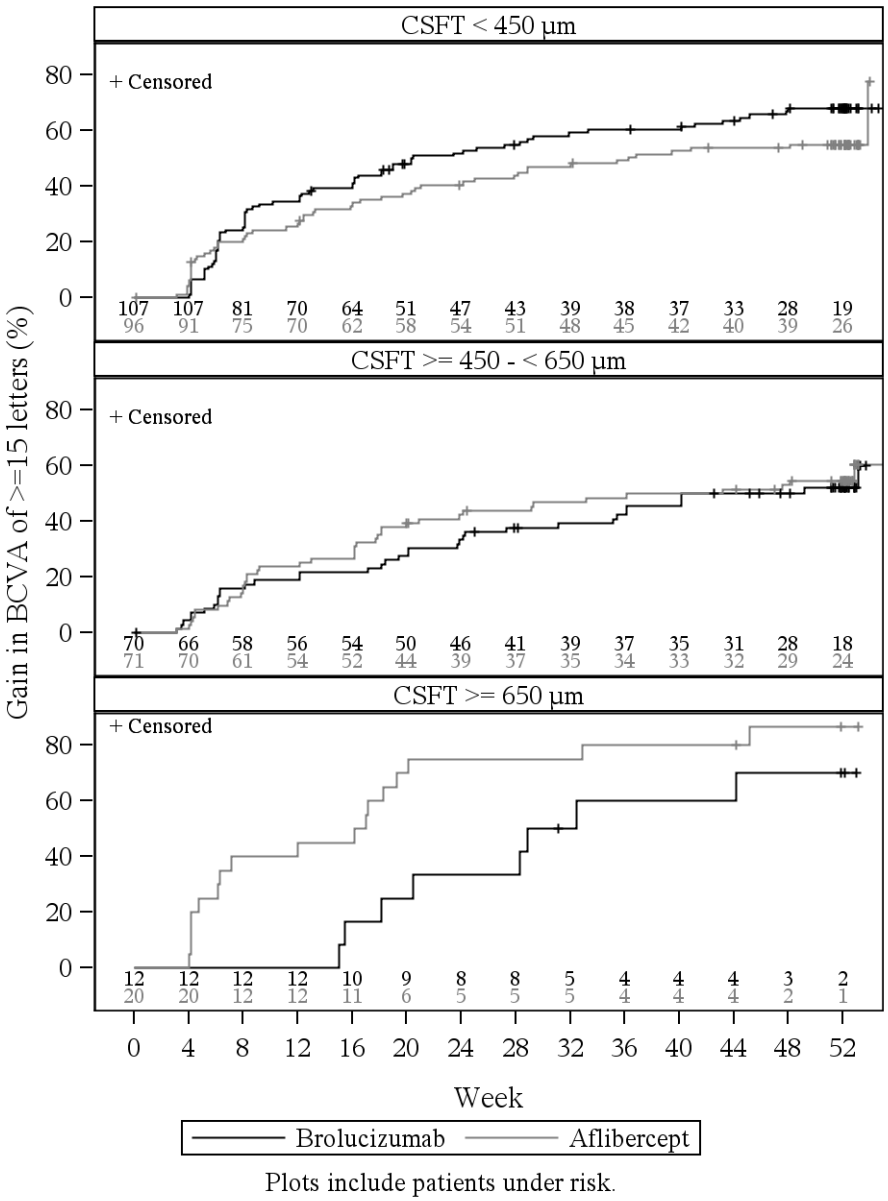


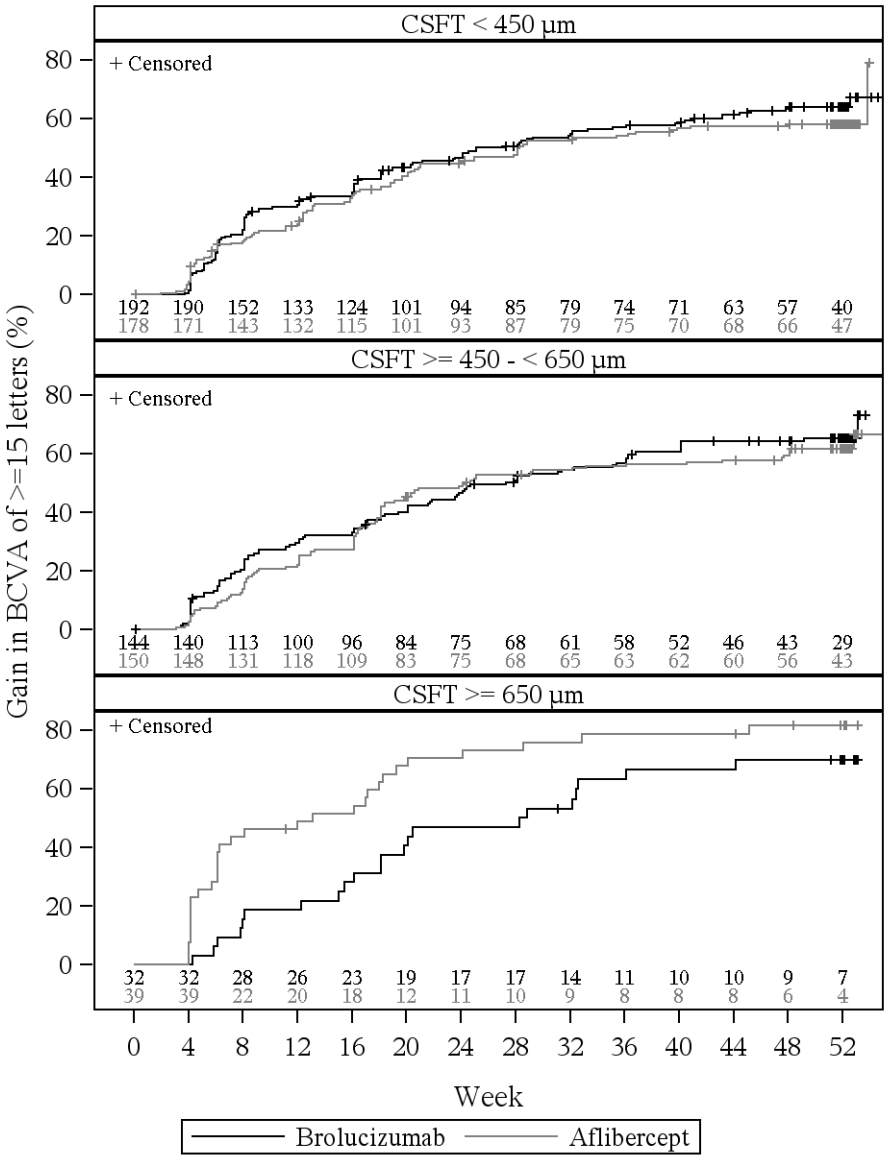
Figure 6.10.2.2 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), Kaplan-Meier plot, week 52, gain of >=15 letters

Figure 6.10.2.2.1 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), Kaplan-Meier plot, week 52, gain of >=15 letters for Kestrel



Plots include patients under risk.

Figure 6.10.2.2.3 BCVA - Gain of 10 respectively 15 letters by CSFT (FAS), Kaplan-Meier plot, week 52, gain of >=15 letters for Pooled Analysis

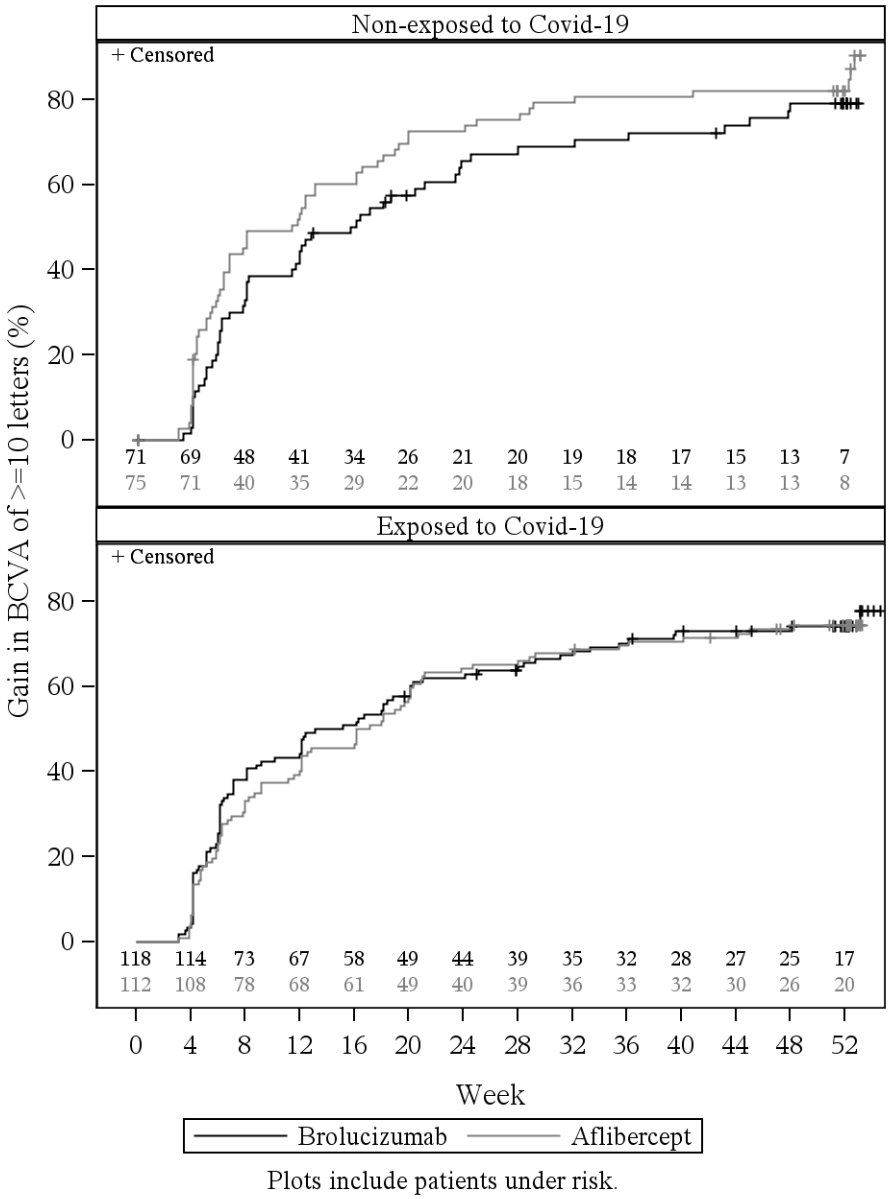


Plots include patients under risk.

Figure 6.12.2 BCVA - Gain of 10 respectively 15 letters by exposure (FAS), Kaplan-Meier plot, week 52

Figure 6.12.2.1 BCVA - Gain of 10 respectively 15 letters by exposure (FAS), Kaplan-Meier plot, week 52, gain of >=10 letters

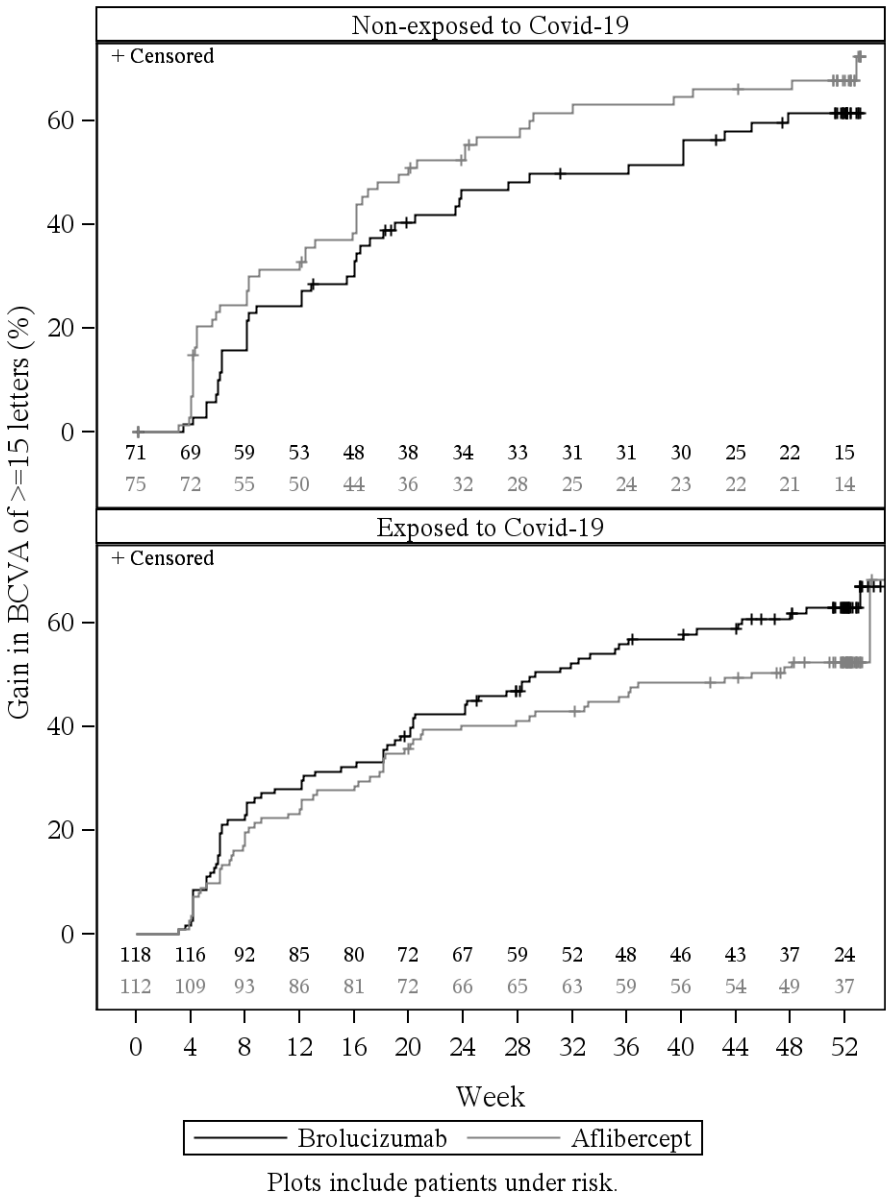
Figure 6.12.2.1.1 BCVA - Gain of 10 respectively 15 letters by exposure (FAS), Kaplan-Meier plot, week 52, gain of >=10 letters for Kestrel



Plots include patients under risk.

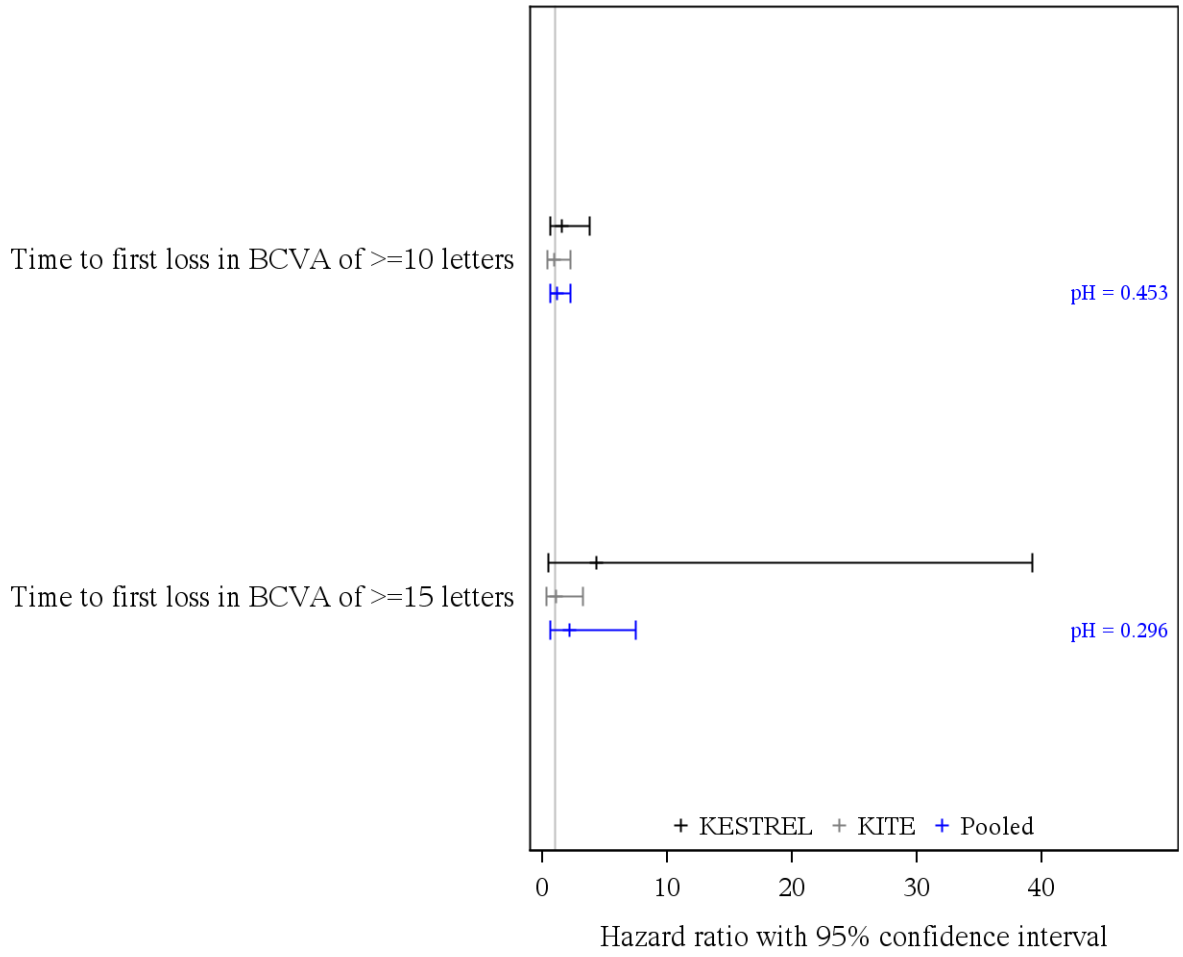
Figure 6.12.2.2 BCVA - Gain of 10 respectively 15 letters by exposure (FAS), Kaplan-Meier plot, week 52, gain of >=15 letters

Figure 6.12.2.2.1 BCVA - Gain of 10 respectively 15 letters by exposure (FAS), Kaplan-Meier plot, week 52, gain of >=15 letters for Kestrel



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

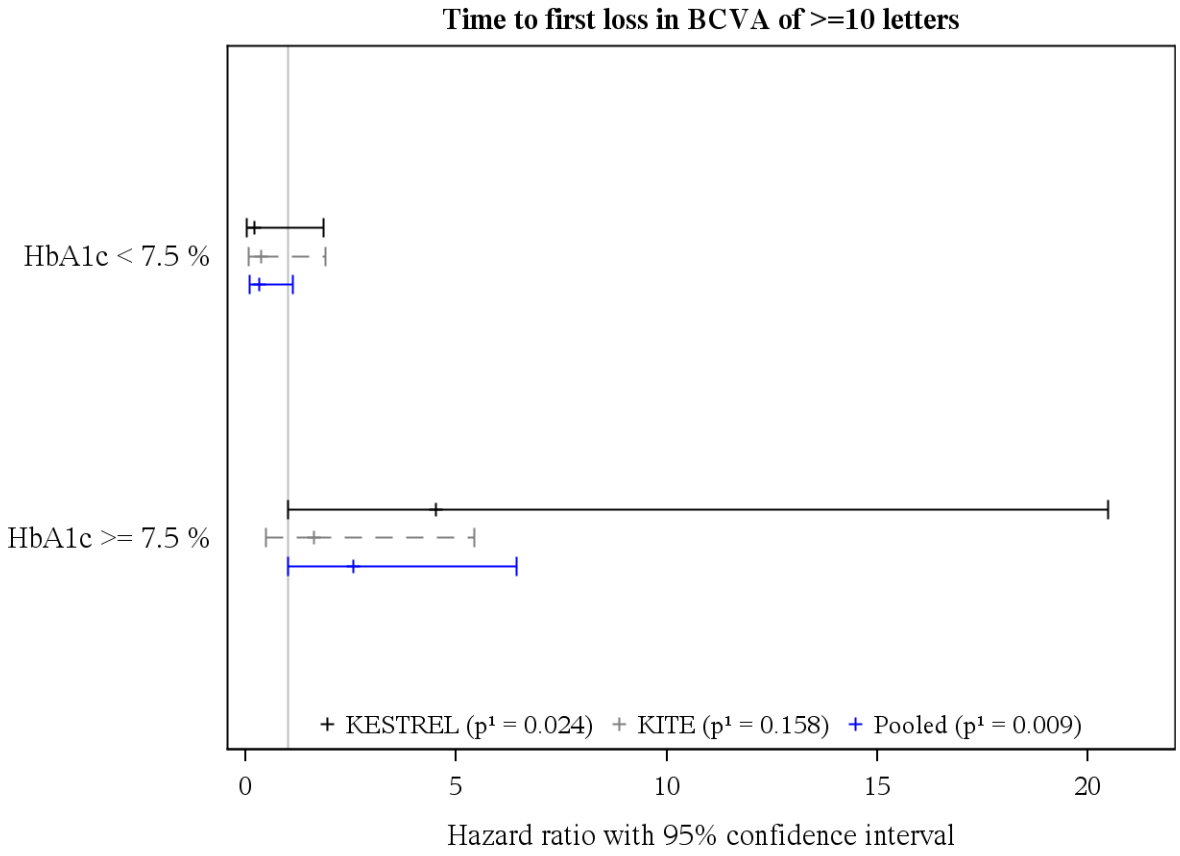
Figure 7.1.1 BCVA - Loss of 10 respectively 15 letters (FAS), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 7.7.1 BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS), forest plot, week 52

Figure 7.7.1.1 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 7.1.2 BCVA - Loss of 10 respectively 15 letters (FAS), Kaplan-Meier plot, week 52

Figure 7.1.2.1 BCVA - Loss of 10 respectively 15 letters (FAS), Kaplan-Meier plot, week 52, loss of >=10 letters

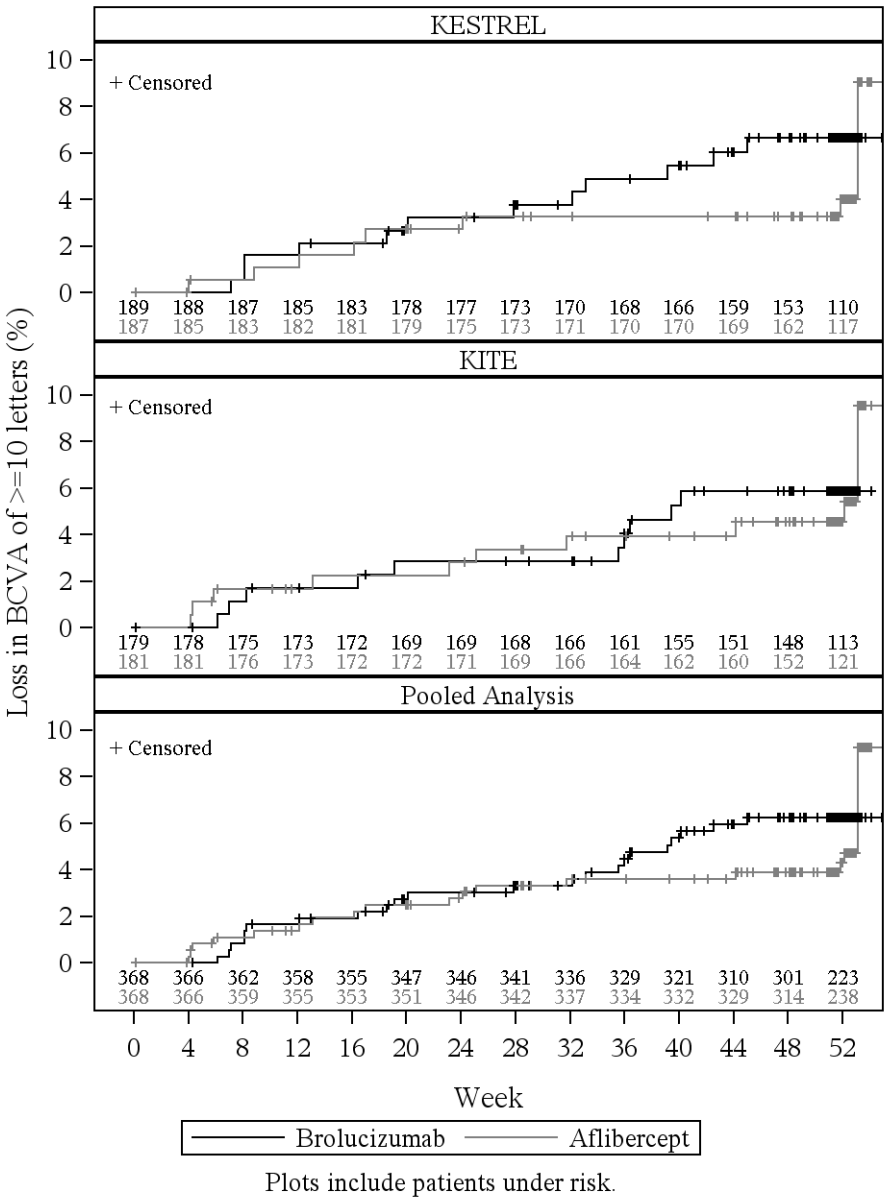
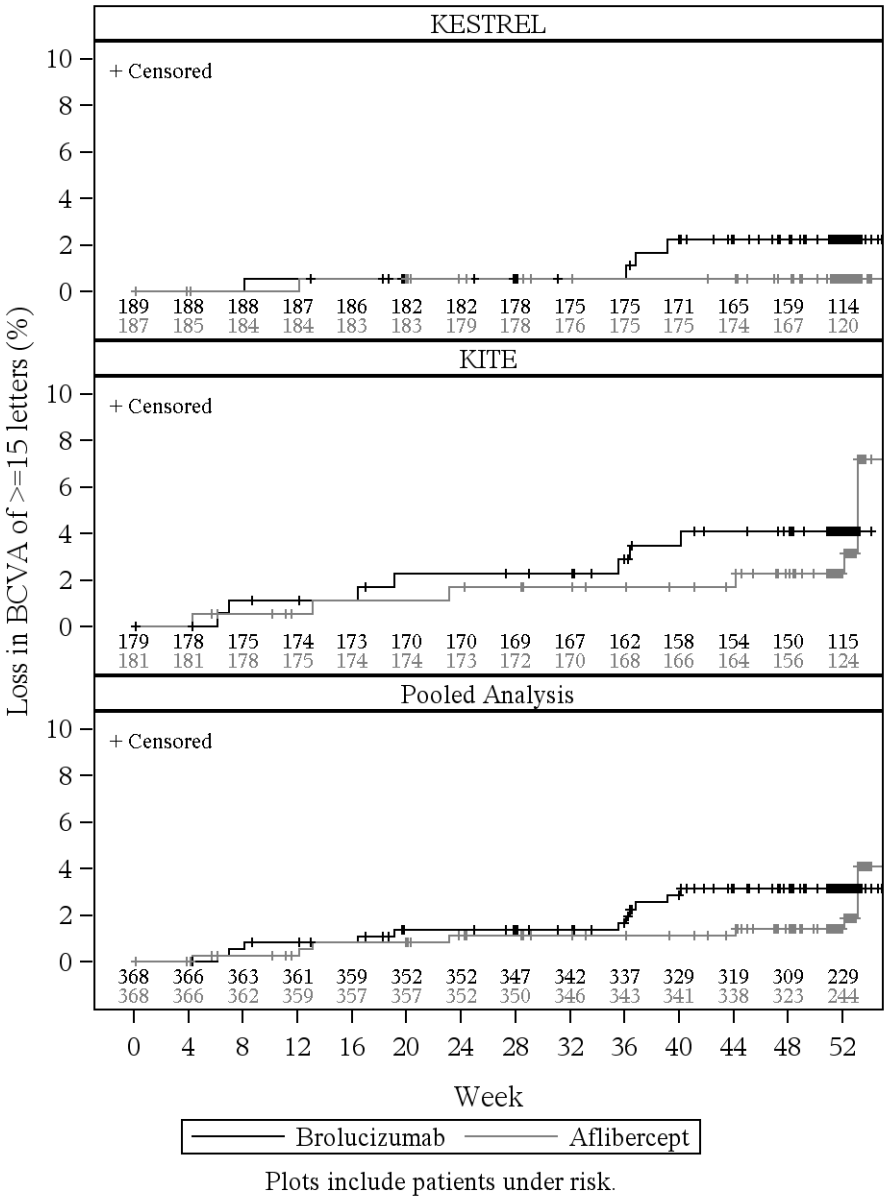


Figure 7.1.2.2 BCVA - Loss of 10 respectively 15 letters (FAS), Kaplan-Meier plot, week 52, loss of >=15 letters

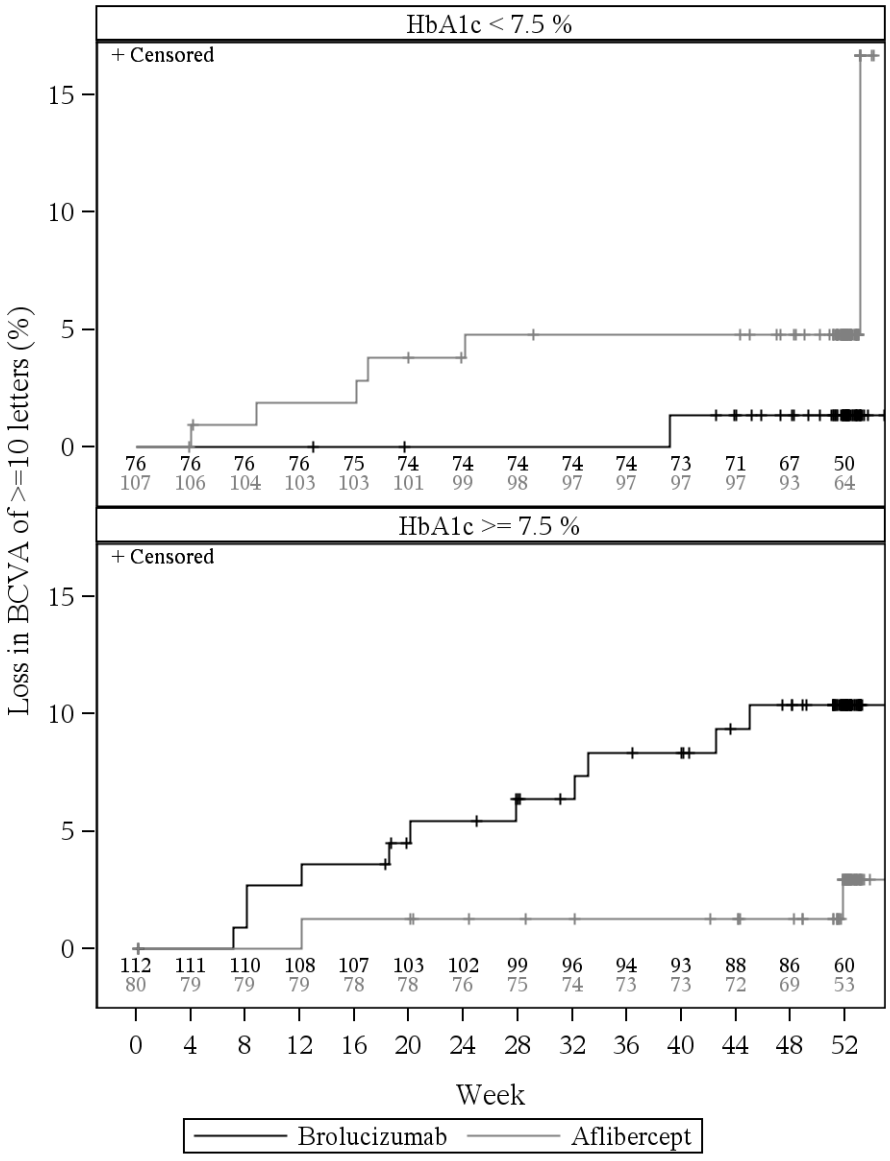


Plots include patients under risk.

Figure 7.7.2 BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS), Kaplan-Meier plot, week 52

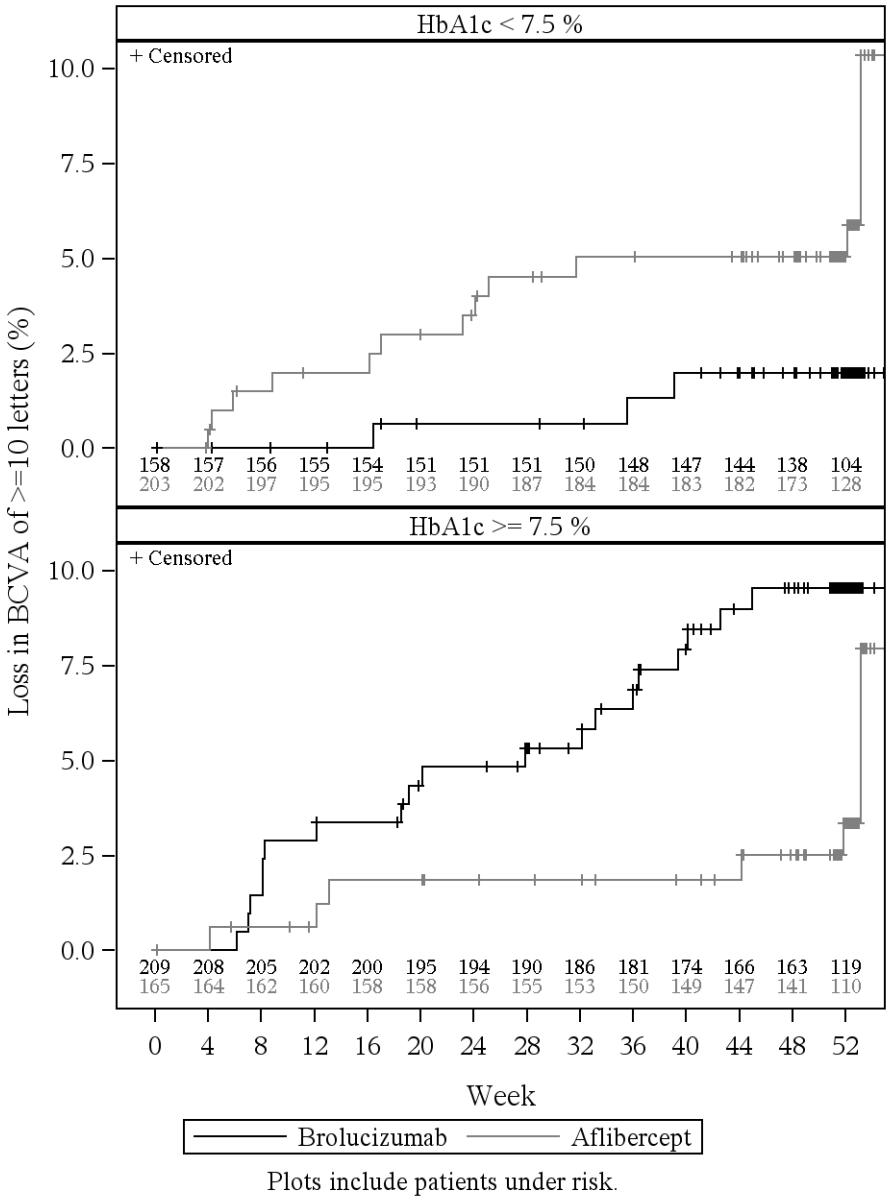
Figure 7.7.2.1 BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS), Kaplan-Meier plot, week 52, loss of >=10 letters

Figure 7.7.2.1.1 BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS), Kaplan-Meier plot, week 52, loss of >=10 letters for Kestrel



Plots include patients under risk.

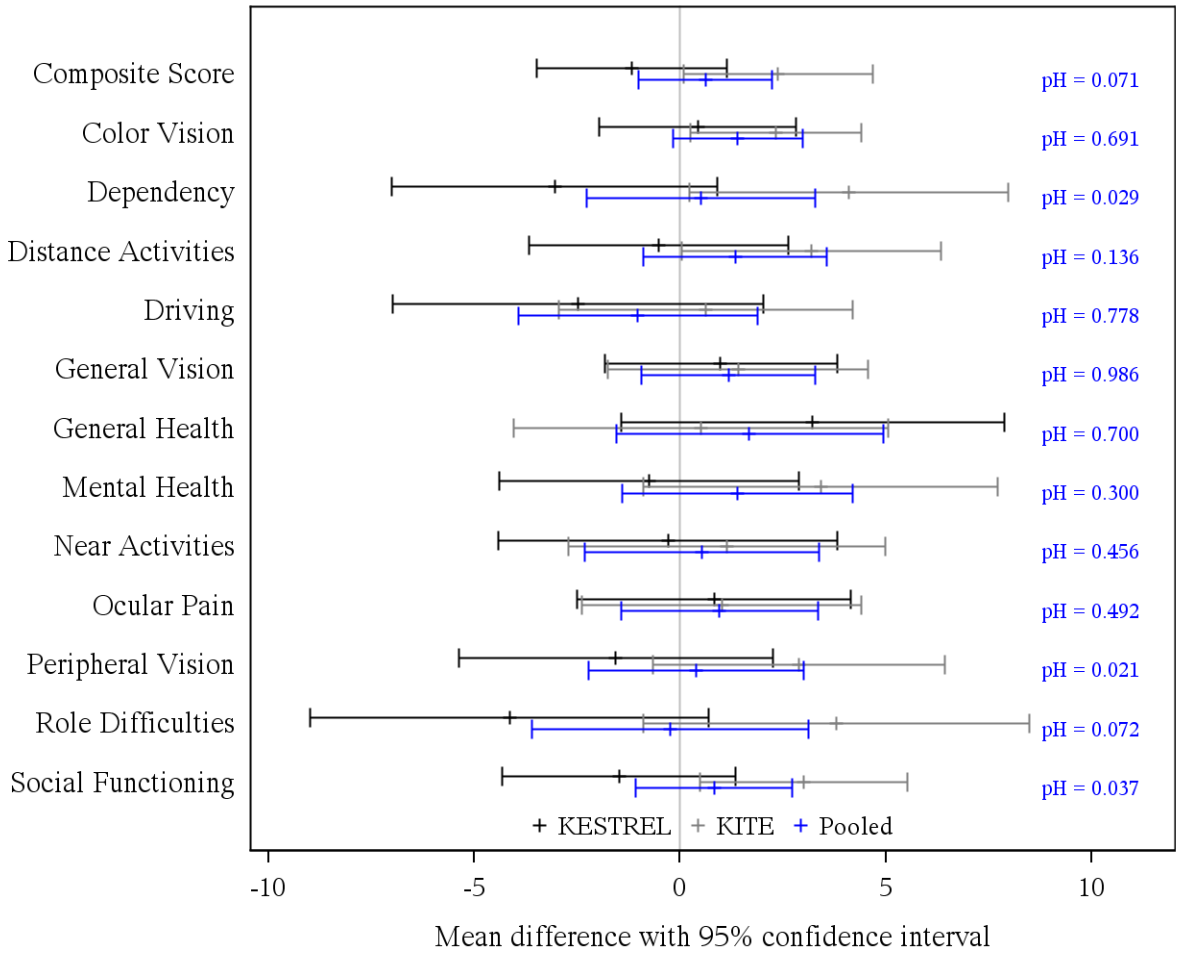
Figure 7.7.2.1.3 BCVA - Loss of 10 respectively 15 letters by HbA1c (FAS), Kaplan-Meier plot, week 52, loss of >=10 letters for Pooled Analysis



Plots include patients under risk.

8 VFQ: Continuous analysis

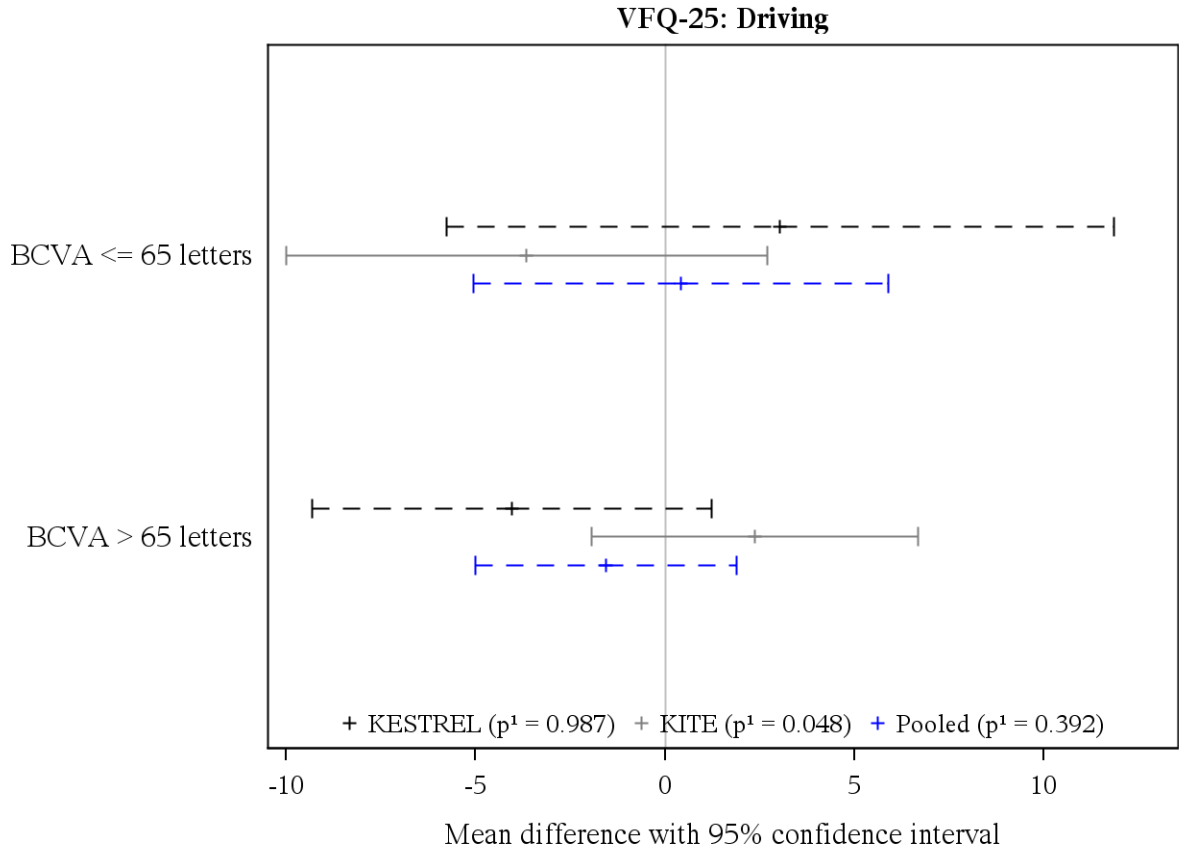
Figure 8.1.1 VFQ (FAS), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 8.4.1 VFQ by BCVA (FAS), forest plot, week 52

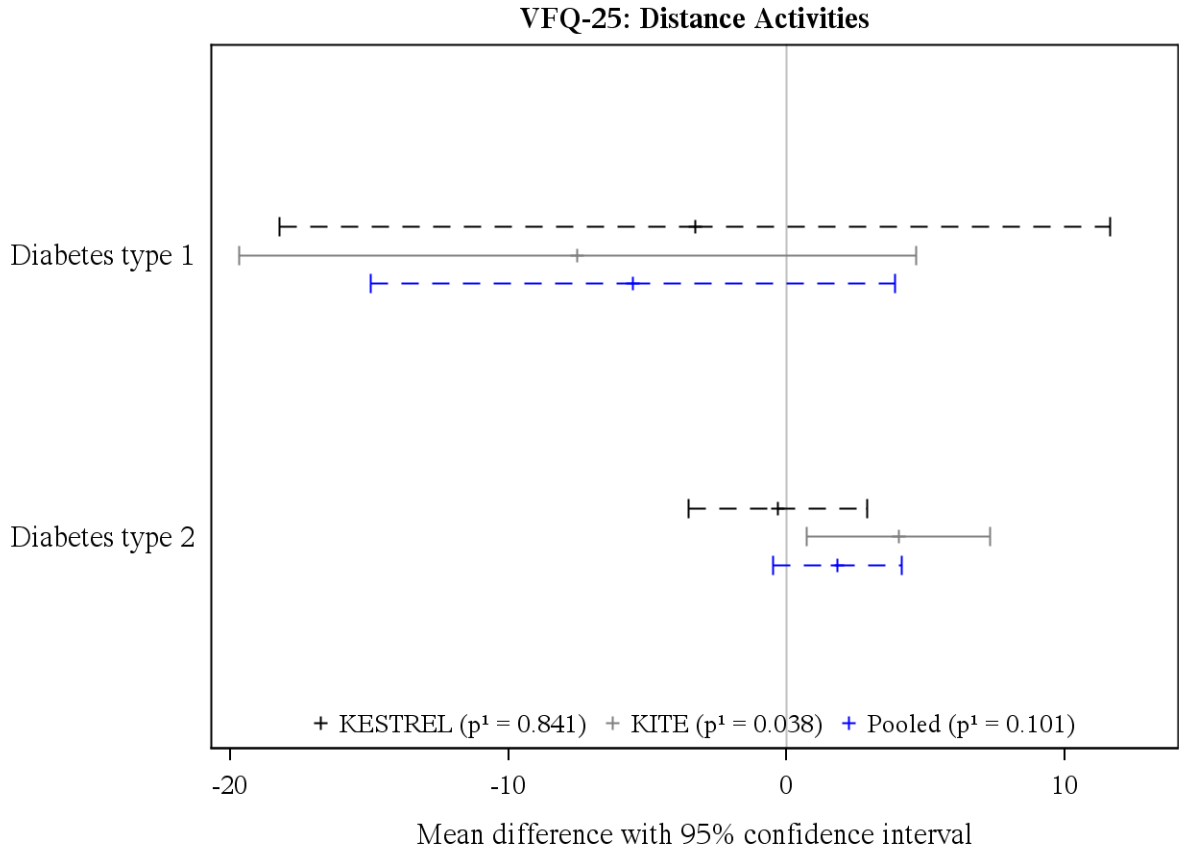
Figure 8.4.1.1 VFQ by BCVA (FAS), forest plot, week 52, Driving



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: $p_H = 0.778$

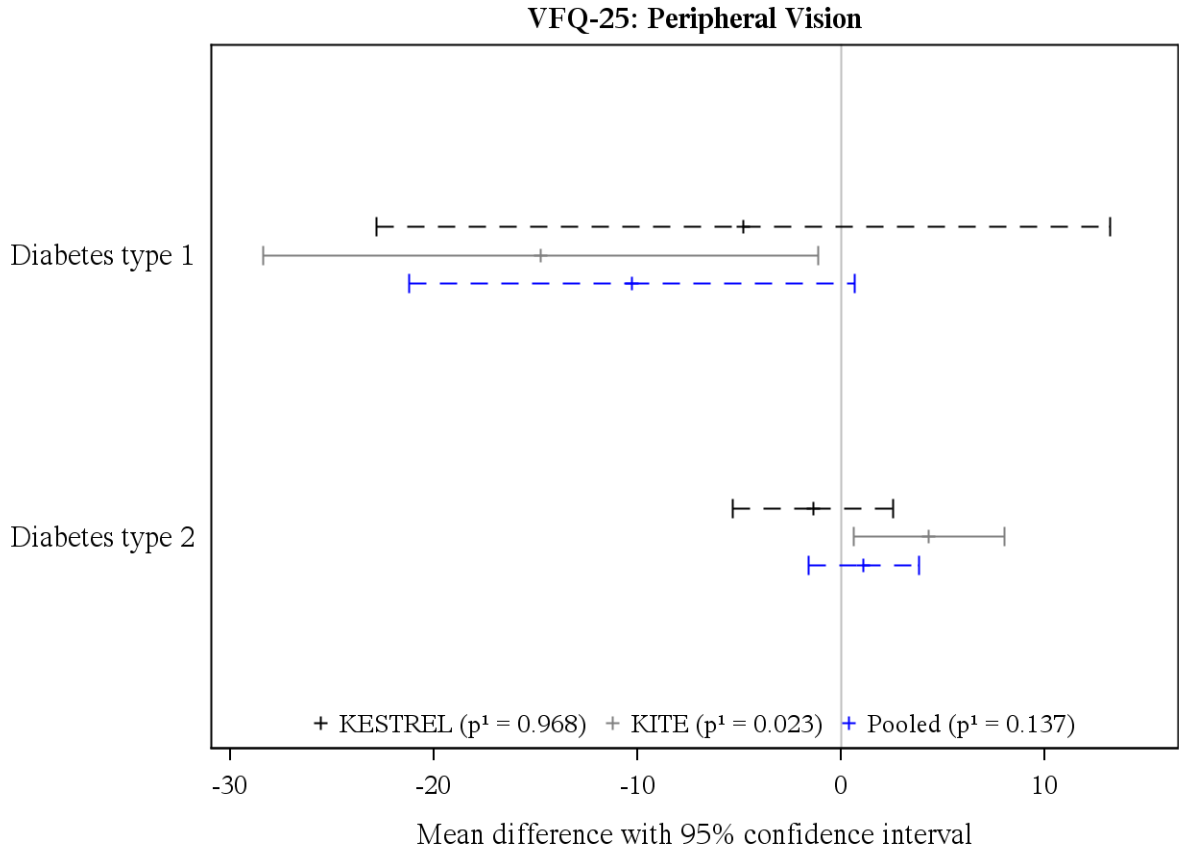
Figure 8.6.1 VFQ by diabetes type (FAS), forest plot, week 52

Figure 8.6.1.1 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: $p_H = 0.136$

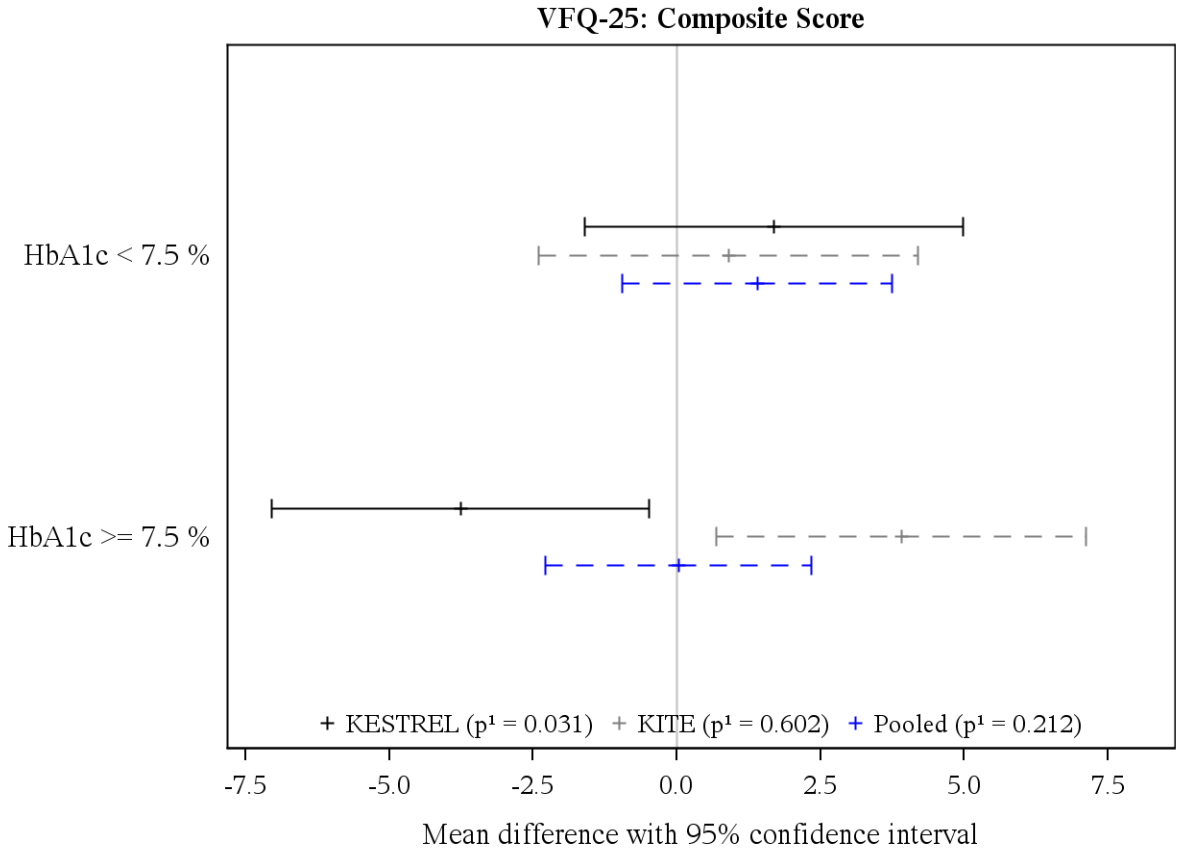
Figure 8.6.1.2 VFQ by diabetes type (FAS), forest plot, week 52, Peripheral Vision



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 = 0.021

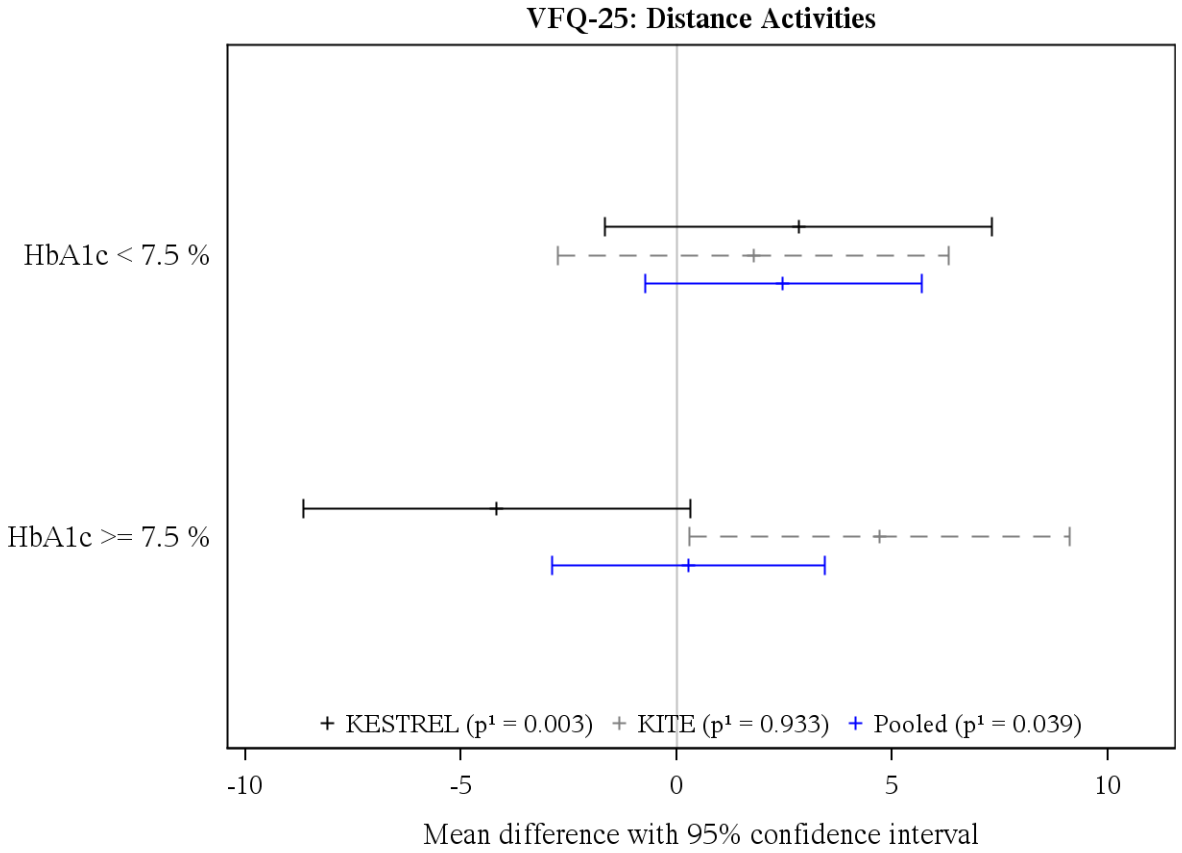
Figure 8.7.1 VFQ by HbA1c (FAS), forest plot, week 52

Figure 8.7.1.1 VFQ by HbA1c (FAS), forest plot, week 52, Composite Score



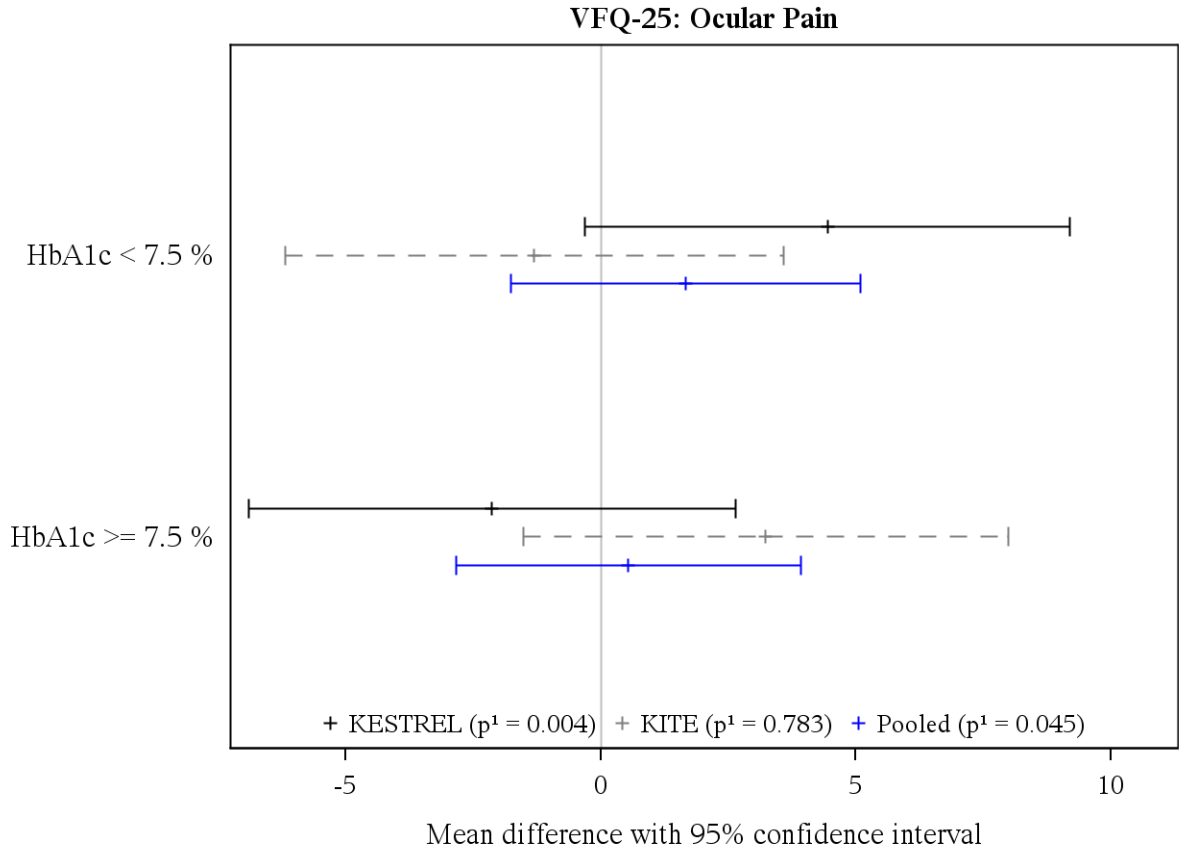
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.071$

Figure 8.7.1.2 VFQ by HbA1c (FAS), forest plot, week 52, Distance Activities



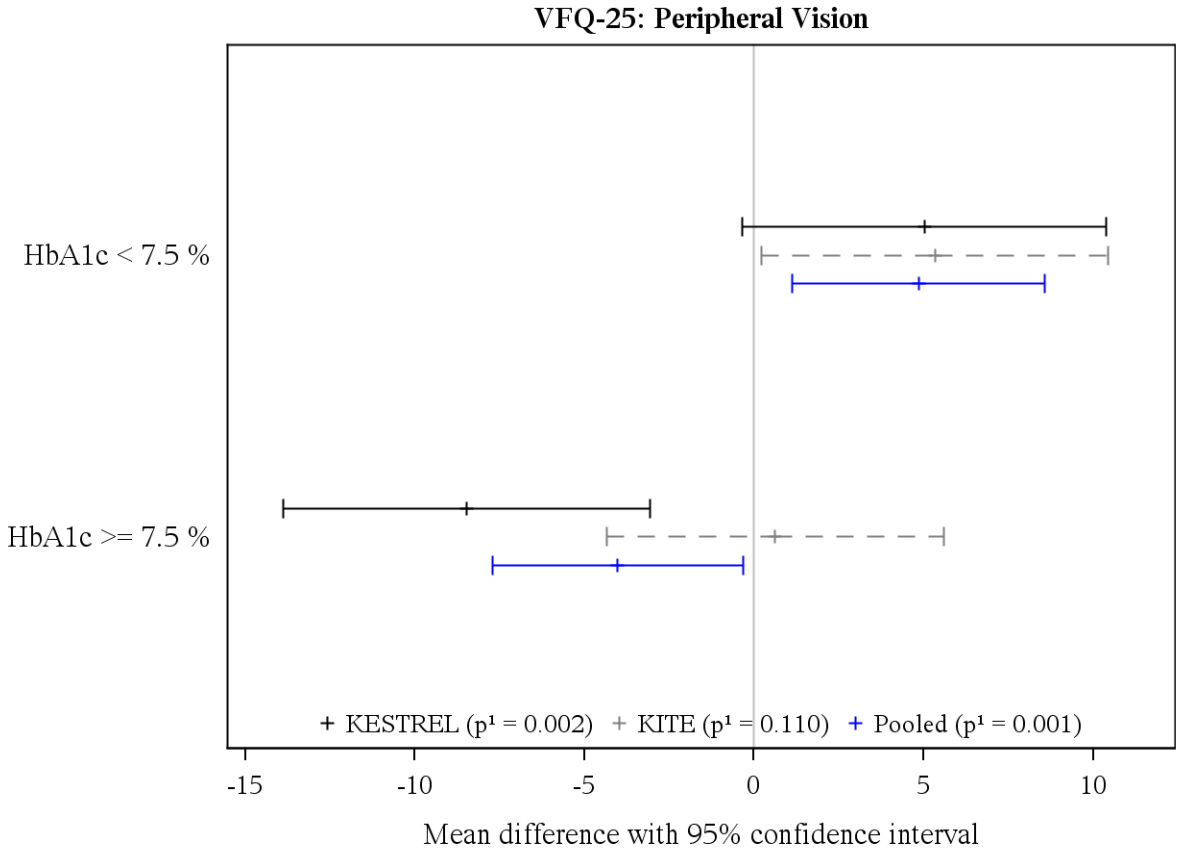
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.136$

Figure 8.7.1.3 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: $p_H = 0.492$

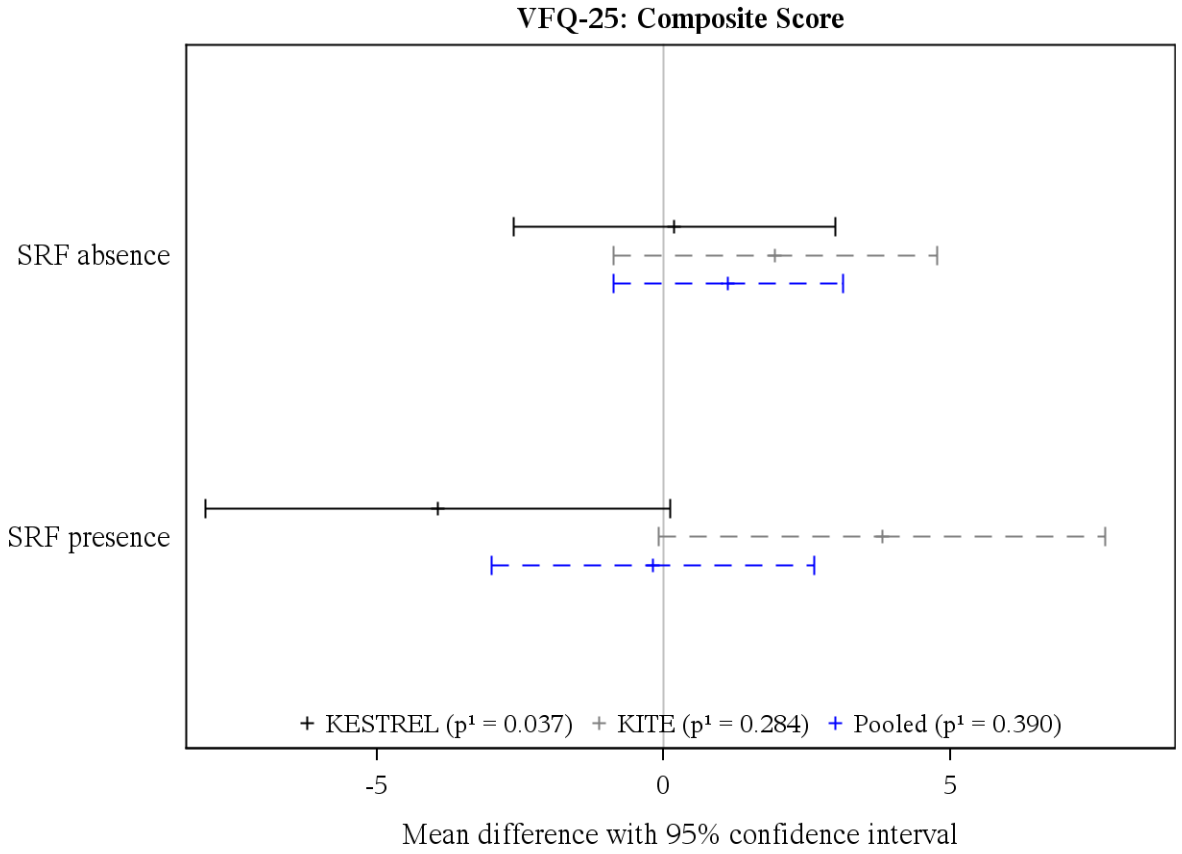
Figure 8.7.1.4 VFQ by HbA1c (FAS), forest plot, week 52, Peripheral Vision



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: $p_H = 0.021$

Figure 8.11.1 VFQ by status of SRF (FAS), forest plot, week 52

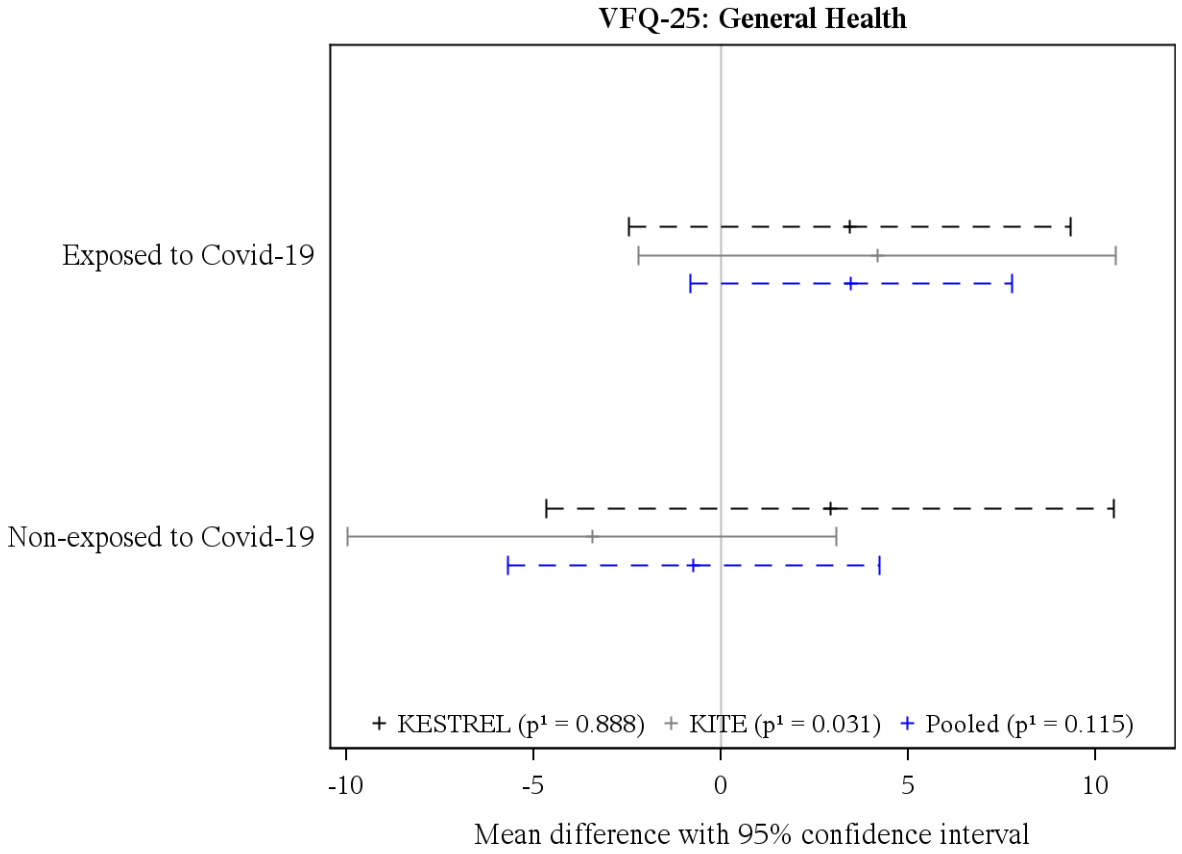
Figure 8.11.1.1 VFQ by status of SRF (FAS), forest plot, week 52, Composite Score



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: $p_H = 0.071$

Figure 8.12.1 VFQ by exposure (FAS), forest plot, week 52

Figure 8.12.1.1 VFQ by exposure (FAS), forest plot, week 52, General Health



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: $p_H = 0.700$

Figure 8.1.2 VFQ (FAS), boxplot, week 52

Figure 8.1.2.1 VFQ (FAS), boxplot, week 52, Composite Score

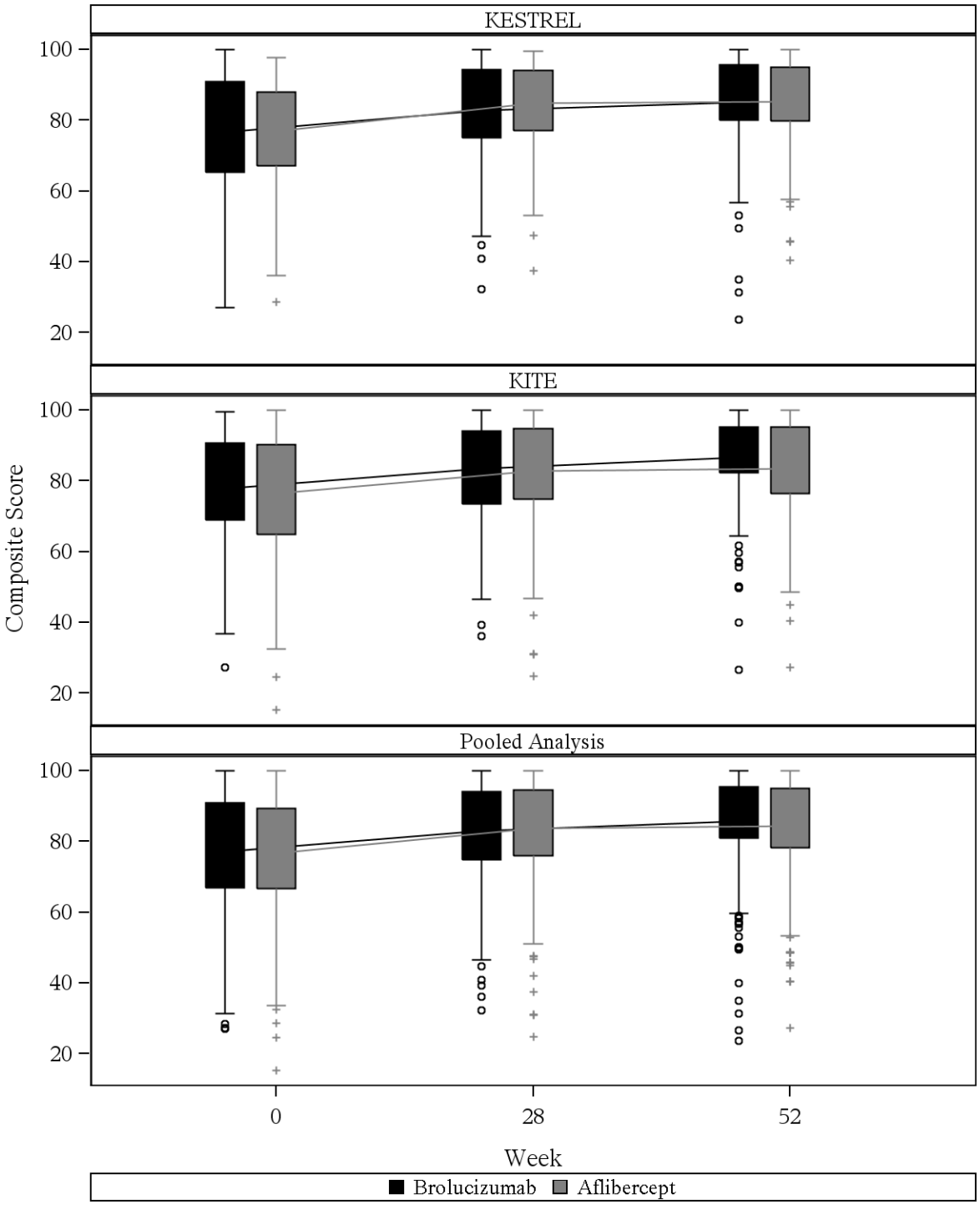


Figure 8.1.2.2 VFQ (FAS), boxplot, week 52, Color Vision

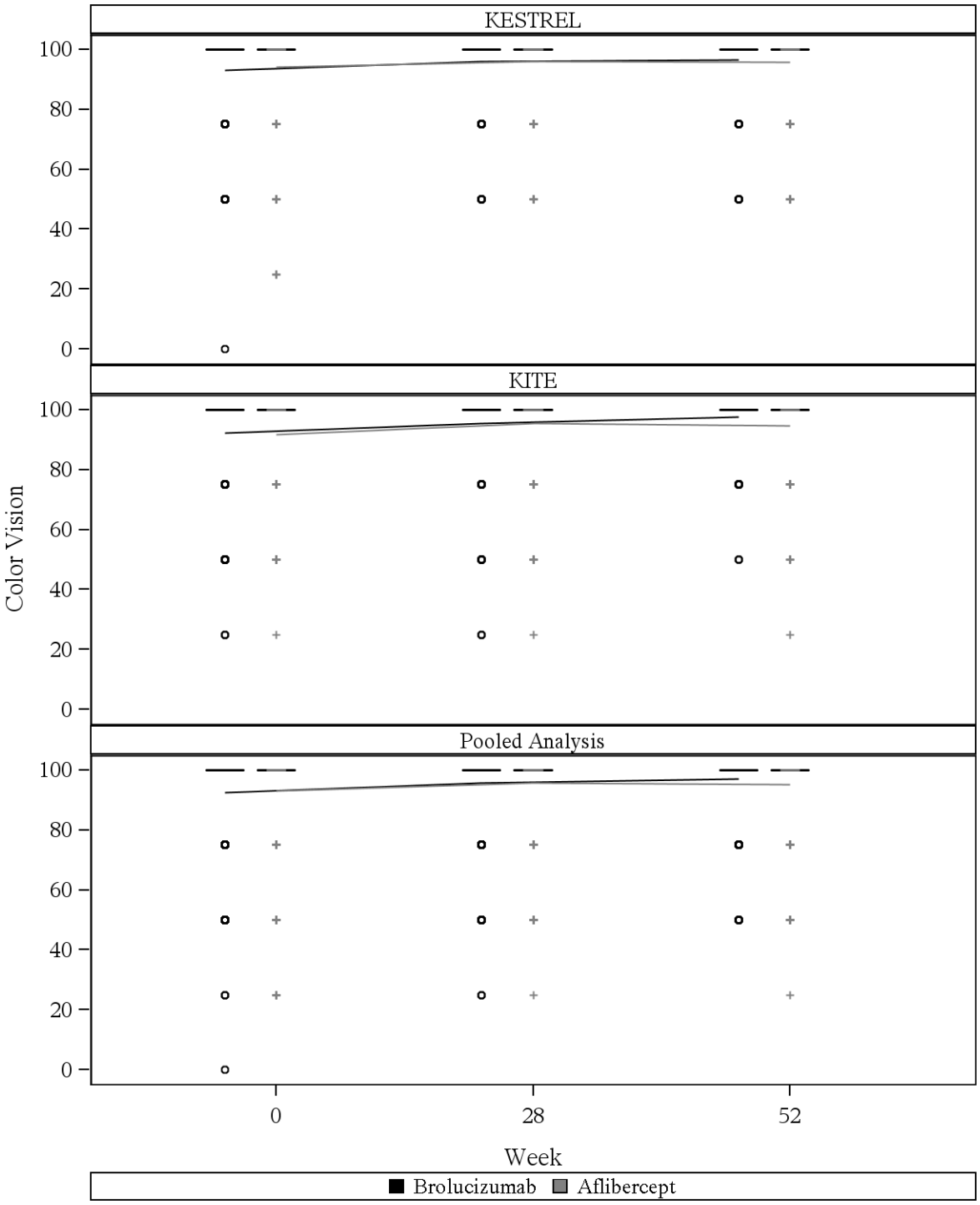


Figure 8.1.2.3 VFQ (FAS), boxplot, week 52, Dependency

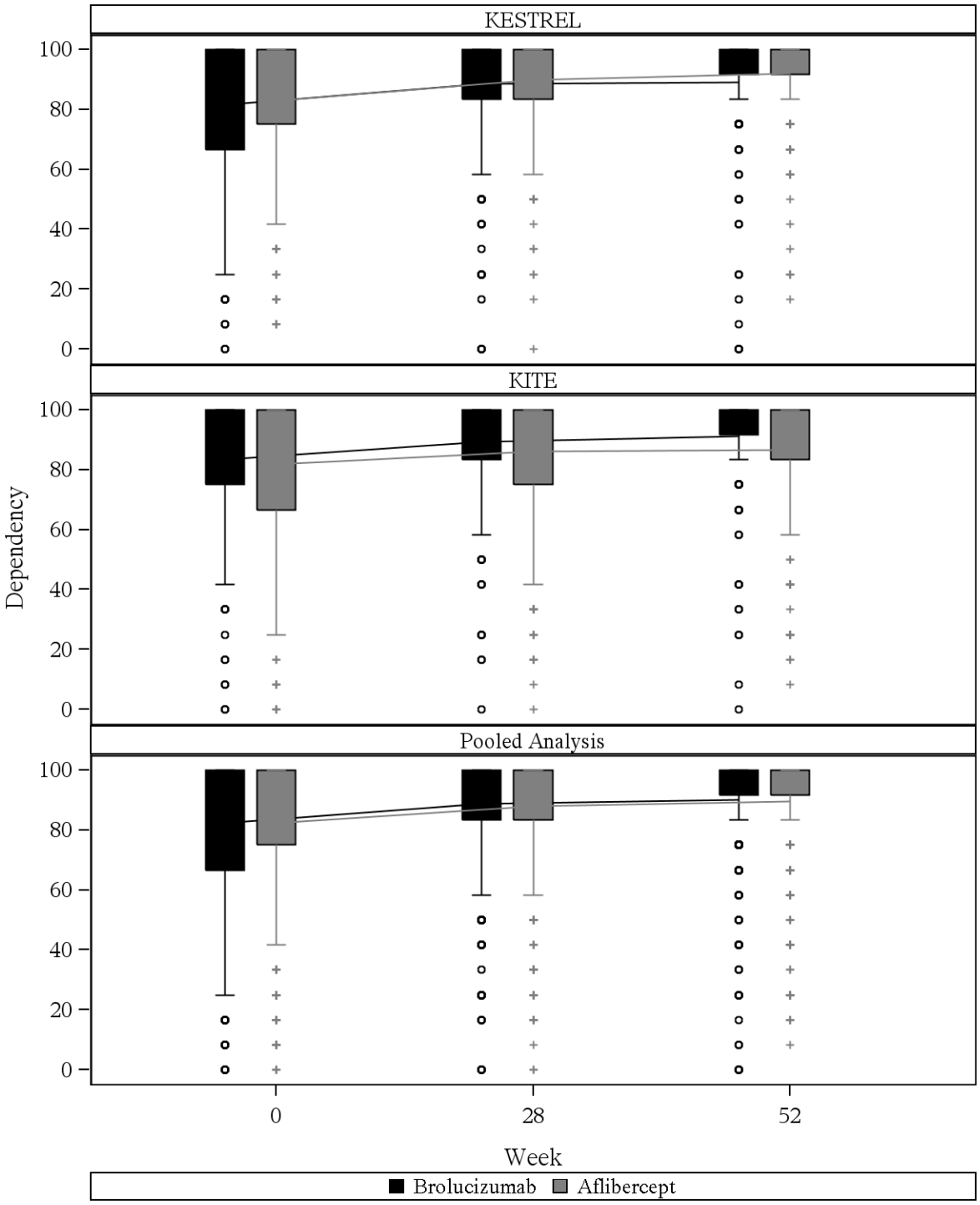


Figure 8.1.2.4 VFQ (FAS), boxplot, week 52, Distance Activities

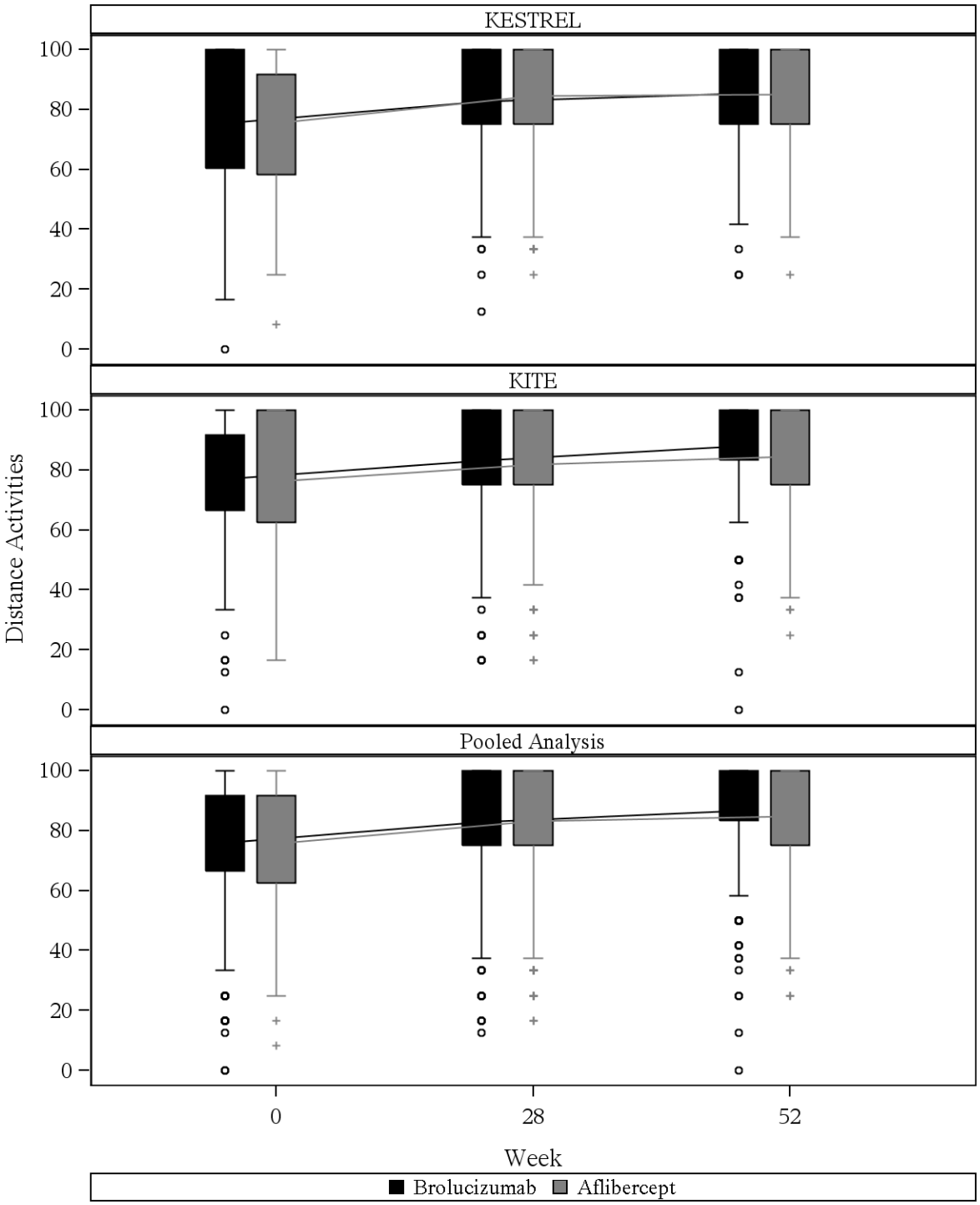


Figure 8.1.2.5 VFQ (FAS), boxplot, week 52, Driving

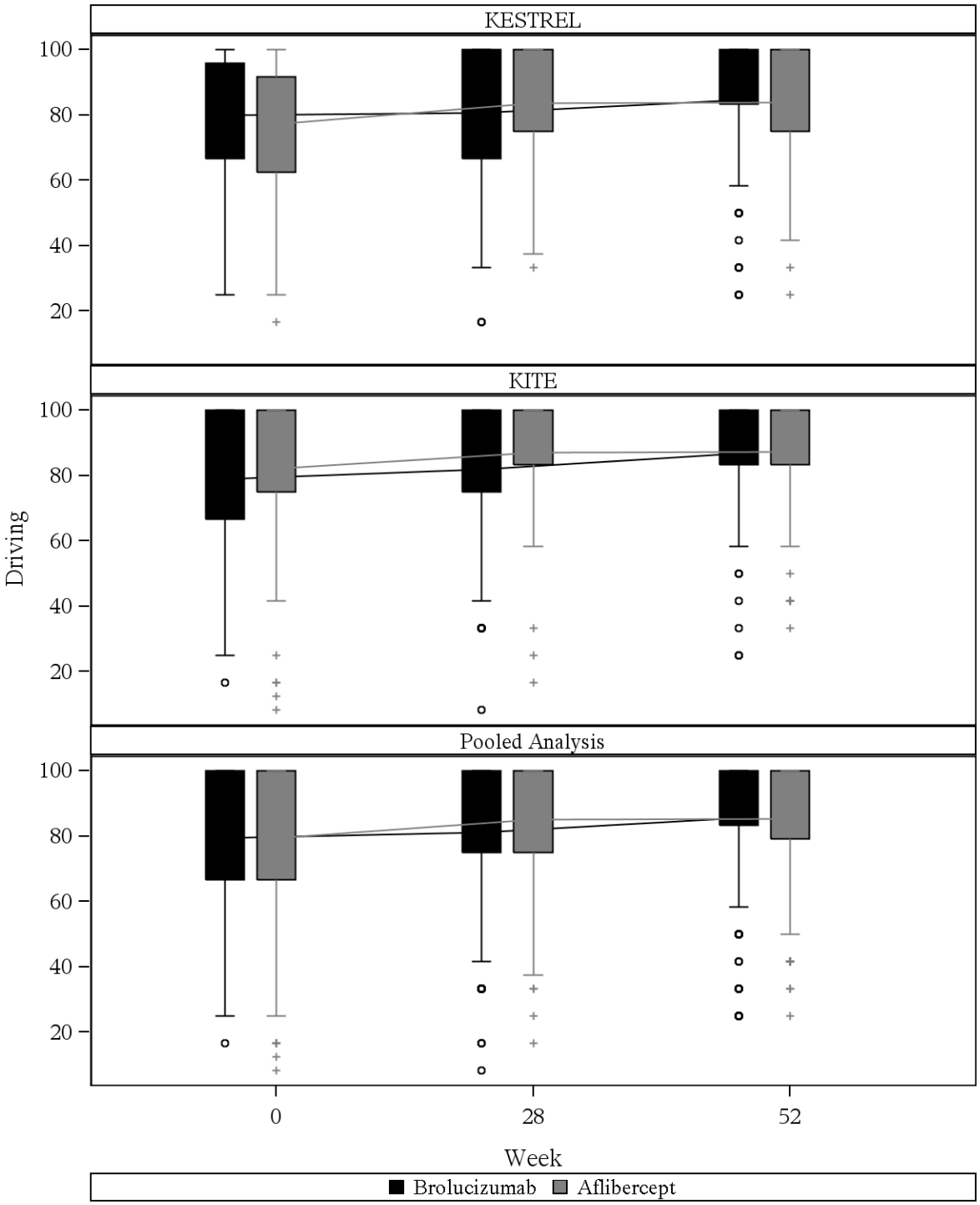


Figure 8.1.2.6 VFQ (FAS), boxplot, week 52, General Vision

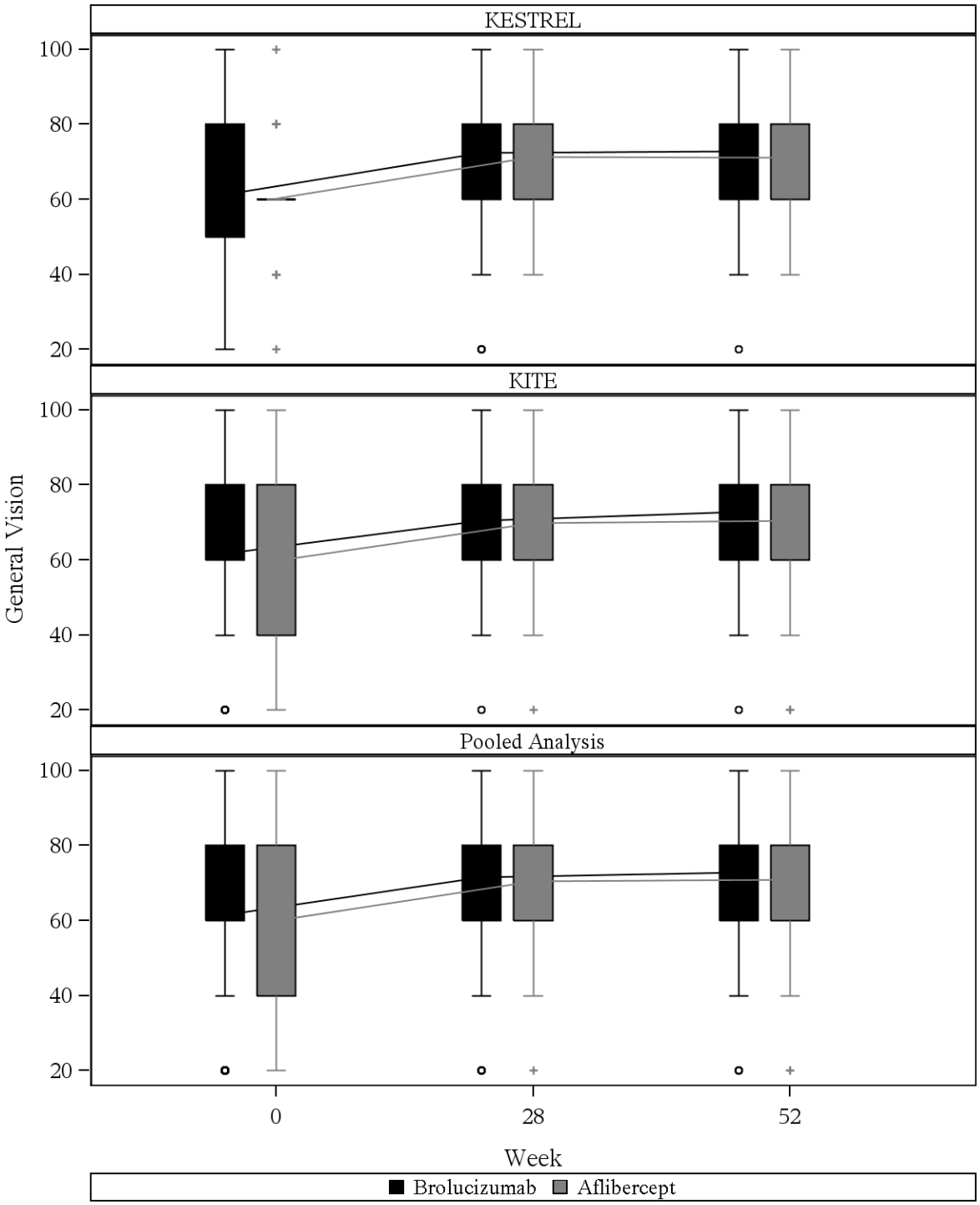


Figure 8.1.2.7 VFQ (FAS), boxplot, week 52, General Health

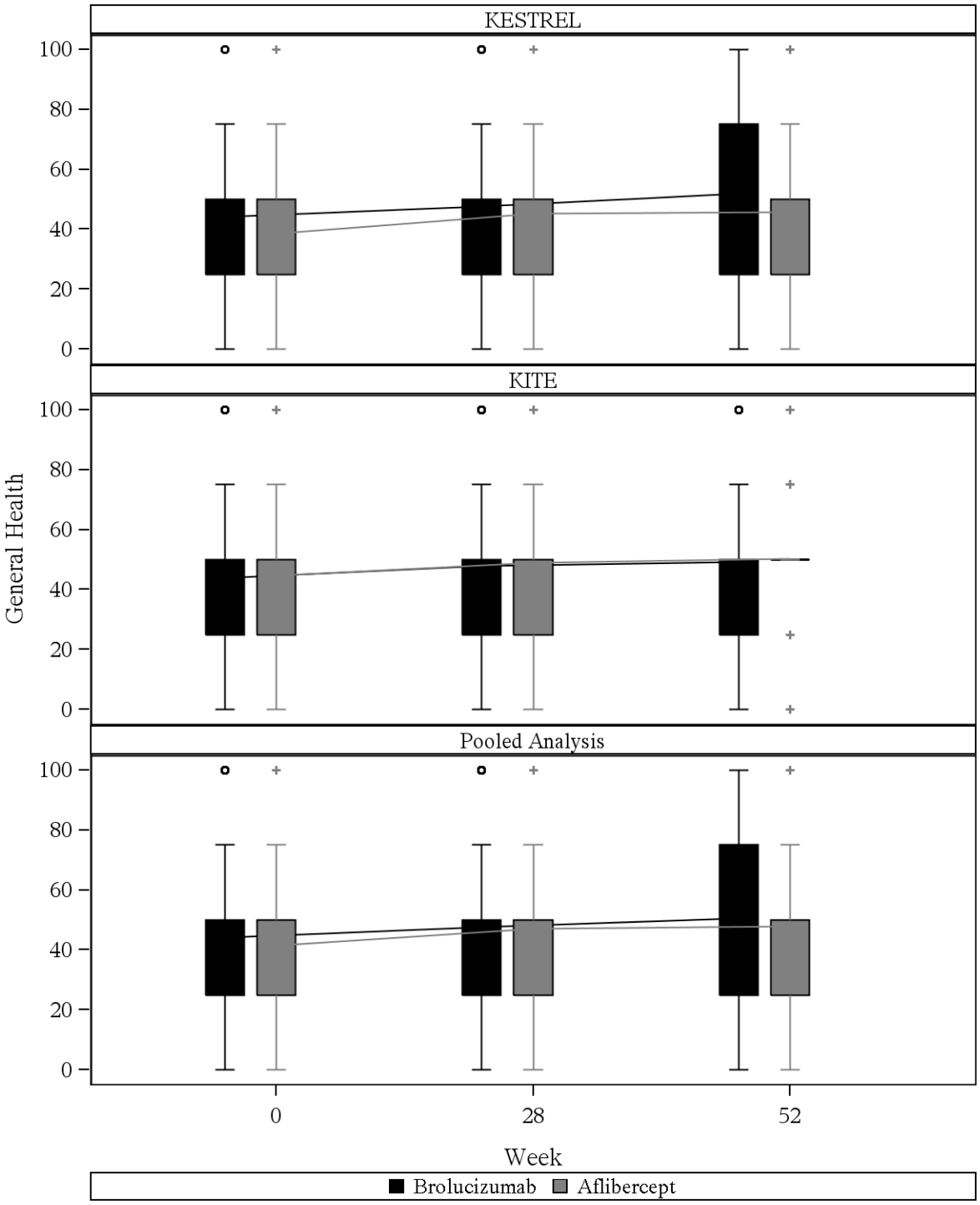


Figure 8.1.2.8 VFQ (FAS), boxplot, week 52, Mental Health

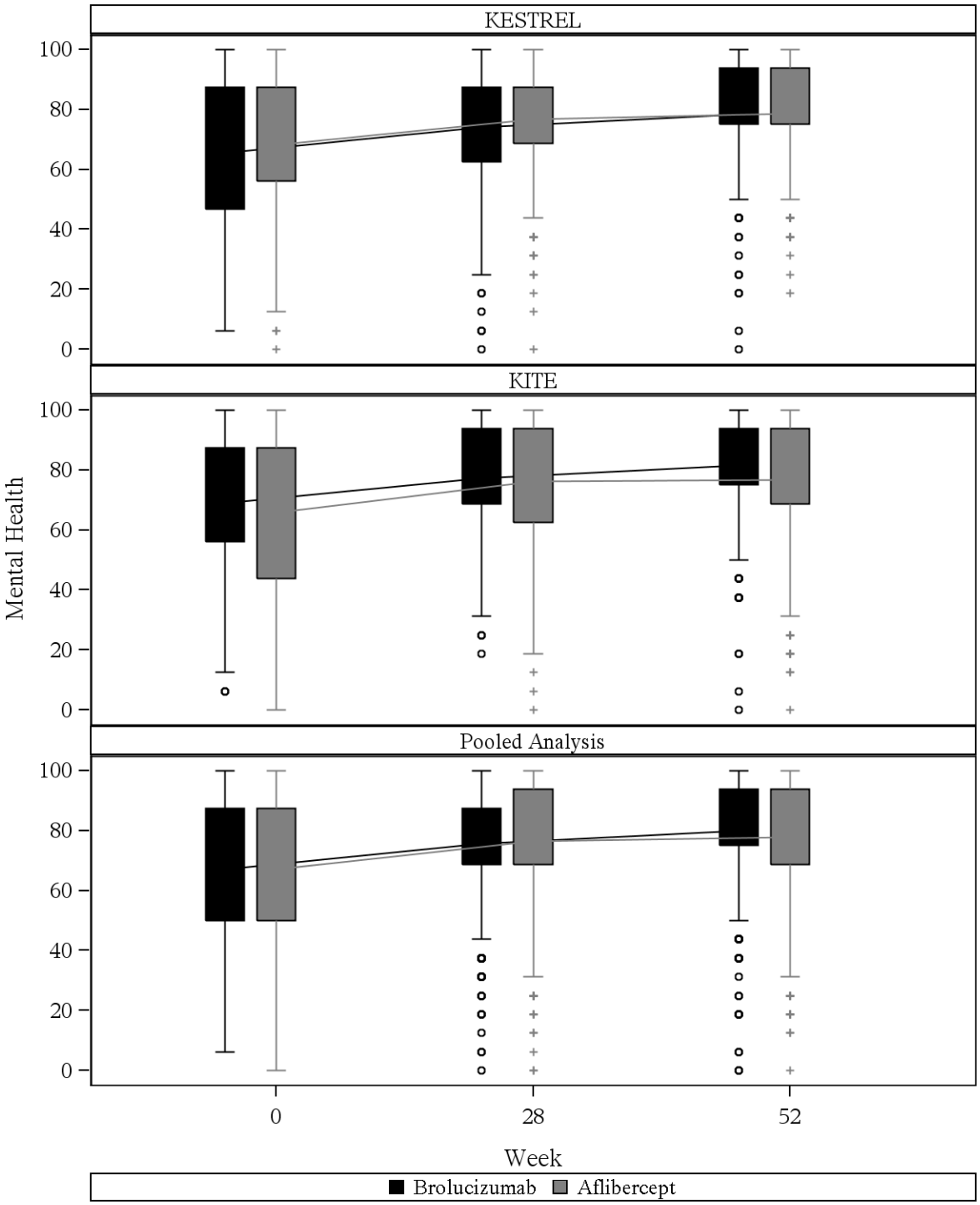


Figure 8.1.2.9 VFQ (FAS), boxplot, week 52, Near Activities

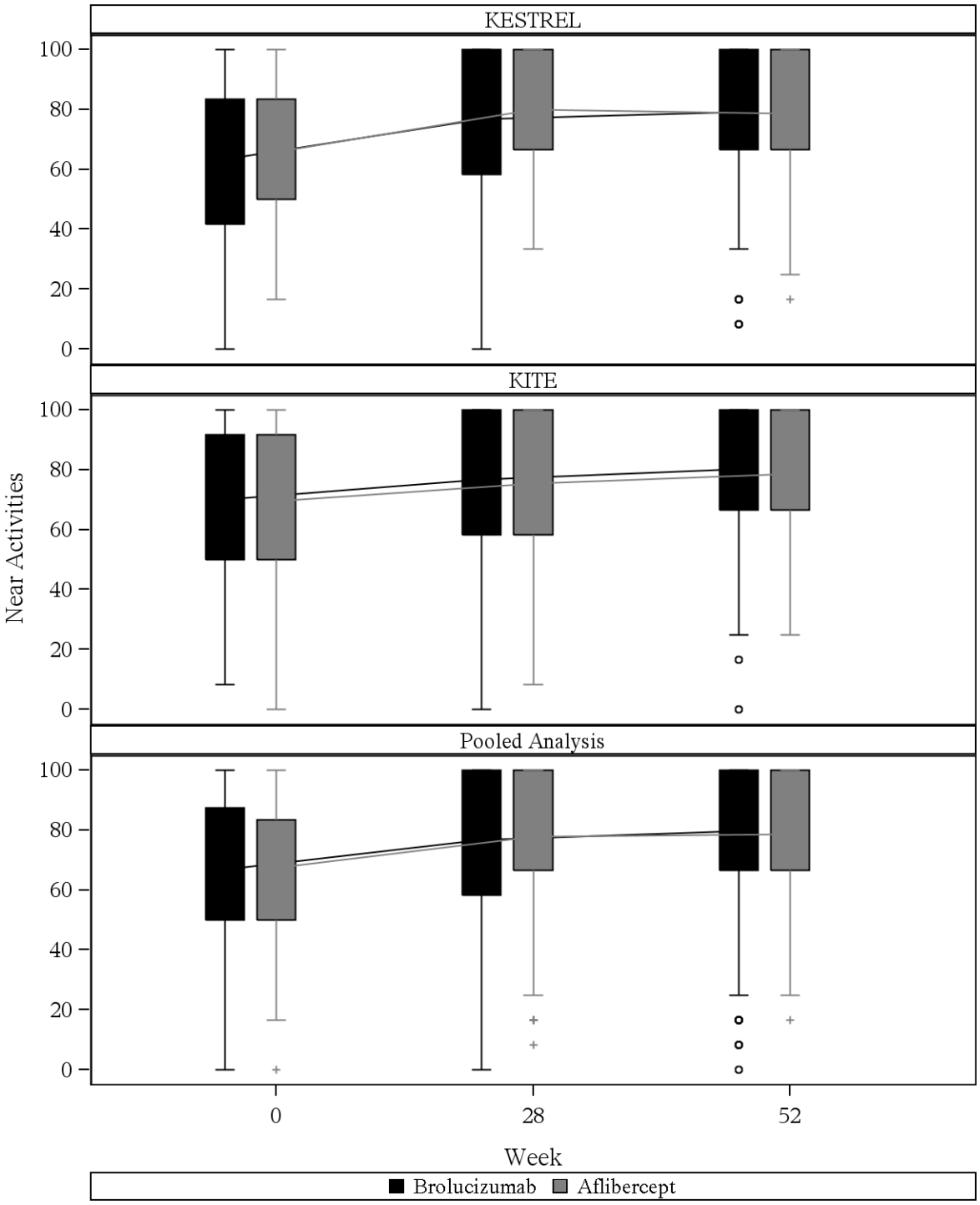


Figure 8.1.2.10 VFQ (FAS), boxplot, week 52, Ocular Pain

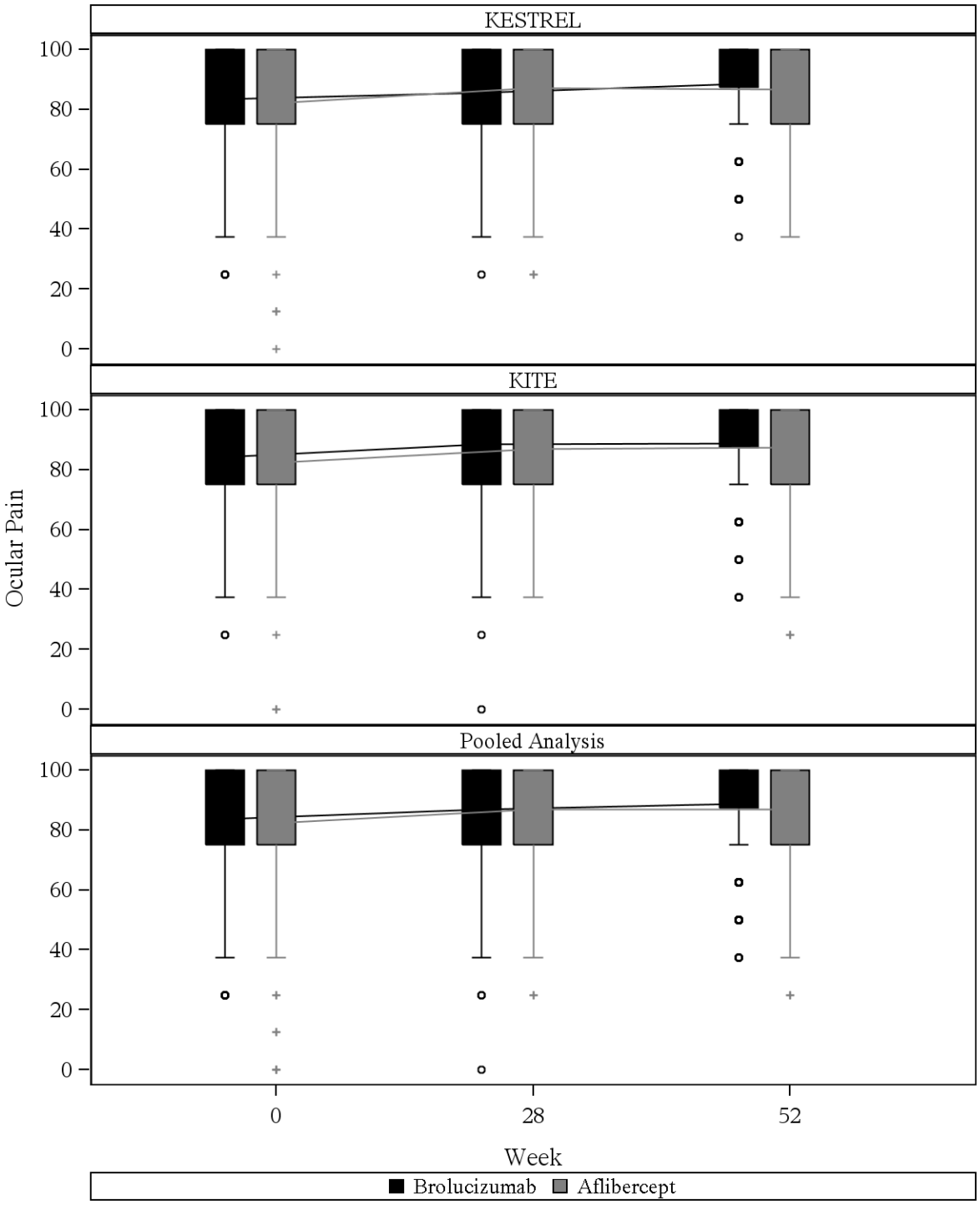


Figure 8.1.2.11 VFQ (FAS), boxplot, week 52, Peripheral Vision

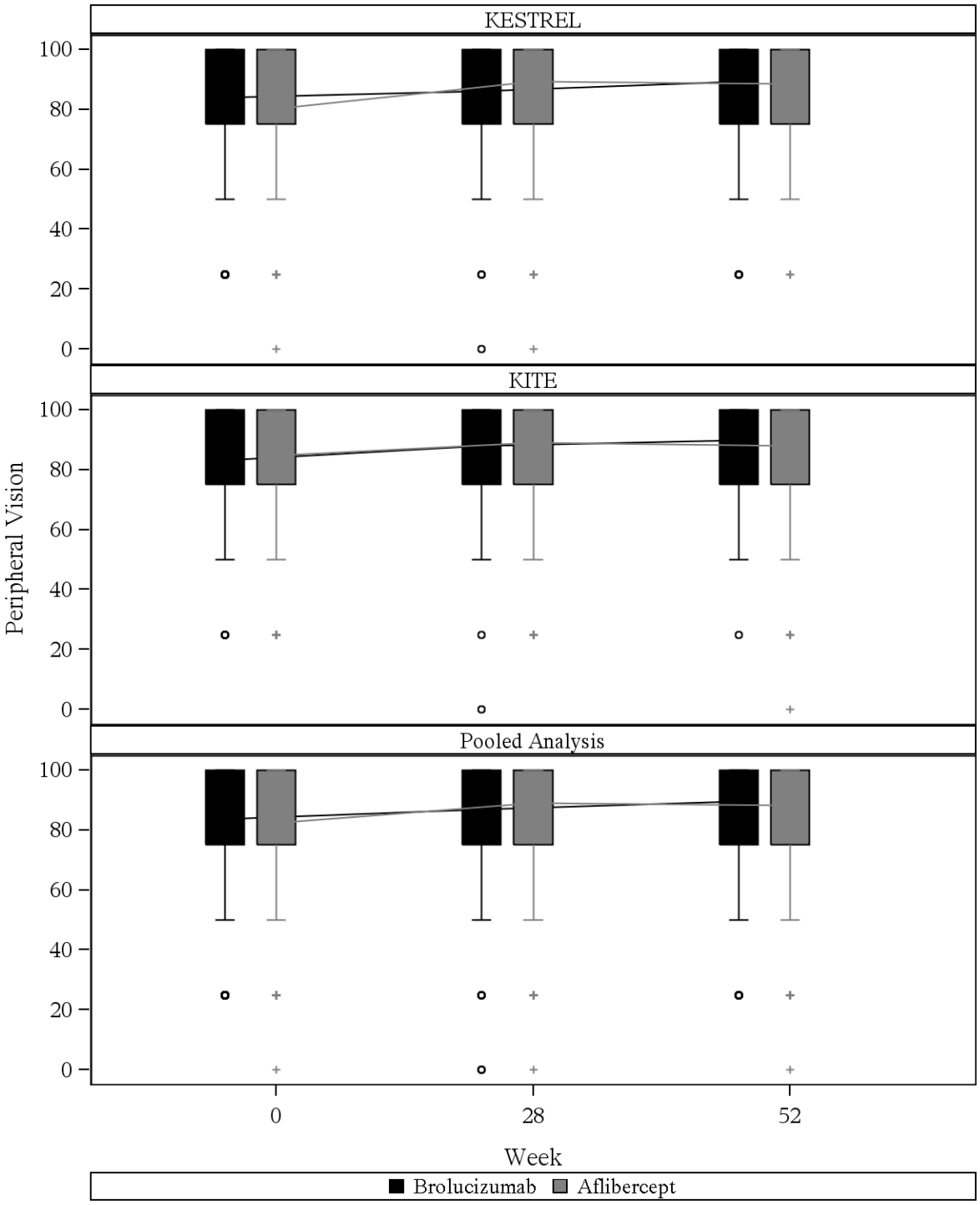


Figure 8.1.2.12 VFQ (FAS), boxplot, week 52, Role Difficulties

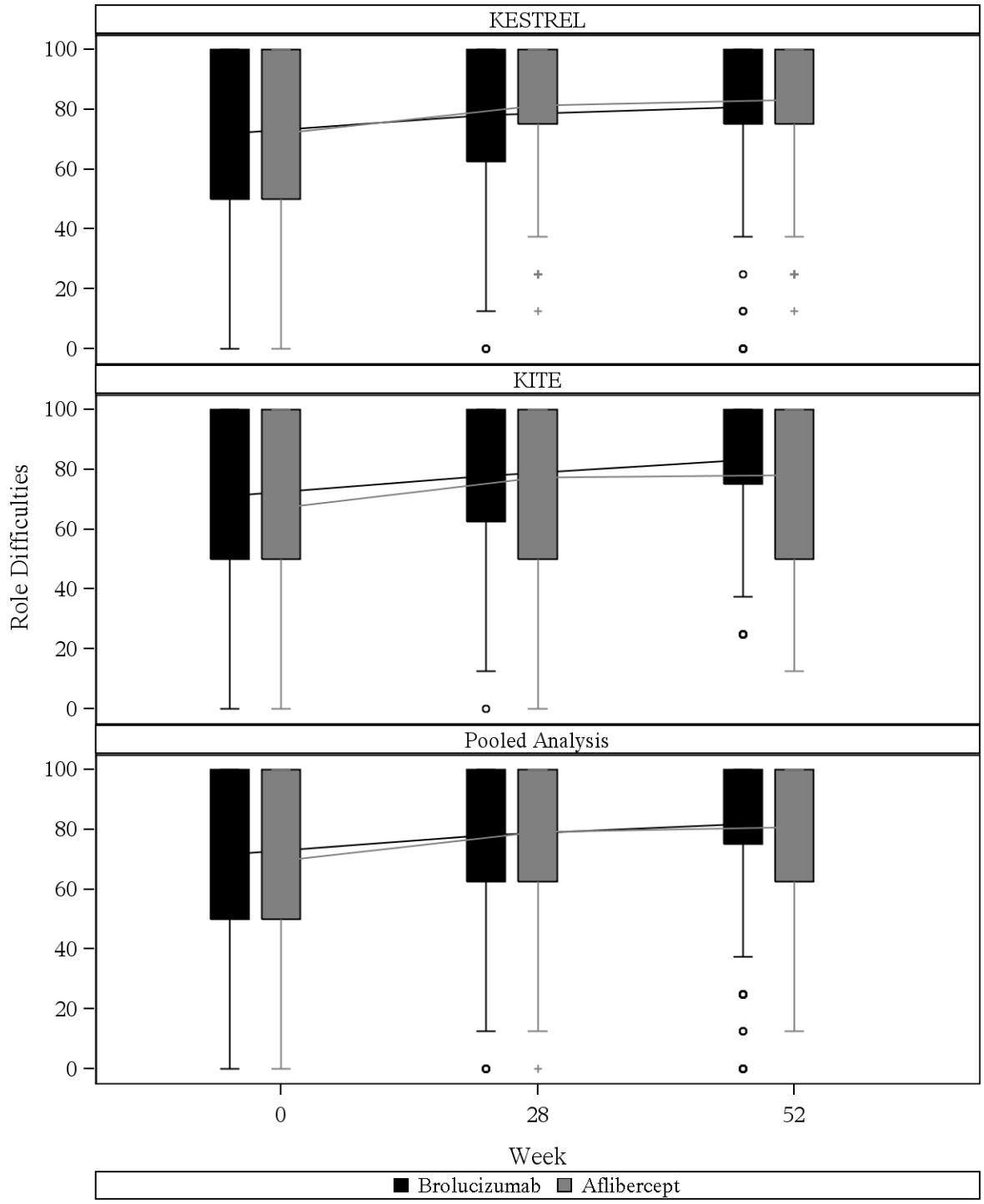


Figure 8.1.2.13 VFQ (FAS), boxplot, week 52, Social Functioning

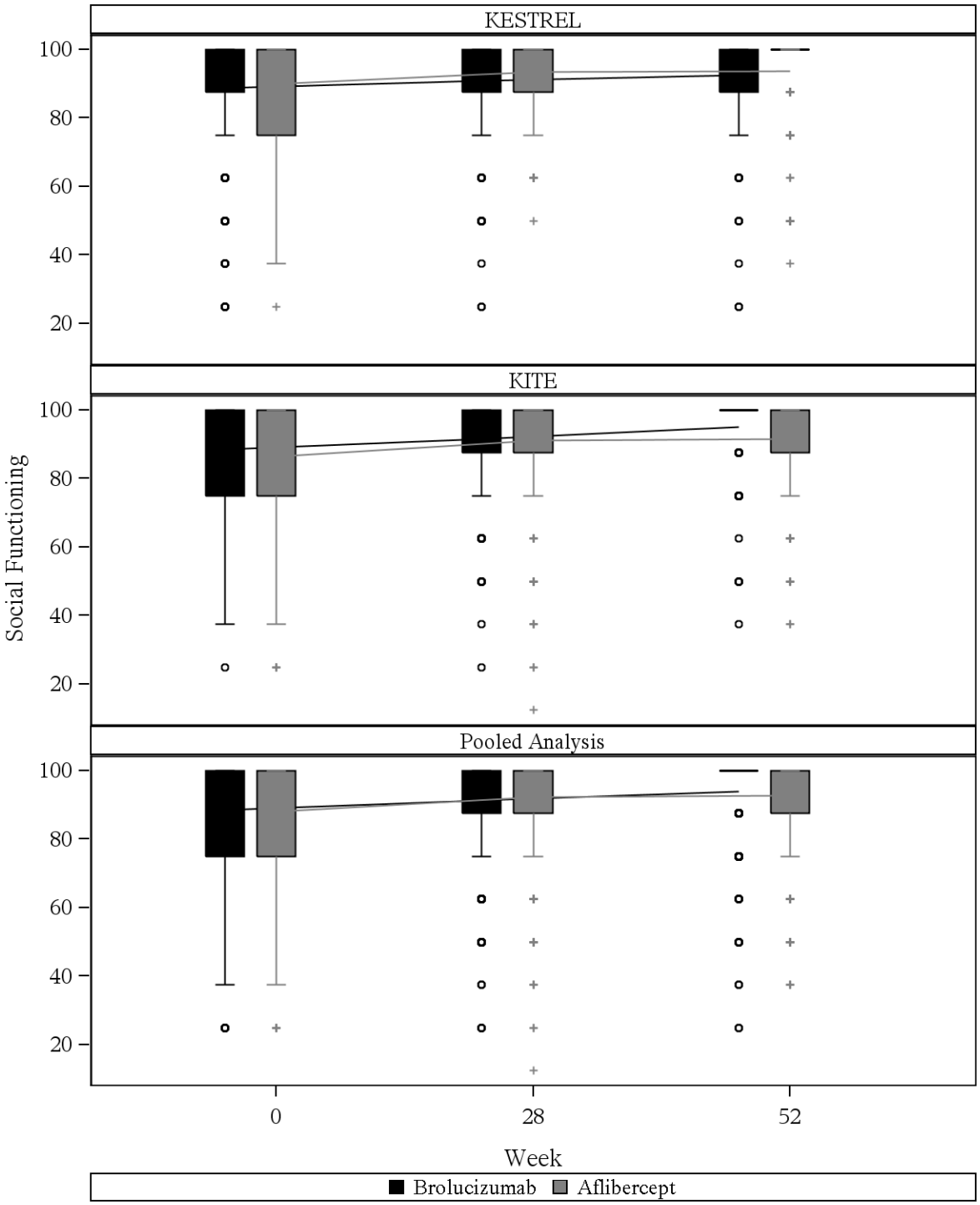


Figure 8.4.2 VFQ by BCVA (FAS), boxplot, week 52

Figure 8.4.2.1 VFQ by BCVA (FAS), boxplot, week 52, Driving

Figure 8.4.2.1.2 VFQ by BCVA (FAS), boxplot, week 52, Driving for Kite

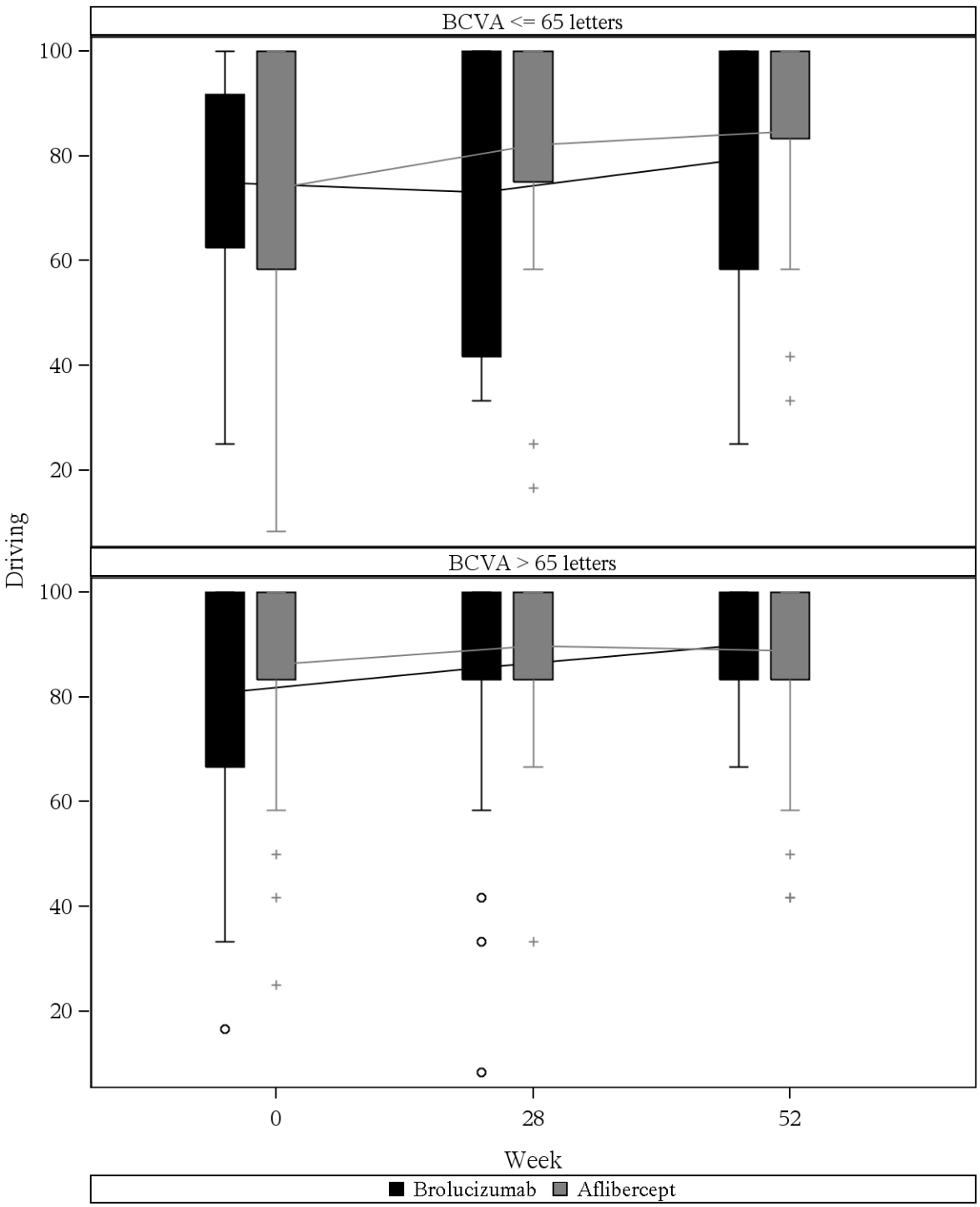


Figure 8.6.2 VFQ by diabetes type (FAS), boxplot, week 52

Figure 8.6.2.1 VFQ by diabetes type (FAS), boxplot, week 52, Distance Activities

Figure 8.6.2.1.2 VFQ by diabetes type (FAS), boxplot, week 52, Distance Activities for Kite

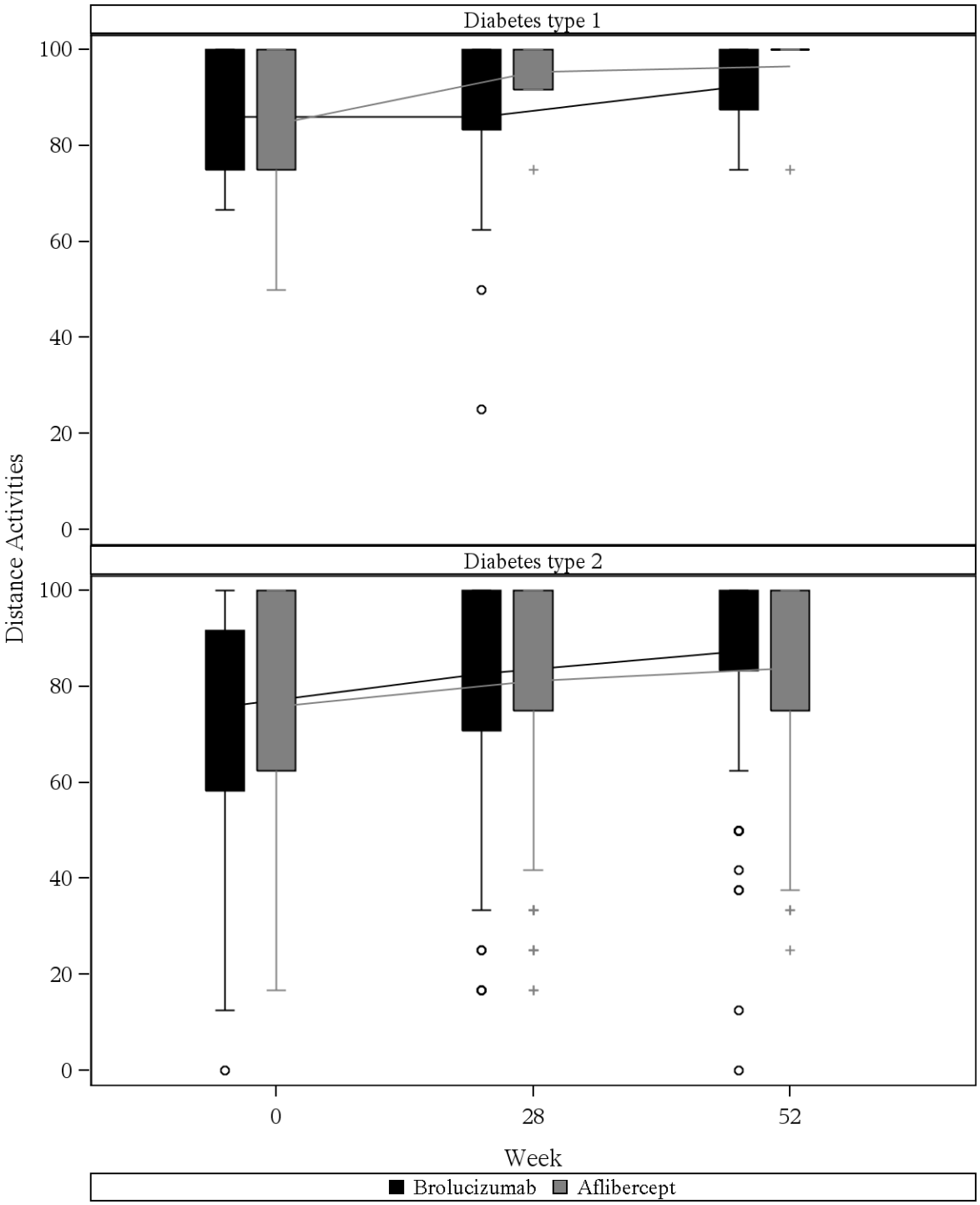


Figure 8.6.2.2 VFQ by diabetes type (FAS), boxplot, week 52, Peripheral Vision

Figure 8.6.2.2.2 VFQ by diabetes type (FAS), boxplot, week 52, Peripheral Vision for Kite

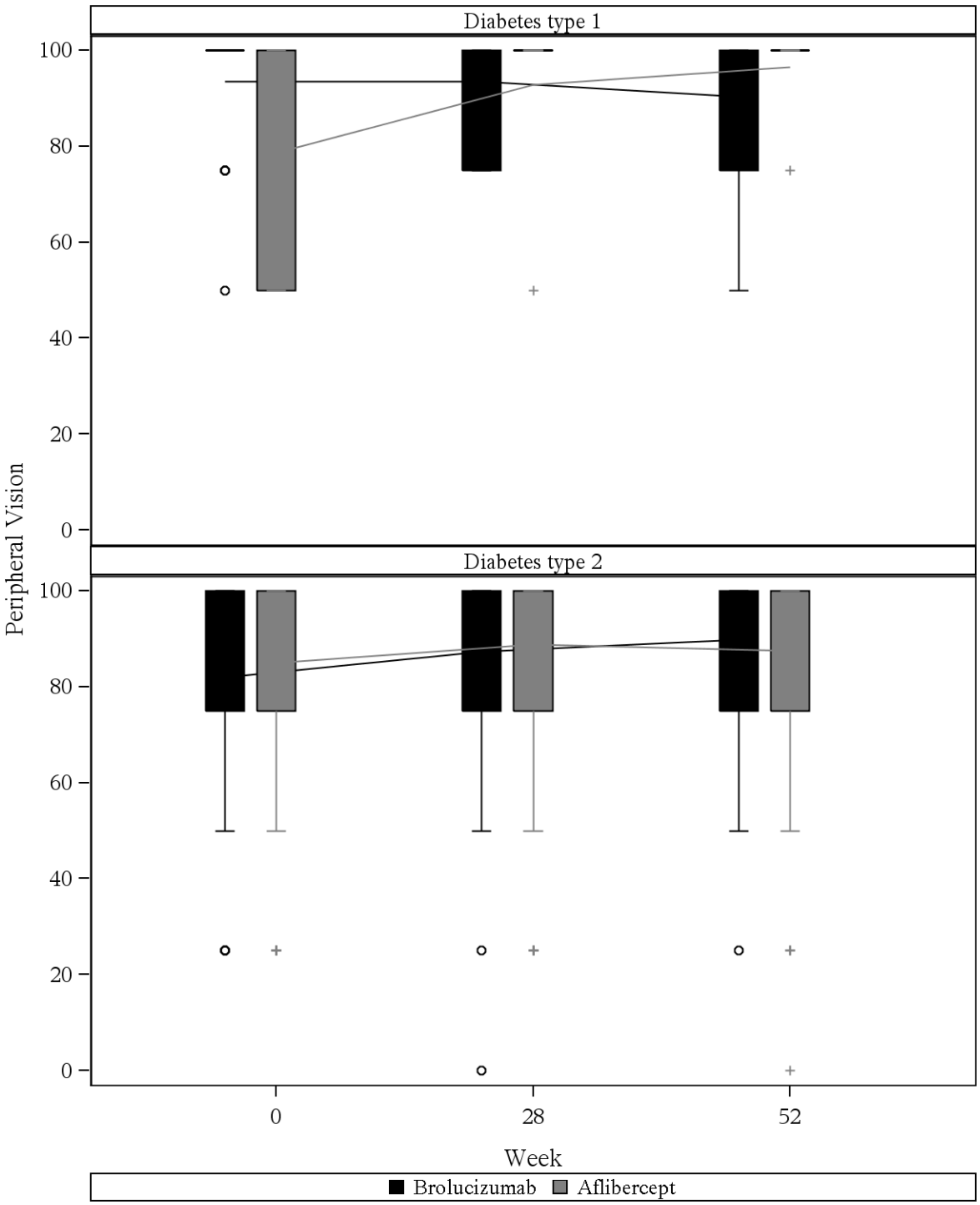


Figure 8.7.2 VFQ by HbA1c (FAS), boxplot, week 52

Figure 8.7.2.1 VFQ by HbA1c (FAS), boxplot, week 52, Composite Score

Figure 8.7.2.1.1 VFQ by HbA1c (FAS), boxplot, week 52, Composite Score for Kestrel

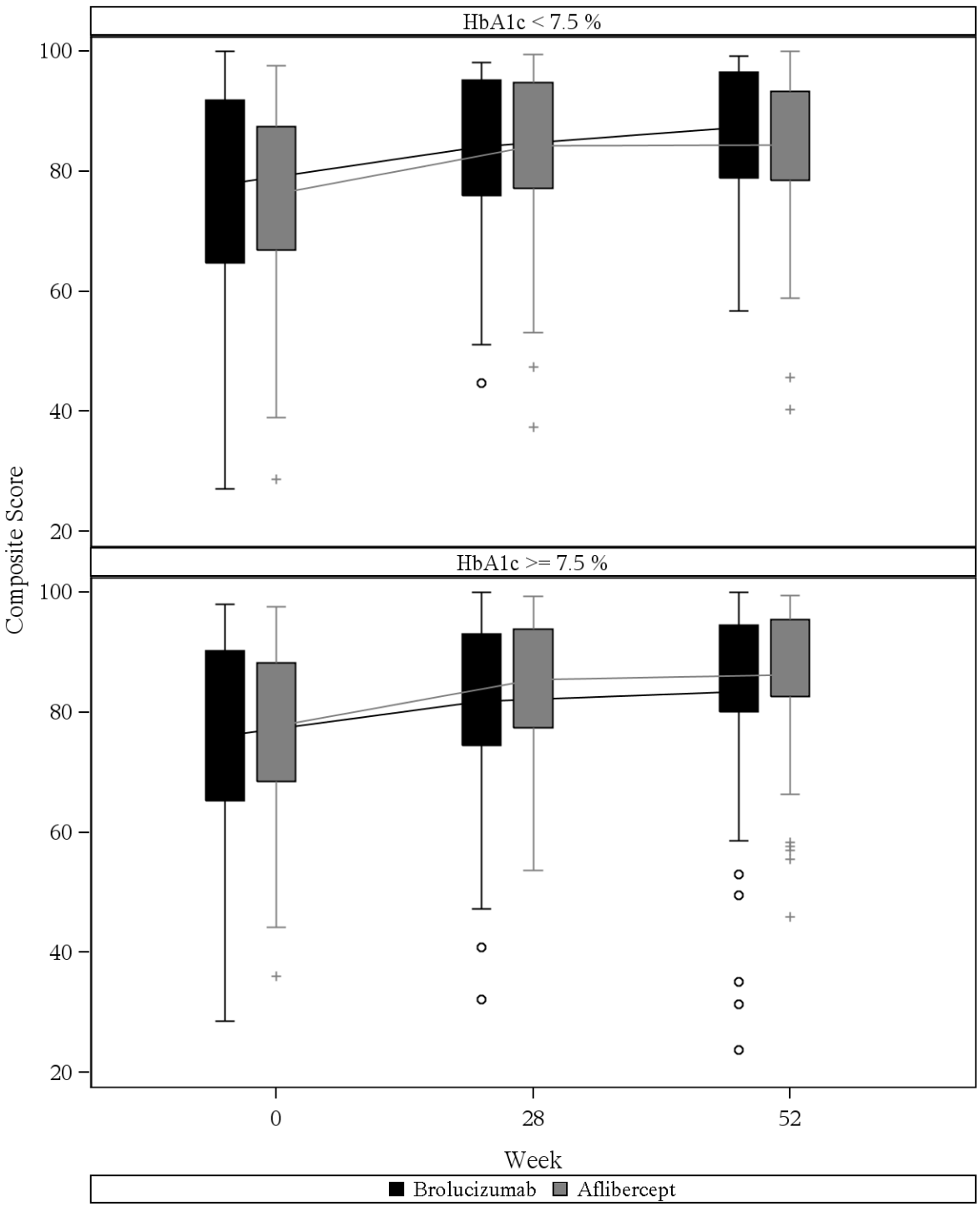


Figure 8.7.2.2 VFQ by HbA1c (FAS), boxplot, week 52, Distance Activities

Figure 8.7.2.2.1 VFQ by HbA1c (FAS), boxplot, week 52, Distance Activities for Kestrel

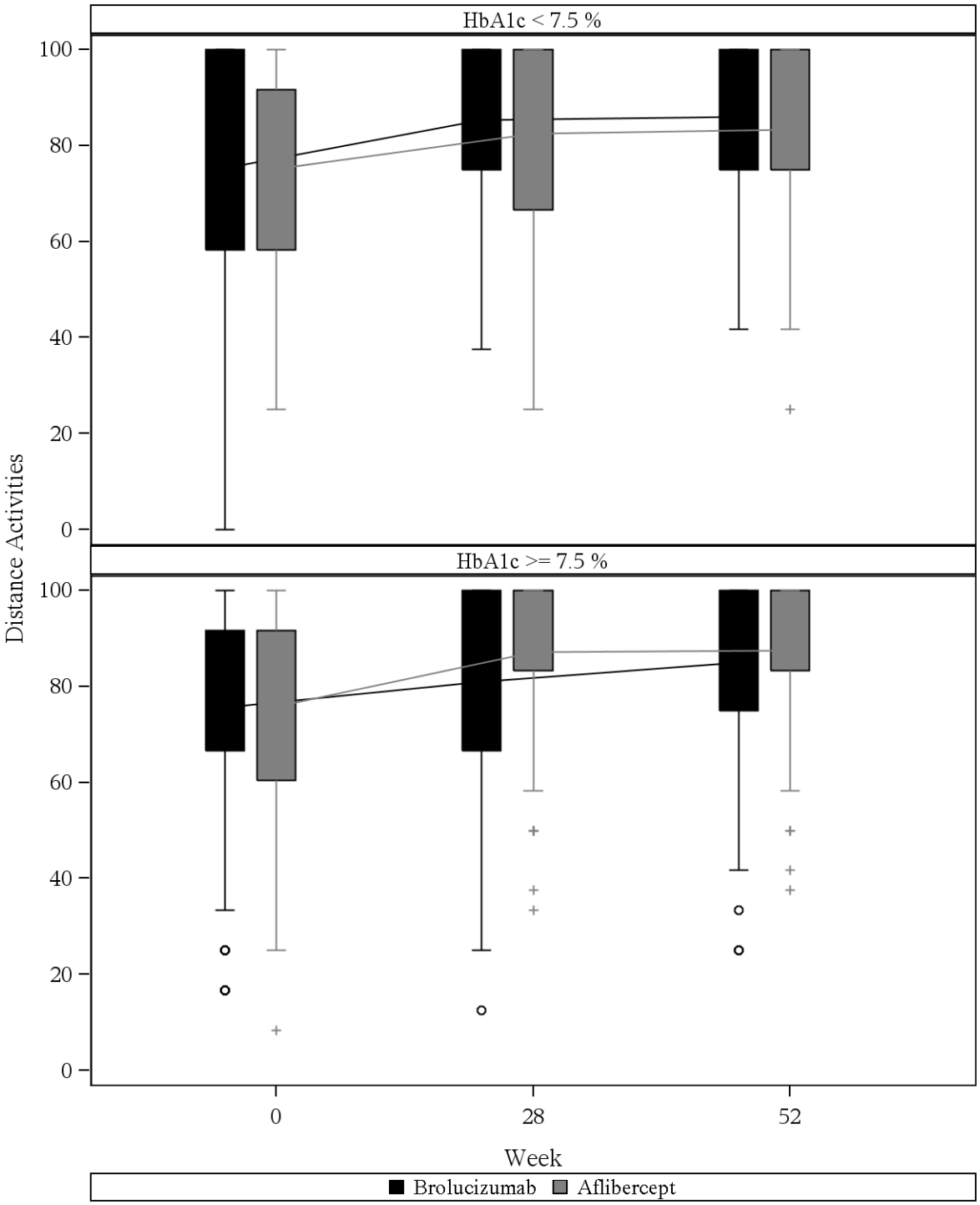


Figure 8.7.2.2.3 VFQ by HbA1c (FAS), boxplot, week 52, Distance Activities for Pooled Analysis

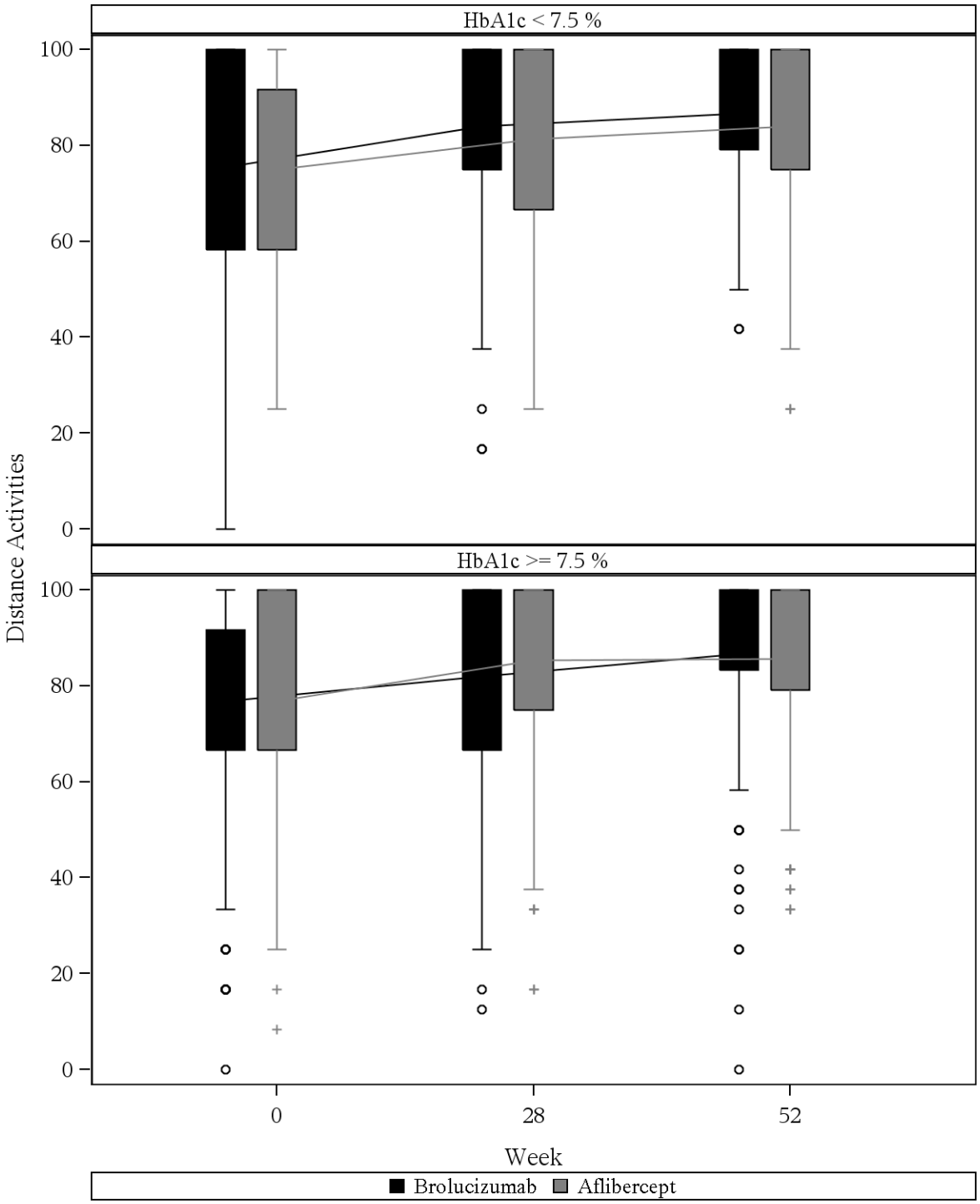


Figure 8.7.2.3 VFQ by HbA1c (FAS), boxplot, week 52, Ocular Pain

Figure 8.7.2.3.1 VFQ by HbA1c (FAS), boxplot, week 52, Ocular Pain for Kestrel

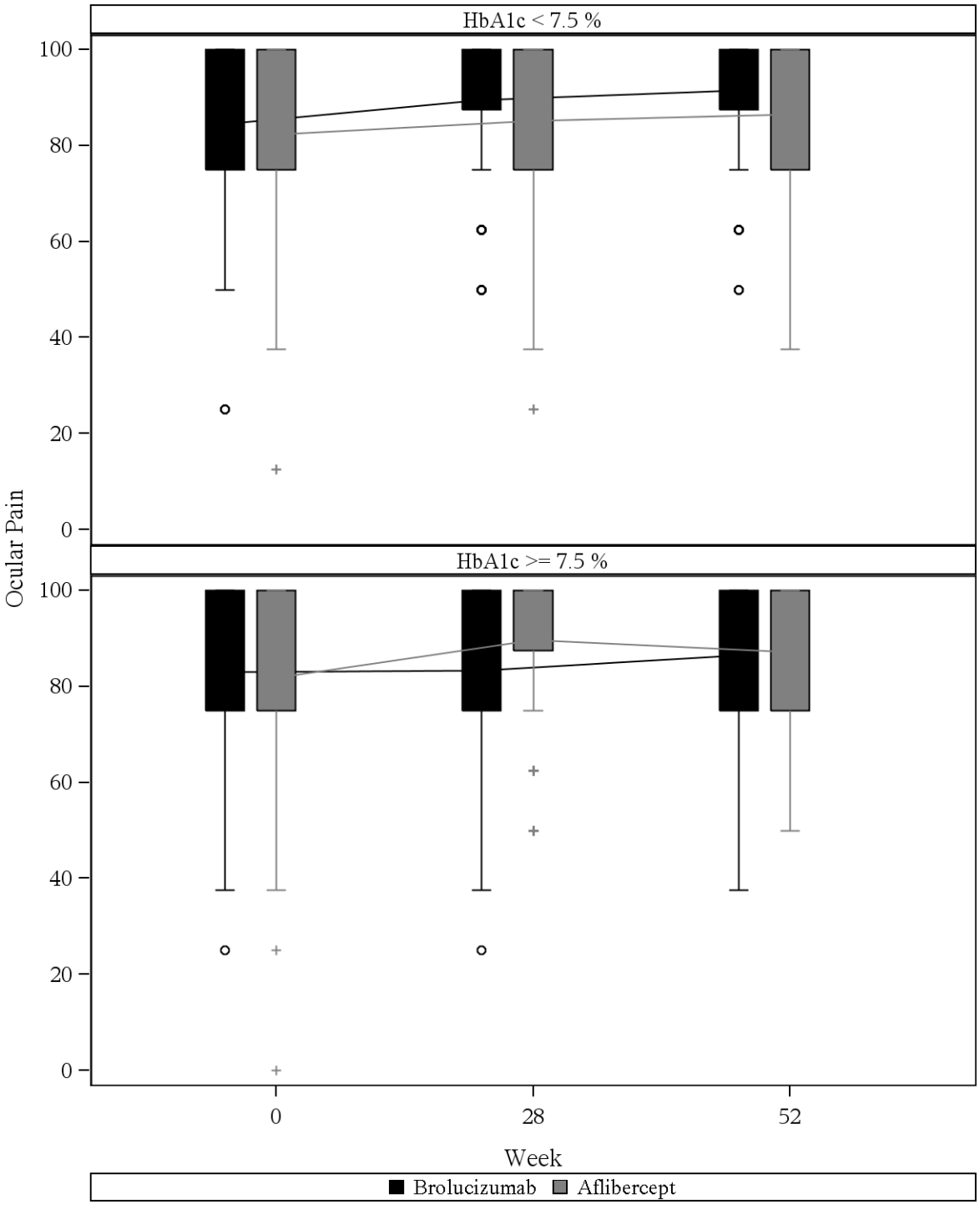


Figure 8.7.2.3.3 VFQ by HbA1c (FAS), boxplot, week 52, Ocular Pain for Pooled Analysis

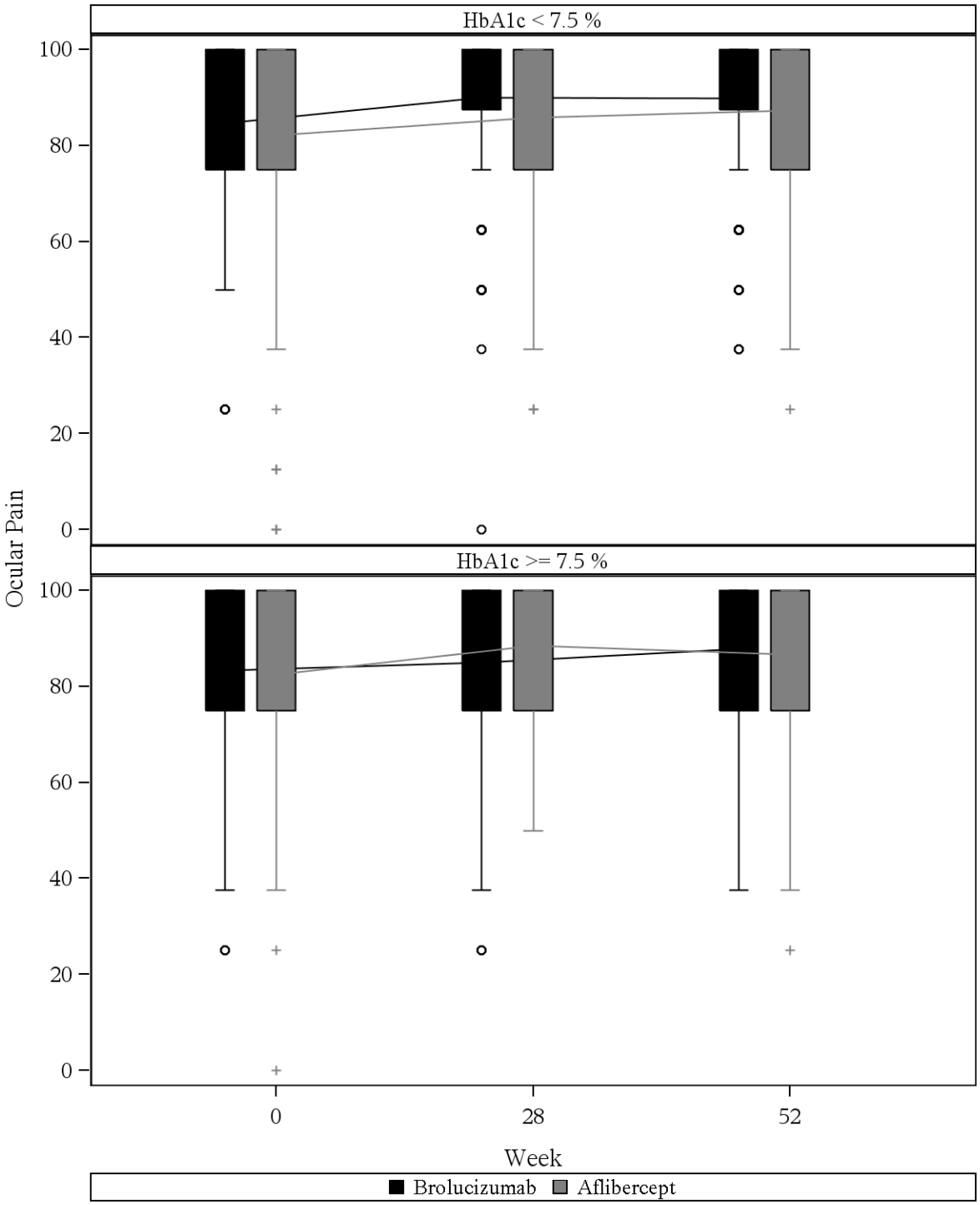


Figure 8.7.2.4 VFQ by HbA1c (FAS), boxplot, week 52, Peripheral Vision

Figure 8.7.2.4.1 VFQ by HbA1c (FAS), boxplot, week 52, Peripheral Vision for Kestrel

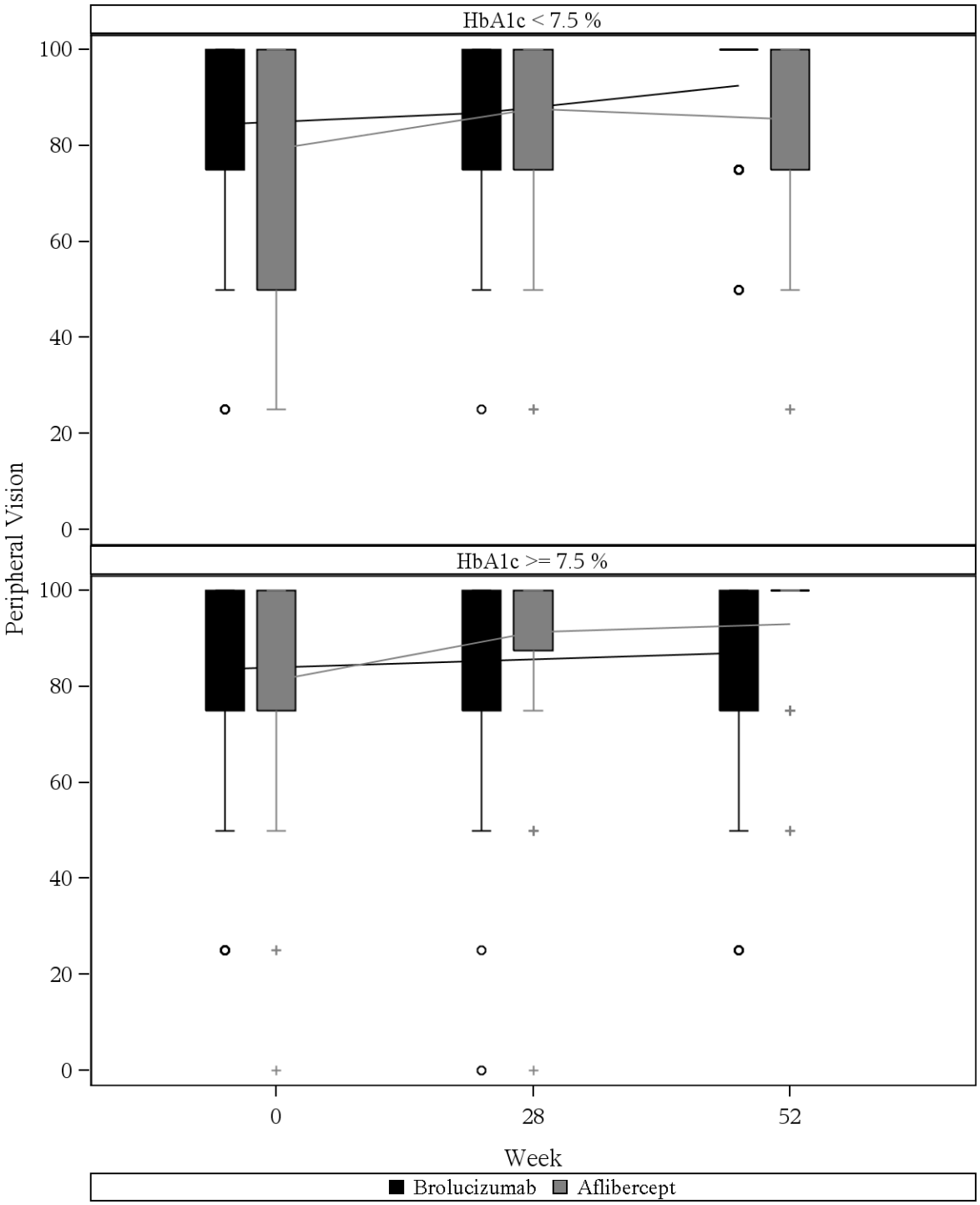


Figure 8.7.2.4.3 VFQ by HbA1c (FAS), boxplot, week 52, Peripheral Vision for Pooled Analysis

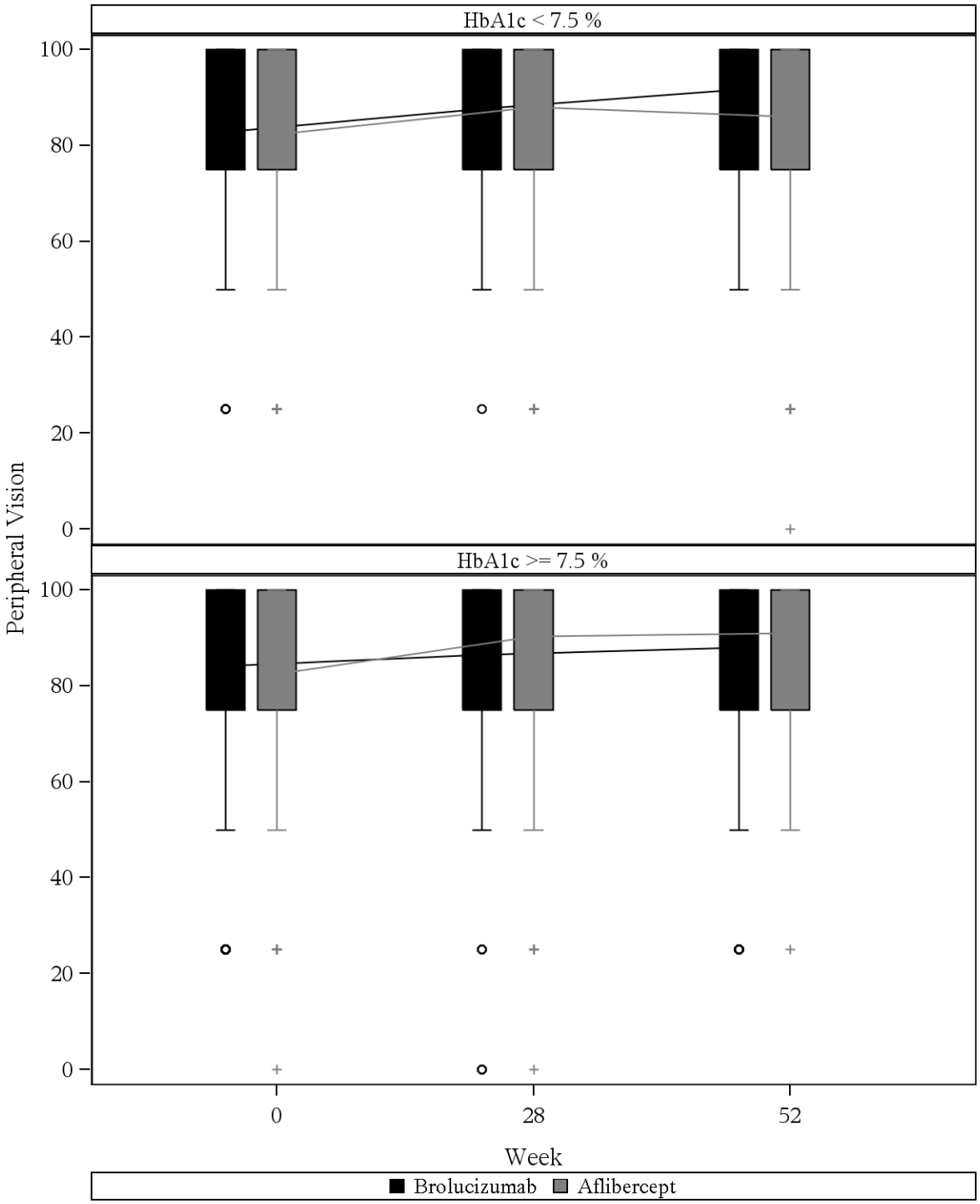


Figure 8.11.2 VFQ by status of SRF (FAS), boxplot, week 52

Figure 8.11.2.1 VFQ by status of SRF (FAS), boxplot, week 52, Composite Score

Figure 8.11.2.1.1 VFQ by status of SRF (FAS), boxplot, week 52, Composite Score for Kestrel

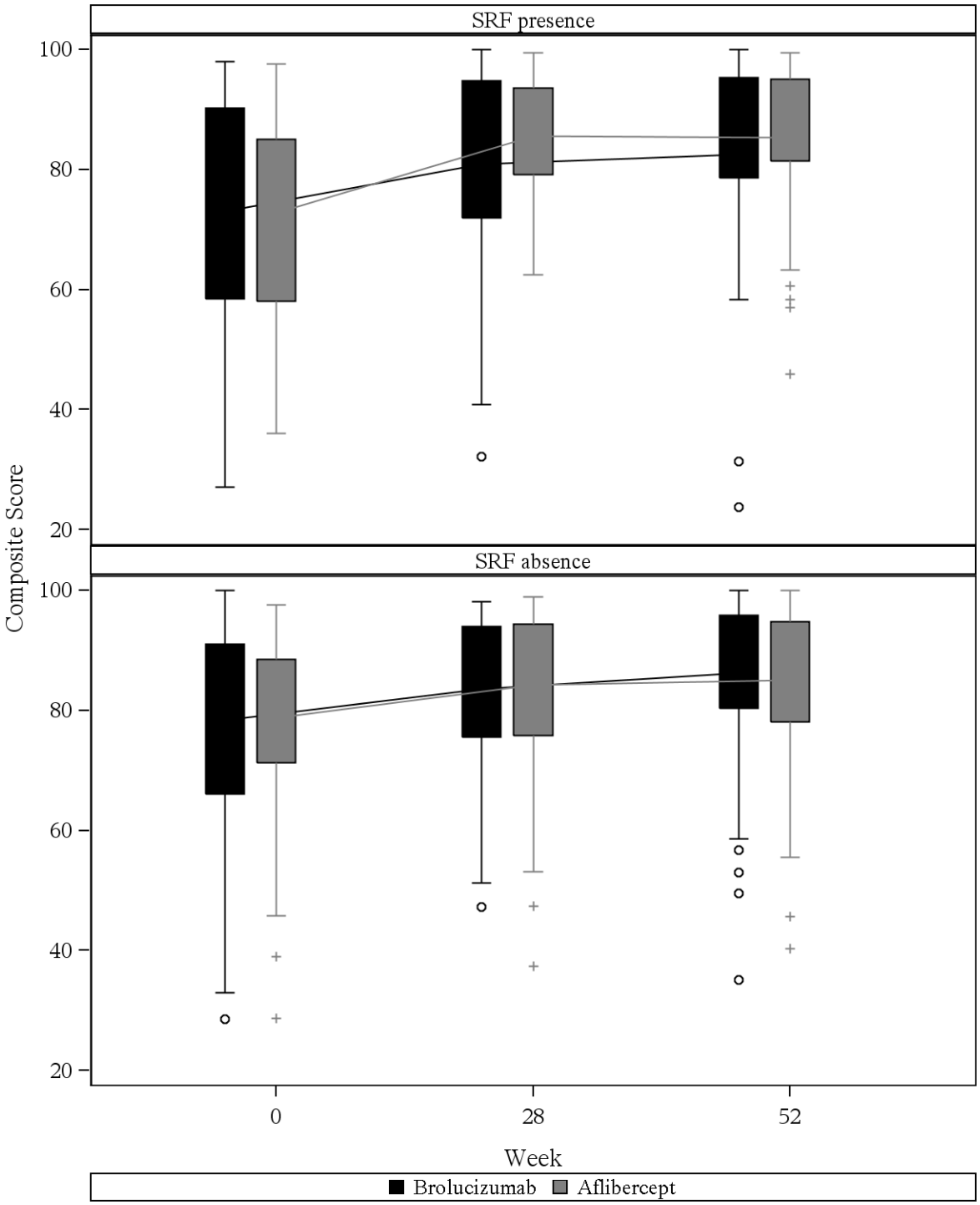
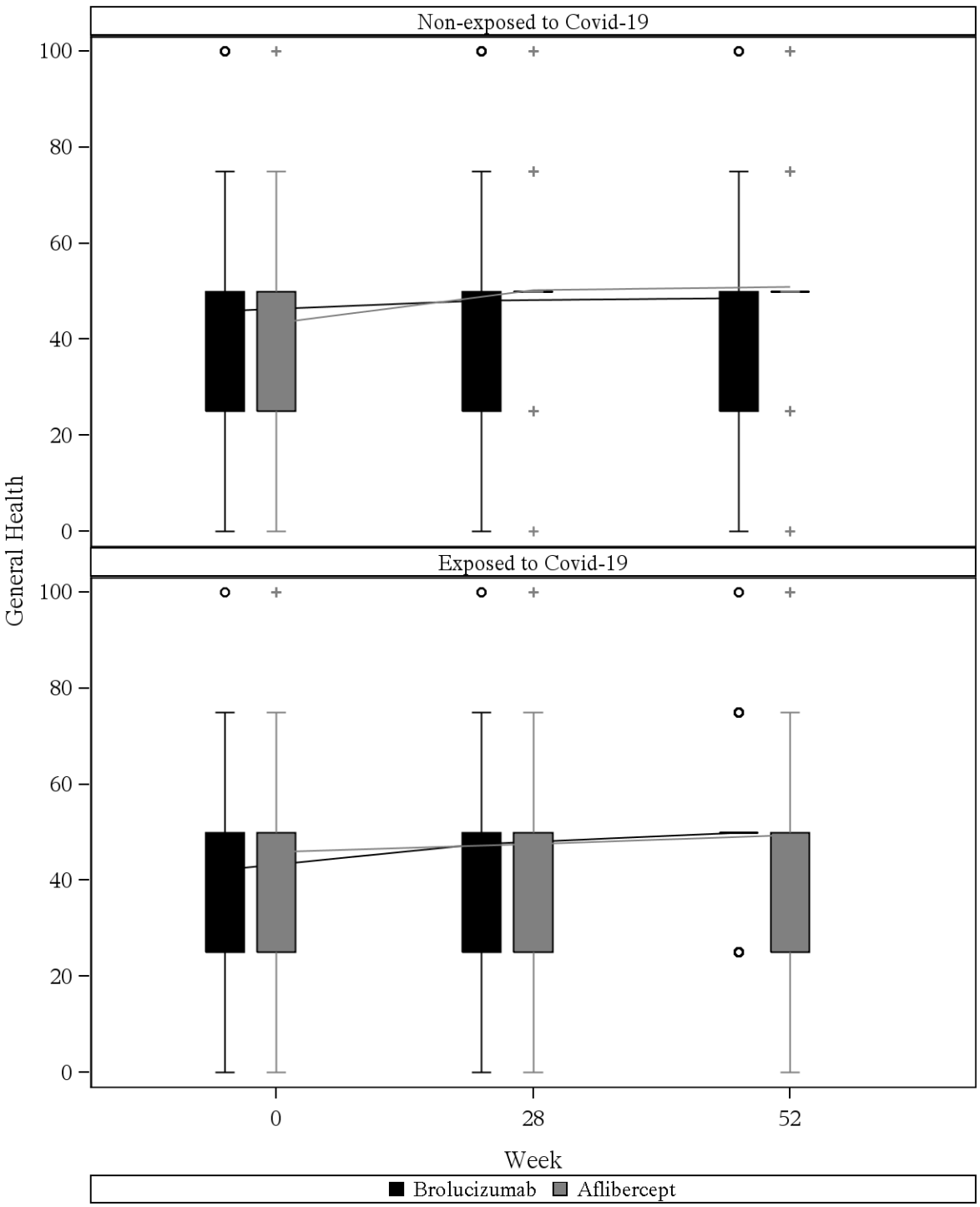


Figure 8.12.2 VFQ by exposure (FAS), boxplot, week 52

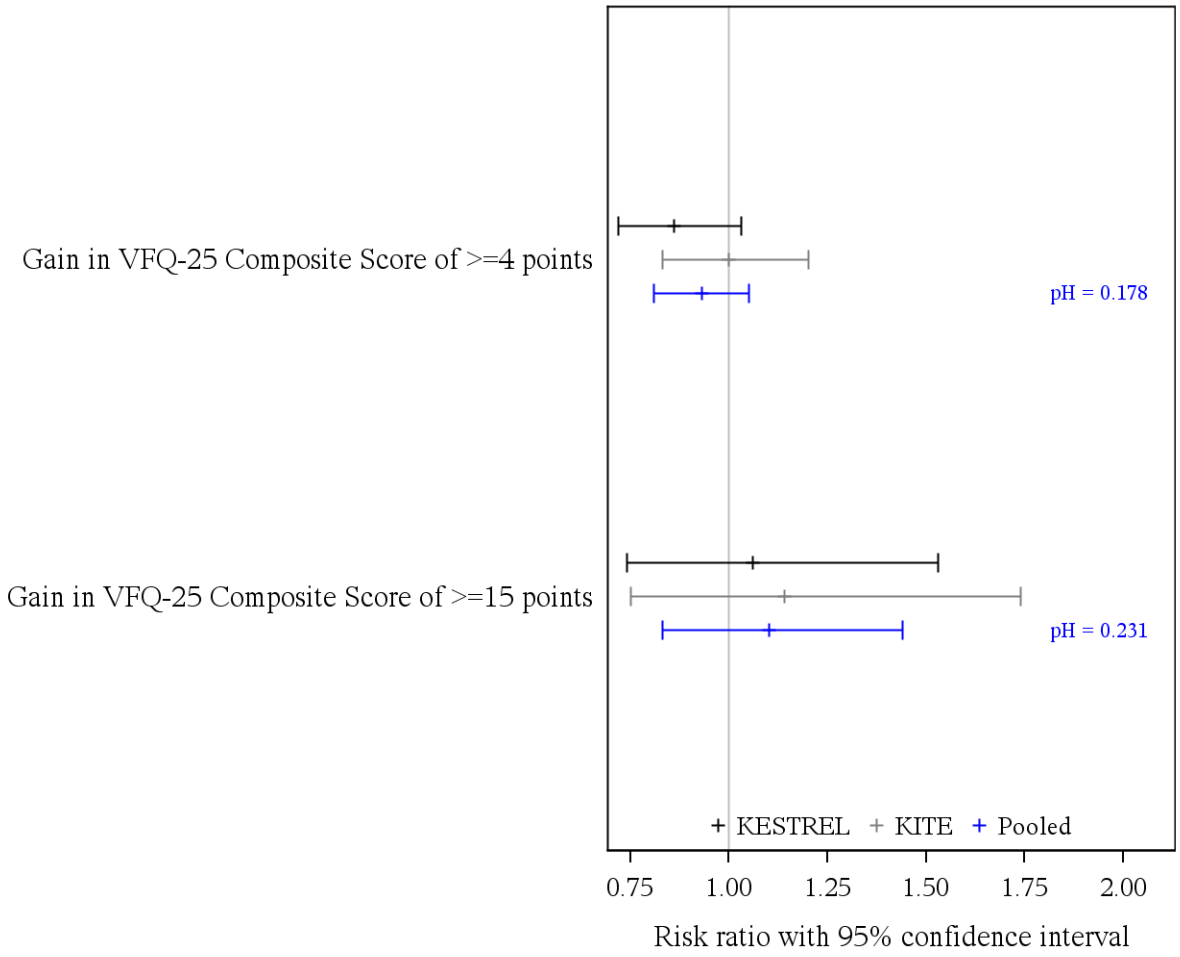
Figure 8.12.2.1 VFQ by exposure (FAS), boxplot, week 52, General Health

Figure 8.12.2.1.2 VFQ by exposure (FAS), boxplot, week 52, General Health for Kite



9 VFQ: Binary analysis (Gain)

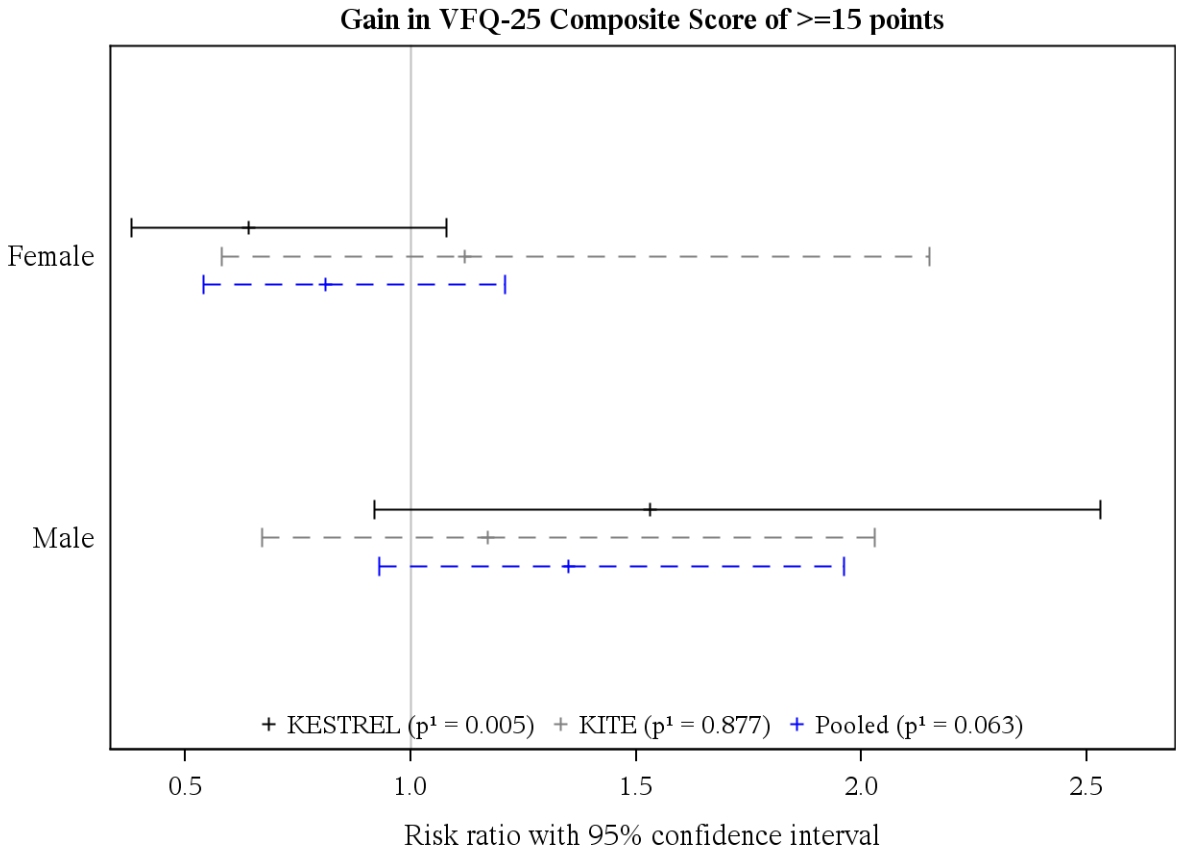
Figure 9.1 VFQ - Gain of 4 respectively 15 points (FAS), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 9.3 VFQ - Gain of 4 respectively 15 points by gender (FAS), forest plot, week 52

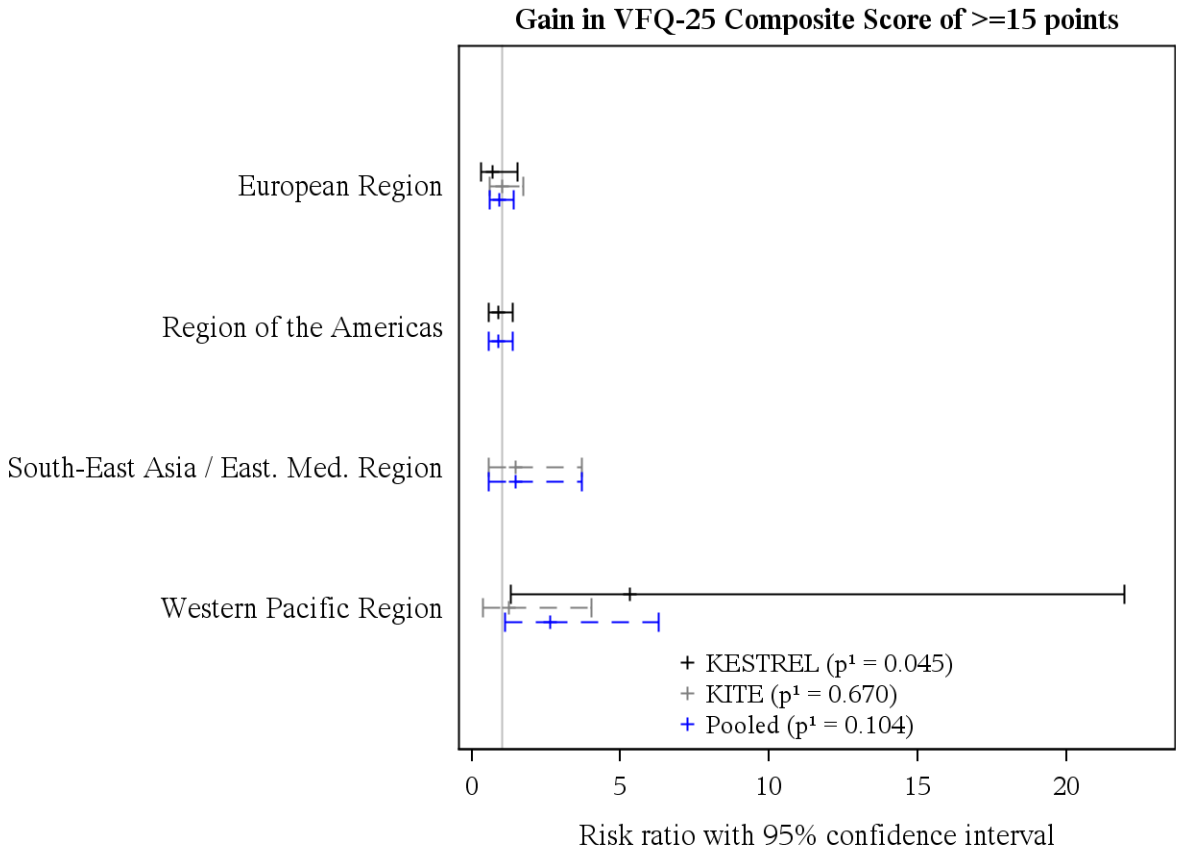
Figure 9.3.1 VFQ - Gain of 4 respectively 15 points by gender (FAS), forest plot, week 52, gain of >=15 points



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 9.5 VFQ - Gain of 4 respectively 15 points by region (FAS), forest plot, week 52

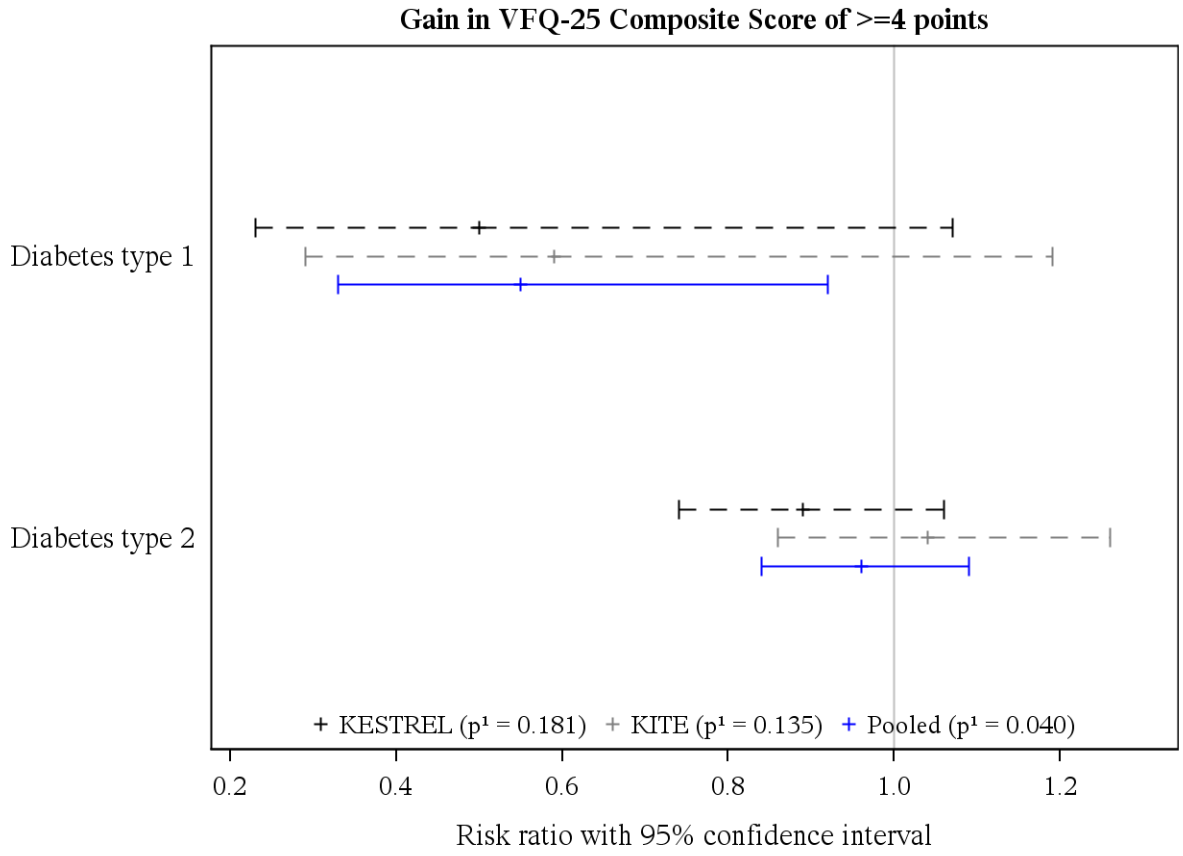
Figure 9.5.1 VFQ - Gain of 4 respectively 15 points by region (FAS), forest plot, week 52, gain of >=15 points



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 9.6 VFQ - Gain of 4 respectively 15 points by diabetes type (FAS), forest plot, week 52

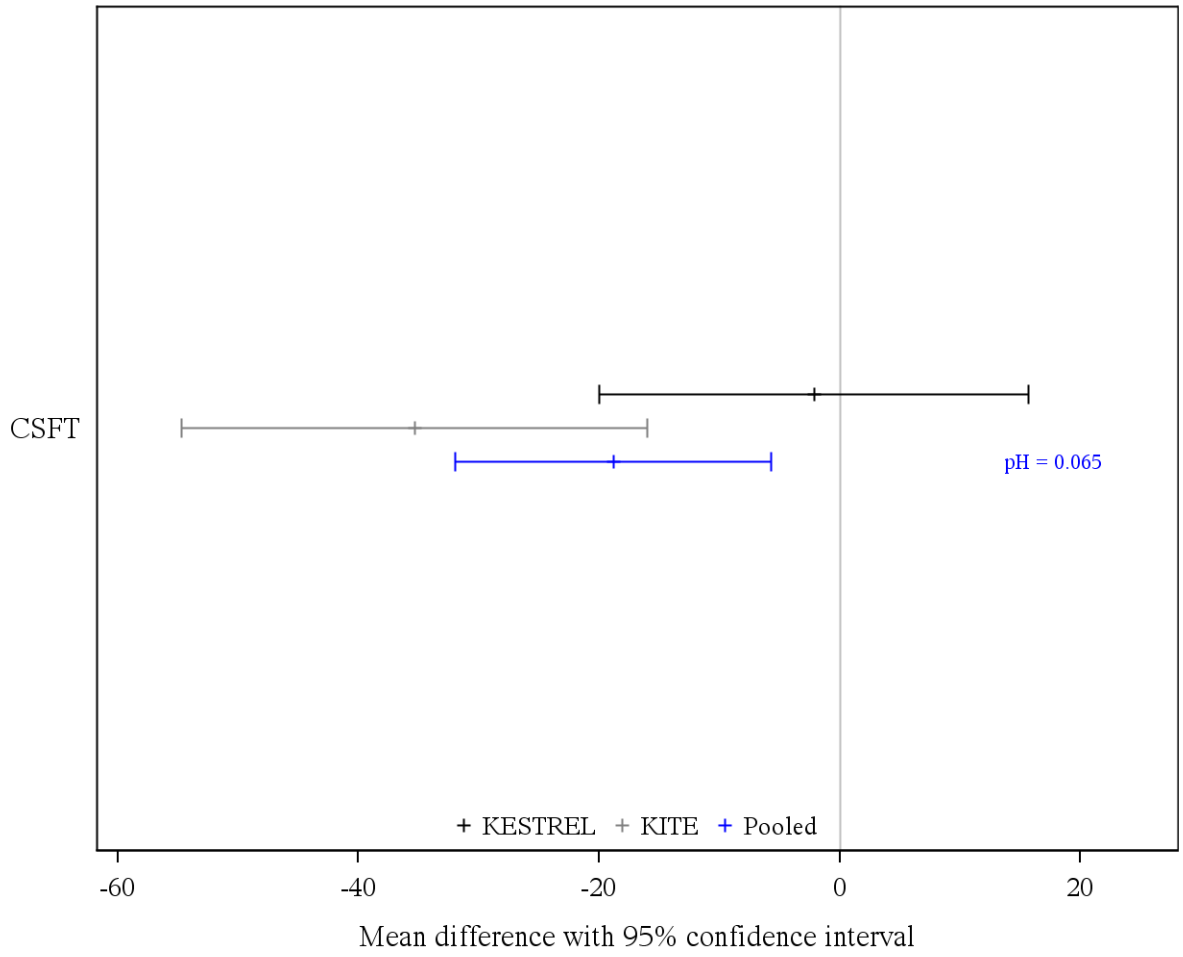
Figure 9.6.1 VFQ - Gain of 4 respectively 15 points by diabetes type (FAS), forest plot, week 52, gain of >=4 points



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: $p_H = 0.178$

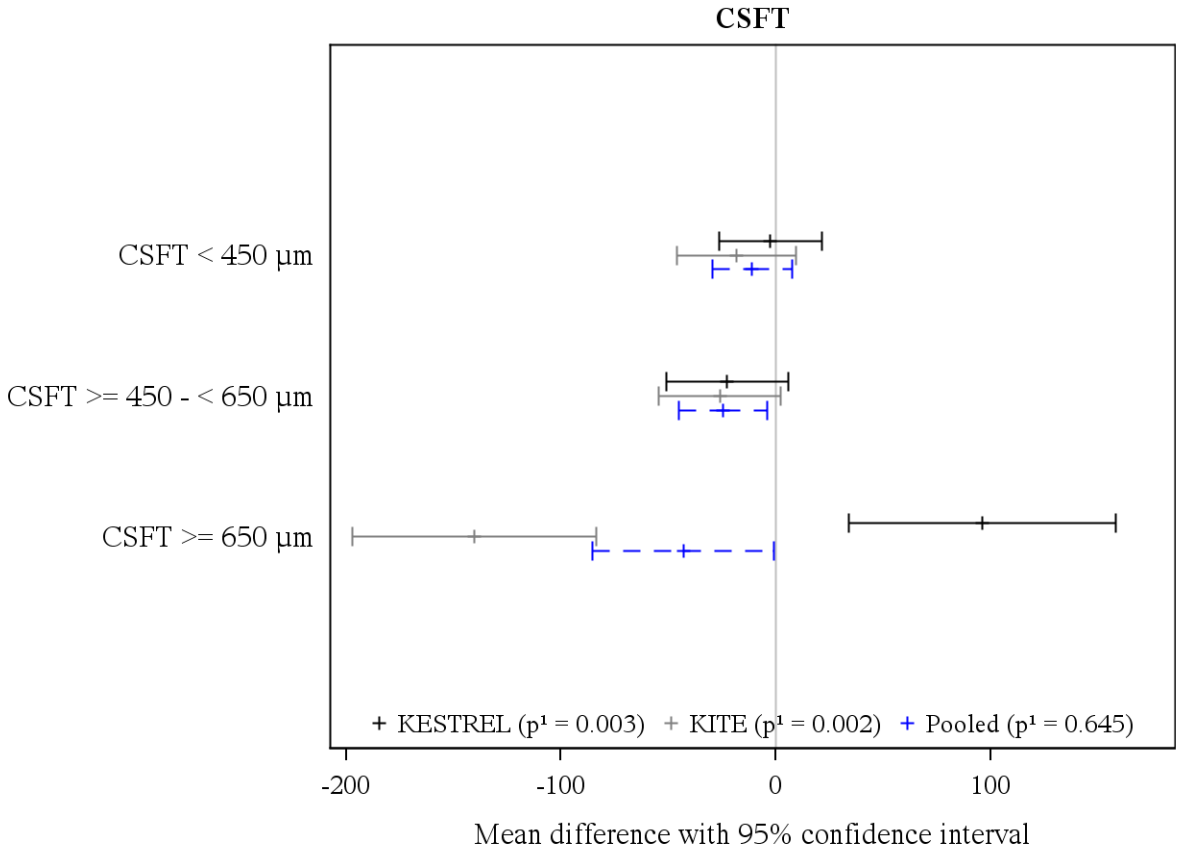
10 CSFT: Continuous analysis

Figure 10.1 CSFT (FAS), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

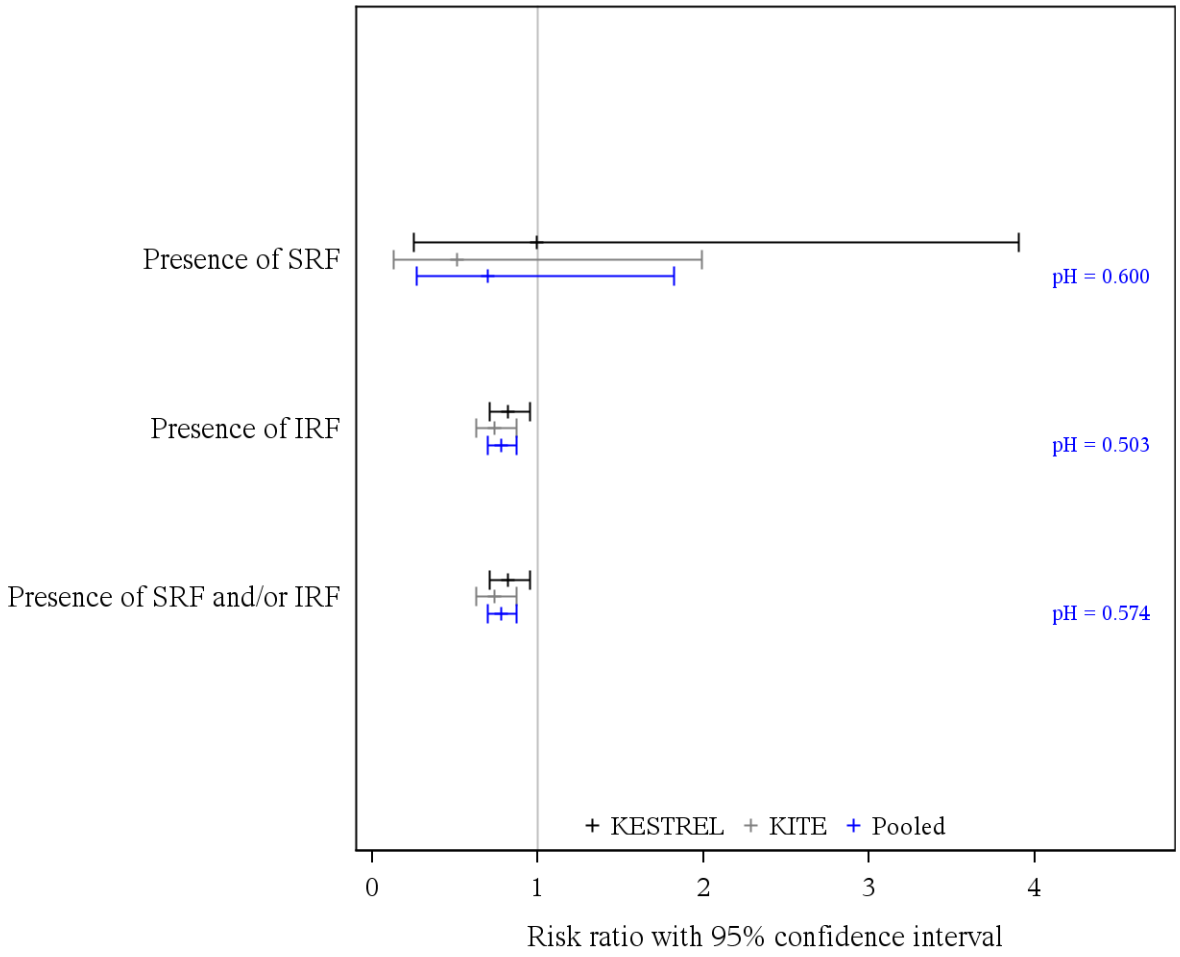
Figure 10.10 CSFT by CSFT (FAS), forest plot, week 52



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: $p_H = 0.065$

11 Presence of SRF and/or IRF in the study eye: Binary analysis

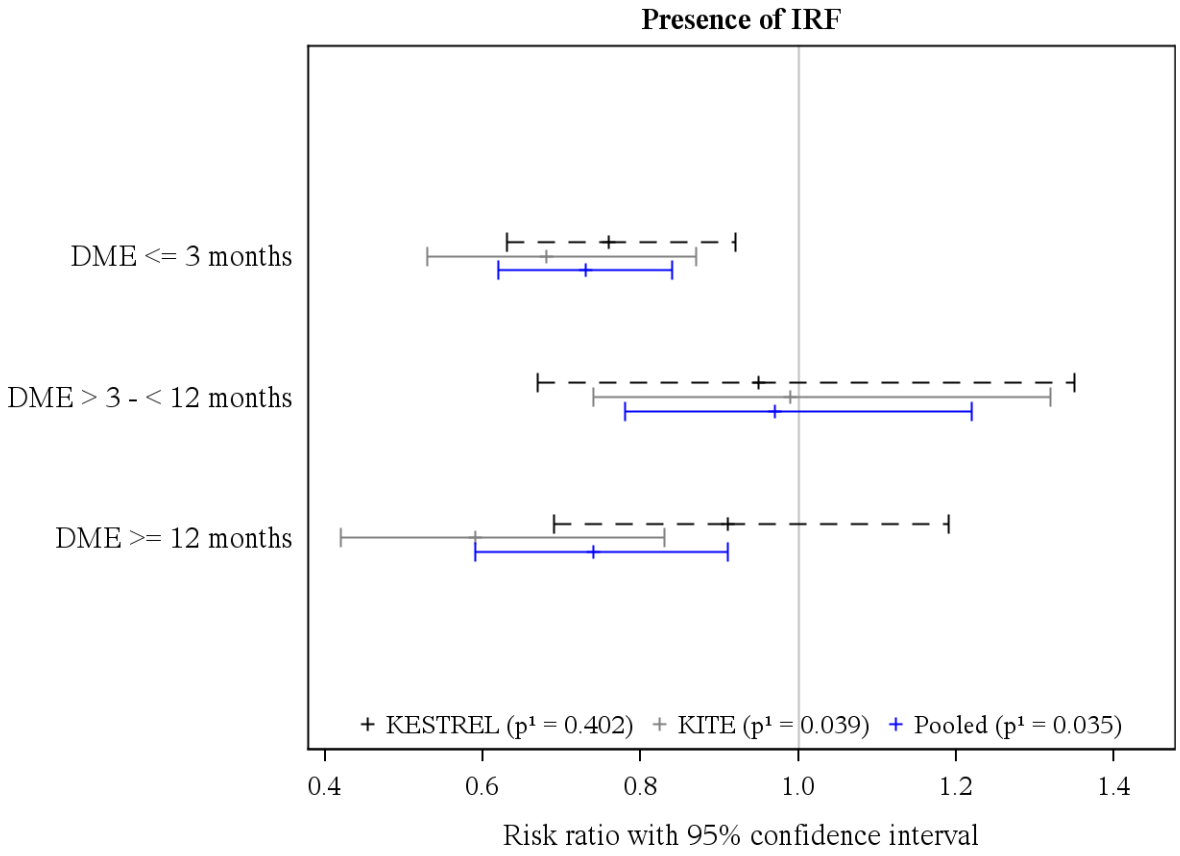
Figure 11.1 Presence of SRF and/or IRF in the study eye (FAS), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 11.8 Presence of SRF and/or IRF in the study eye by duration of DME (FAS), forest plot, week 52

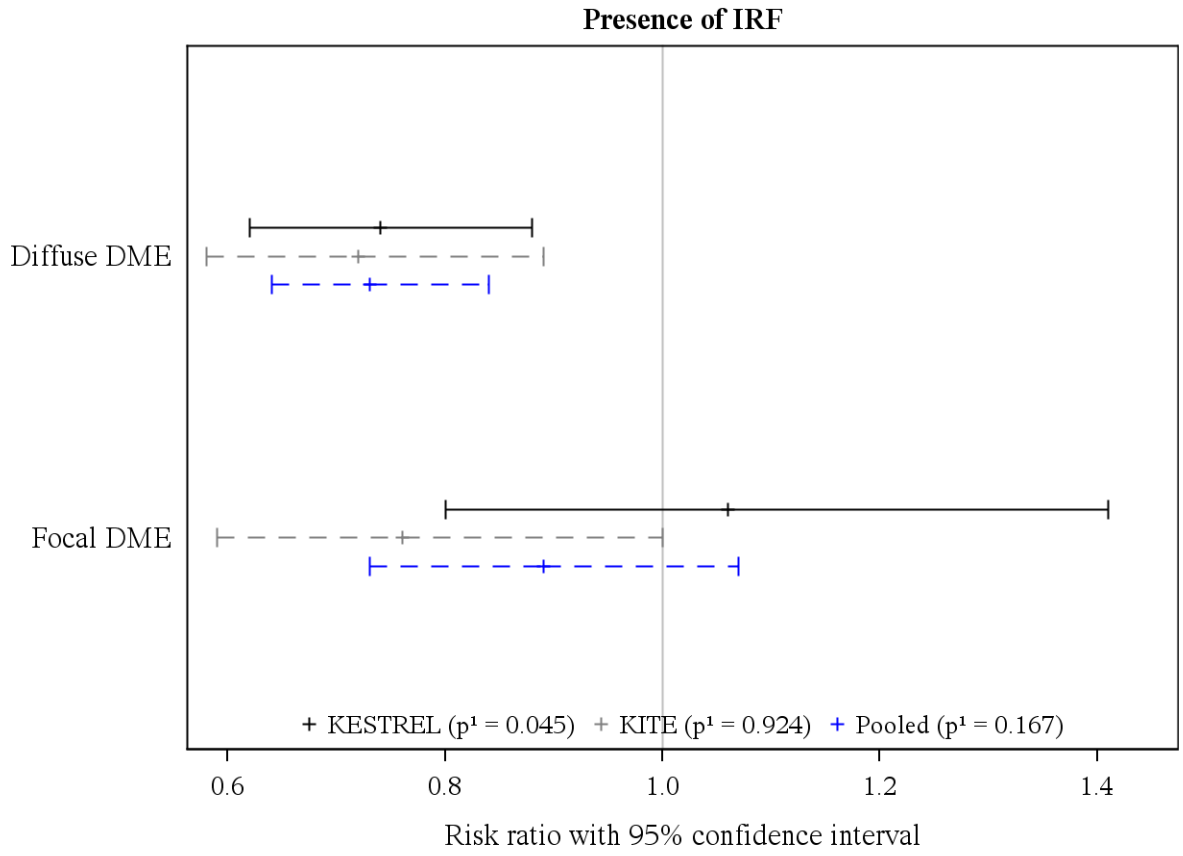
Figure 11.8.1 Presence of SRF and/or IRF in the study eye by duration of DME (FAS), forest plot, week 52, Presence of IRF



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: $p_H = 0.503$

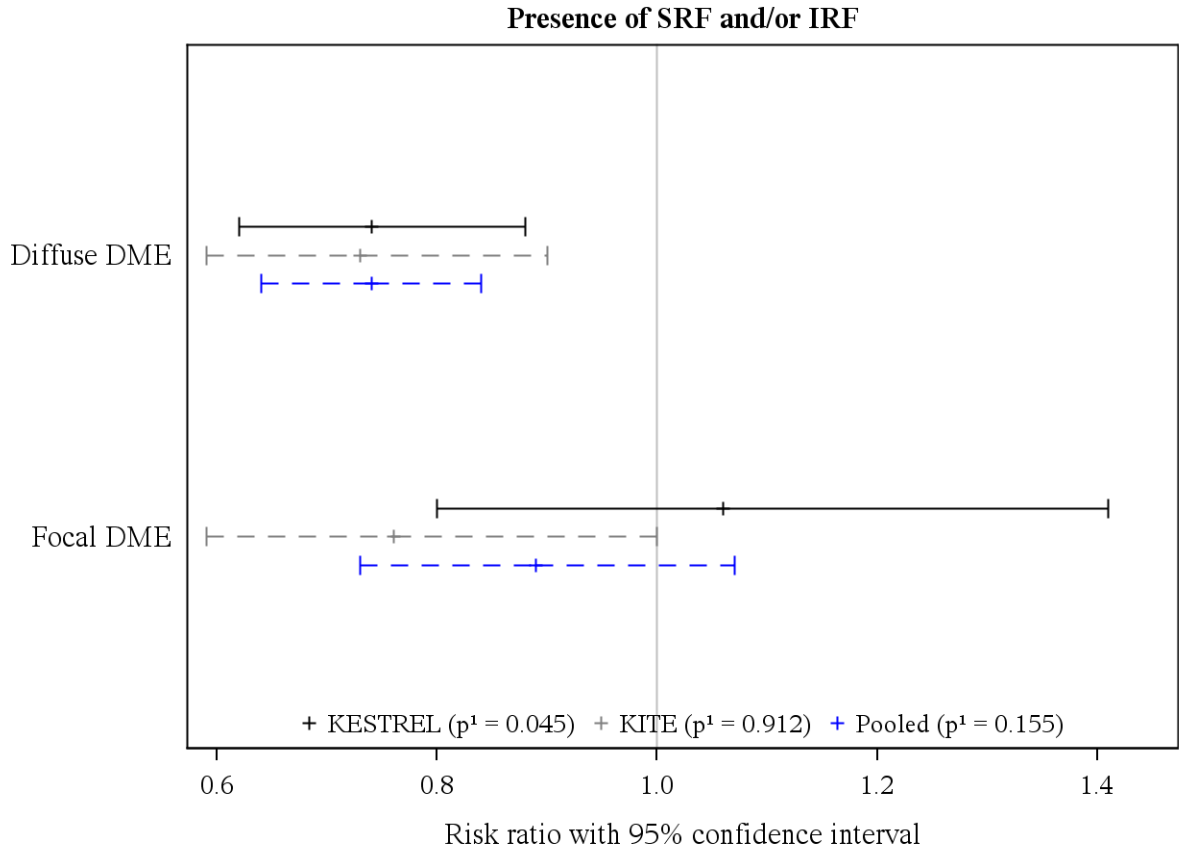
Figure 11.9 Presence of SRF and/or IRF in the study eye by DME type (FAS), forest plot, week 52

Figure 11.9.1 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: $p_H = 0.503$

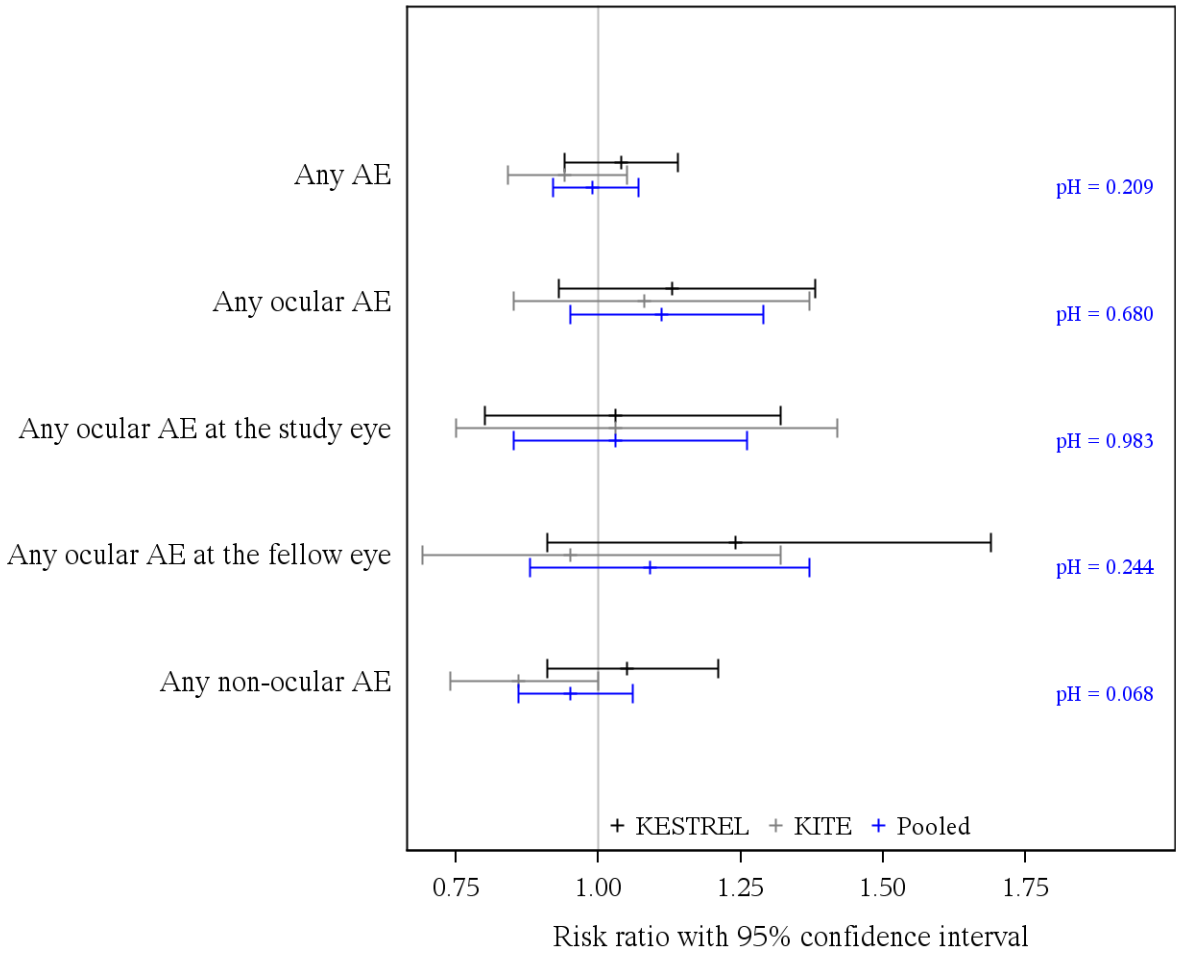
Figure 11.9.2 Presence of SRF and/or IRF in the study eye by DME type (FAS), forest plot, week 52, Presence of SRF and/or IRF



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: $p_H = 0.574$

12 Safety analysis: Any adverse event

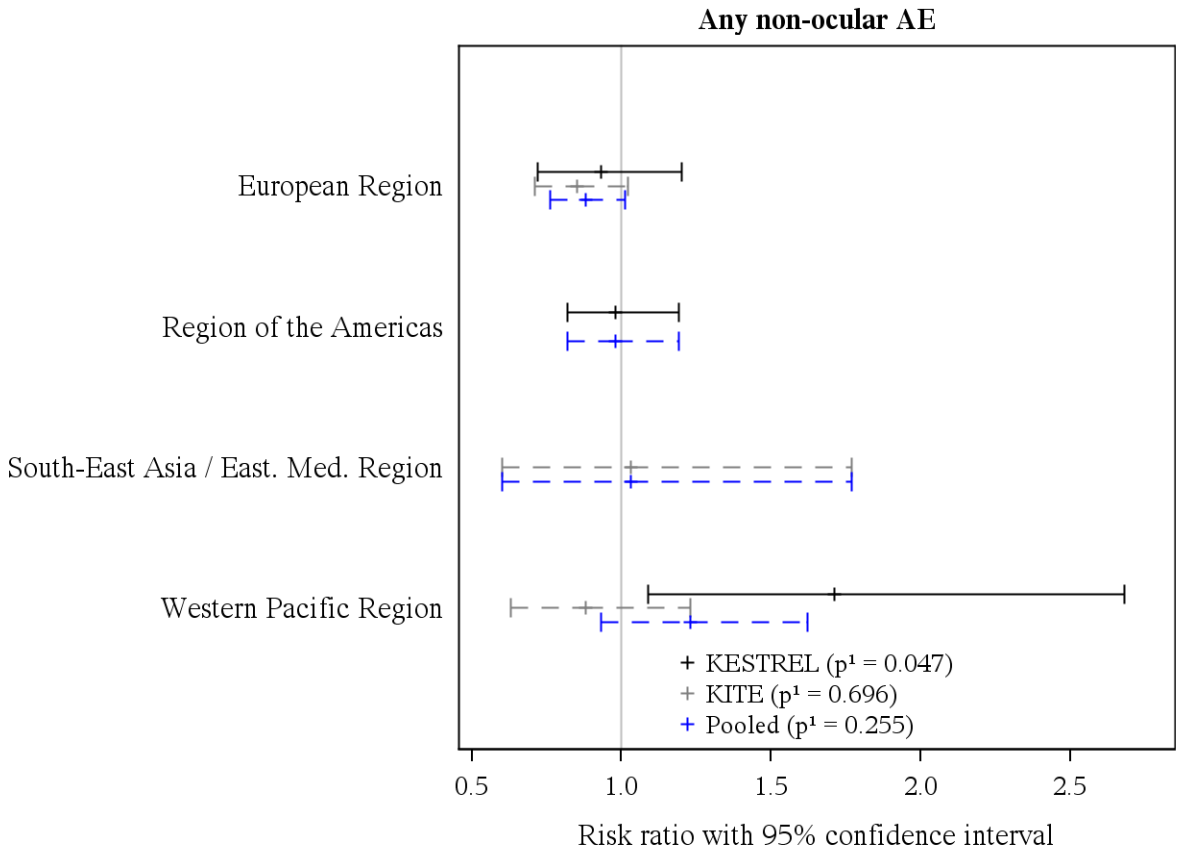
Figure 12.1 Any adverse event (SAF), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 12.5 Any adverse event by region (SAF), forest plot, week 52

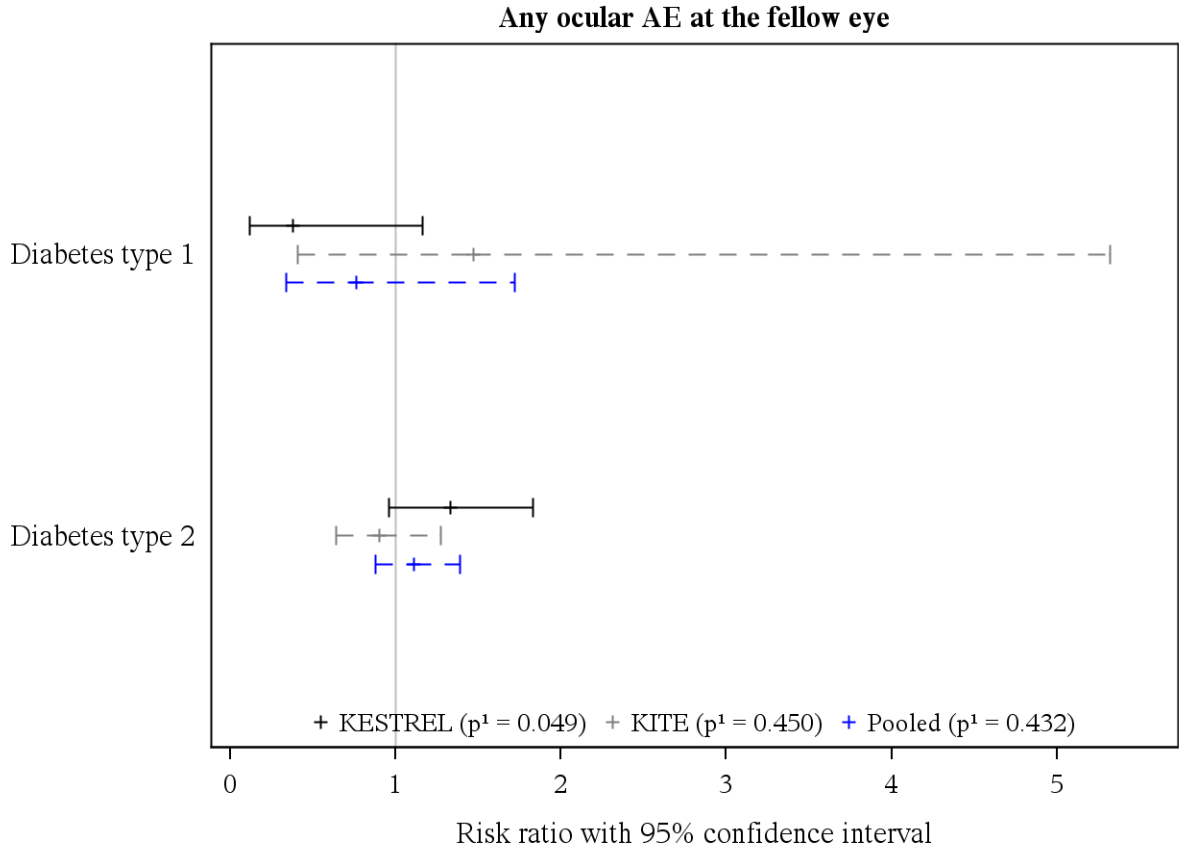
Figure 12.5.1 Any adverse event by region (SAF), forest plot, week 52, any non-ocular AE



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 12.6 Any adverse event by diabetes type (SAF), forest plot, week 52

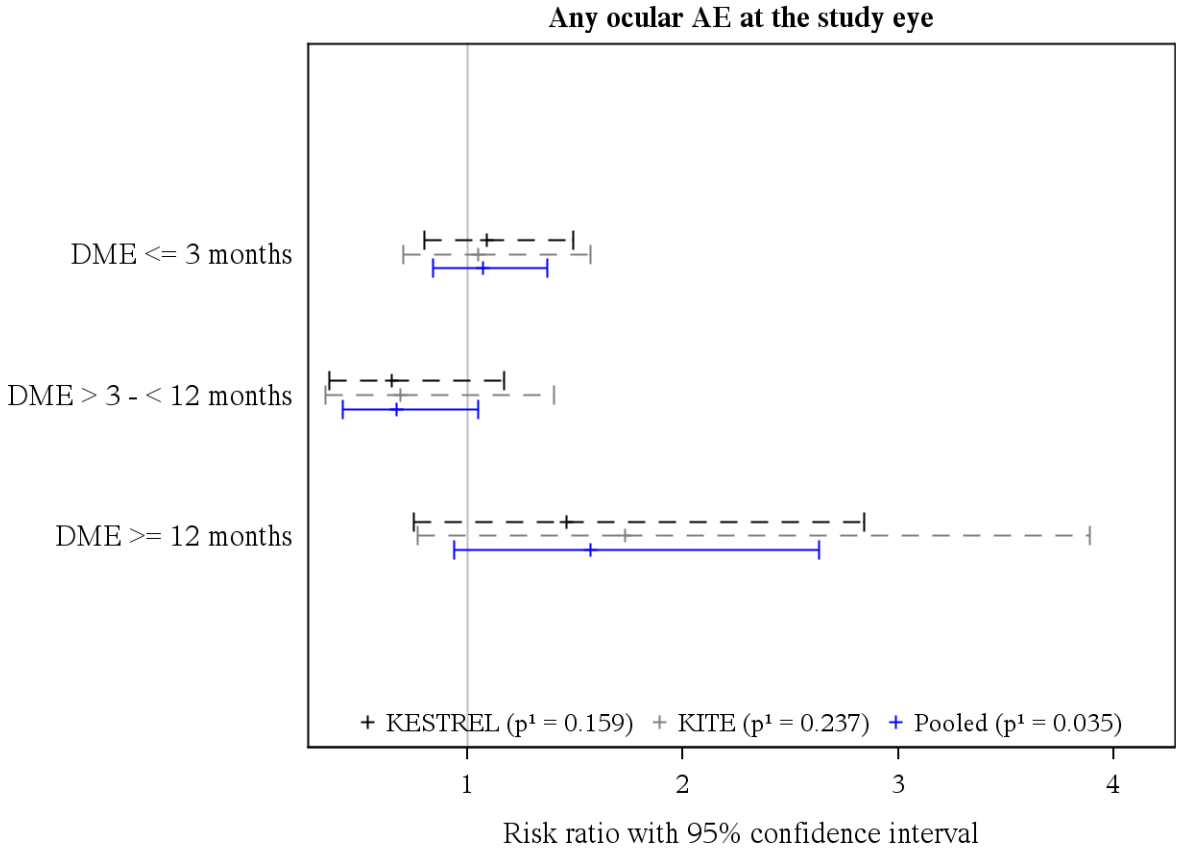
Figure 12.6.1 Any adverse event by diabetes type (SAF), forest plot, week 52, any ocular AE at the fellow eye



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 12.8 Any adverse event by duration of DME (SAF), forest plot, week 52

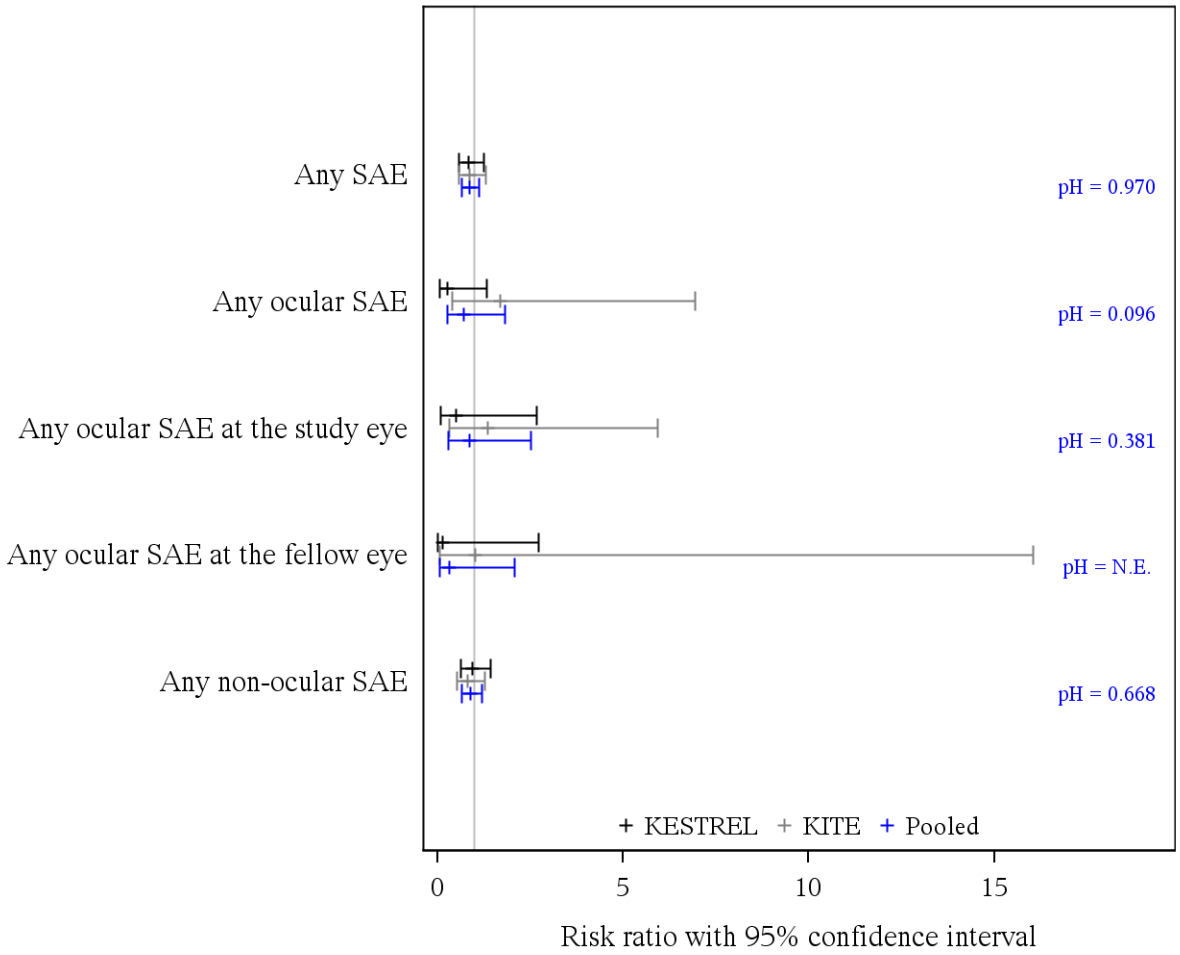
Figure 12.8.1 Any adverse event by duration of DME (SAF), forest plot, week 52, any ocular AE at the study eye



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: $p_H = 0.983$

13 Safety analysis: Any serious adverse event

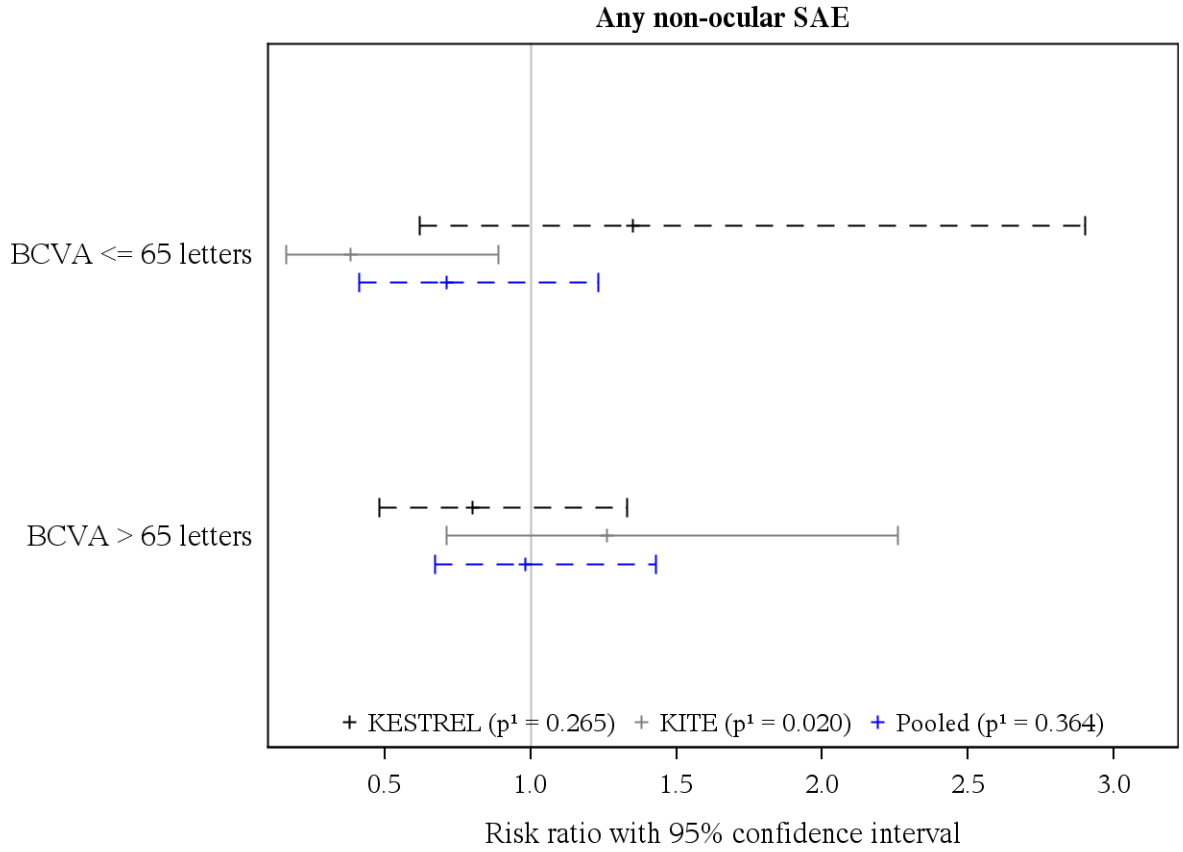
Figure 13.1 Any serious adverse event (SAF), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 13.4 Any serious adverse event by BCVA (SAF), forest plot, week 52

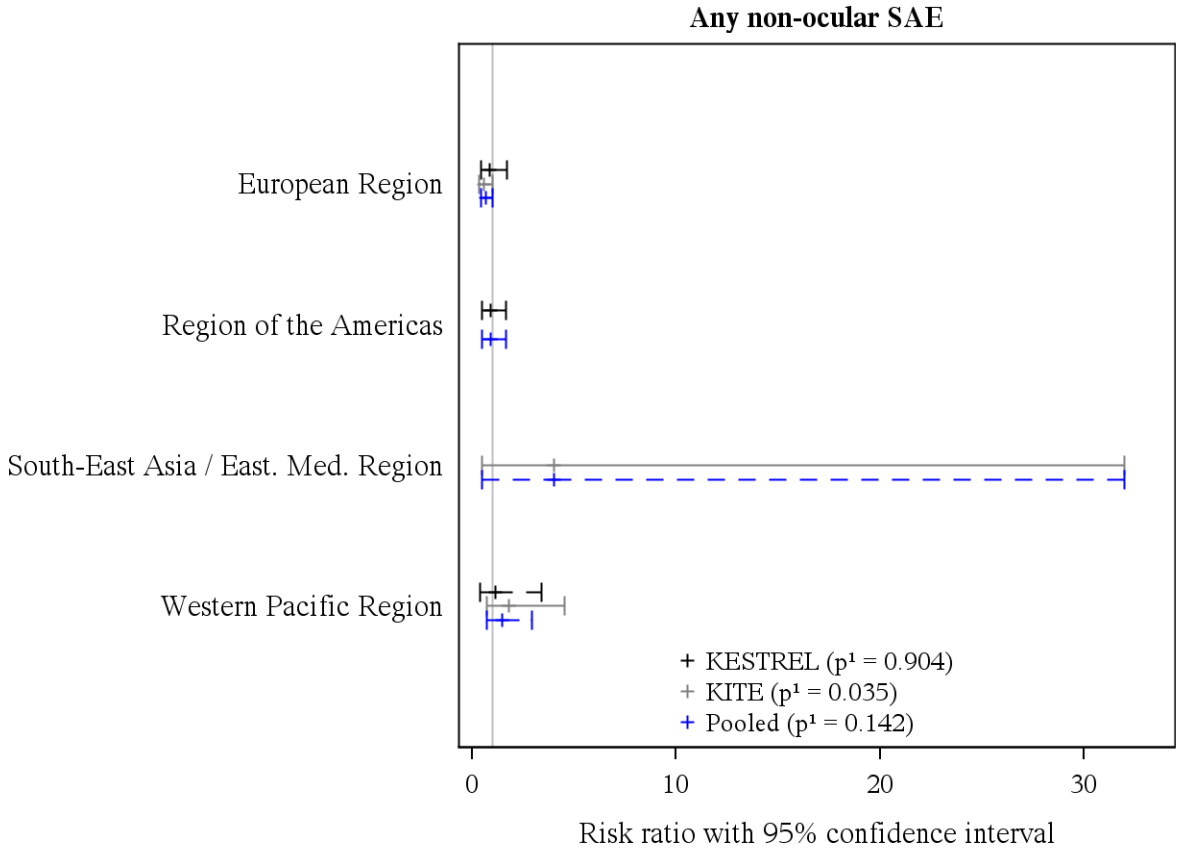
Figure 13.4.1 Any serious adverse event by BCVA (SAF), forest plot, week 52, any non-ocular SAE



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 13.5 Any serious adverse event by region (SAF), forest plot, week 52

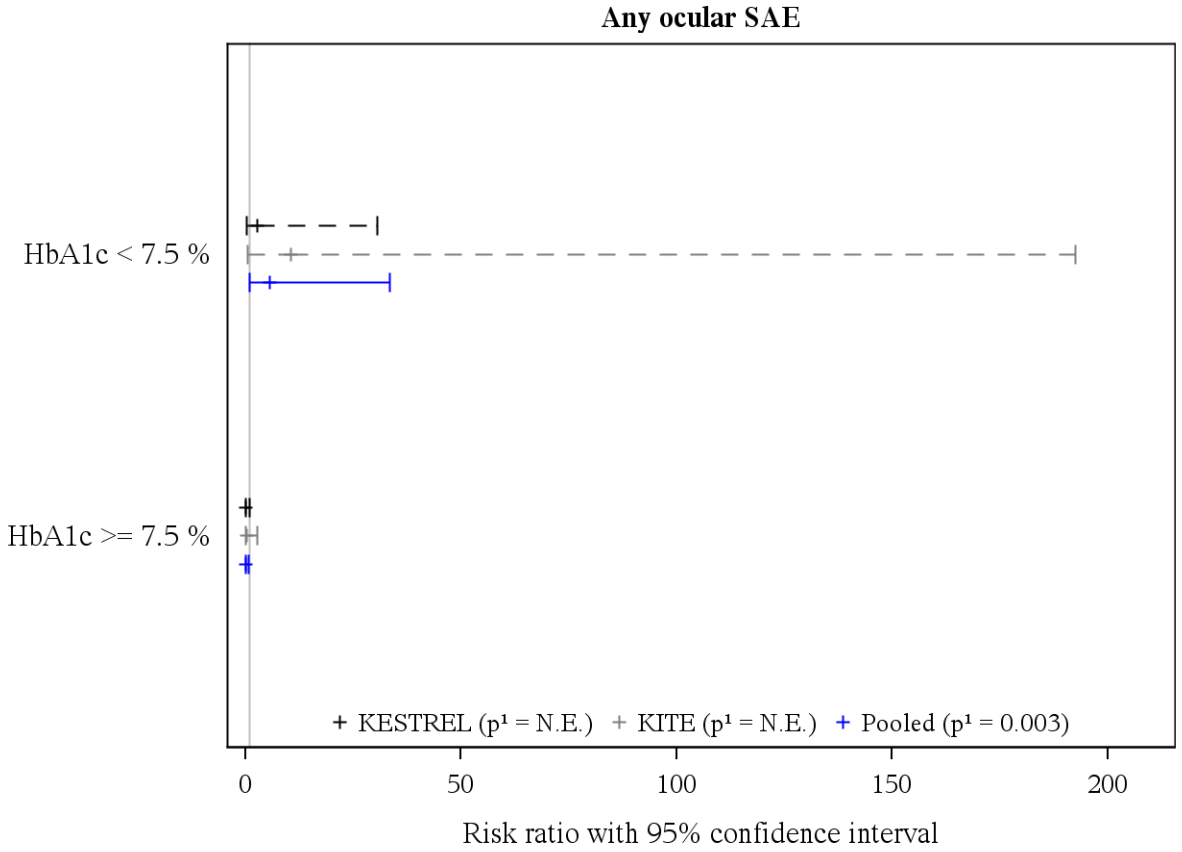
Figure 13.5.1 Any serious adverse event by region (SAF), forest plot, week 52, any non-ocular SAE



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 13.7 Any serious adverse event by HbA1c (SAF), forest plot, week 52

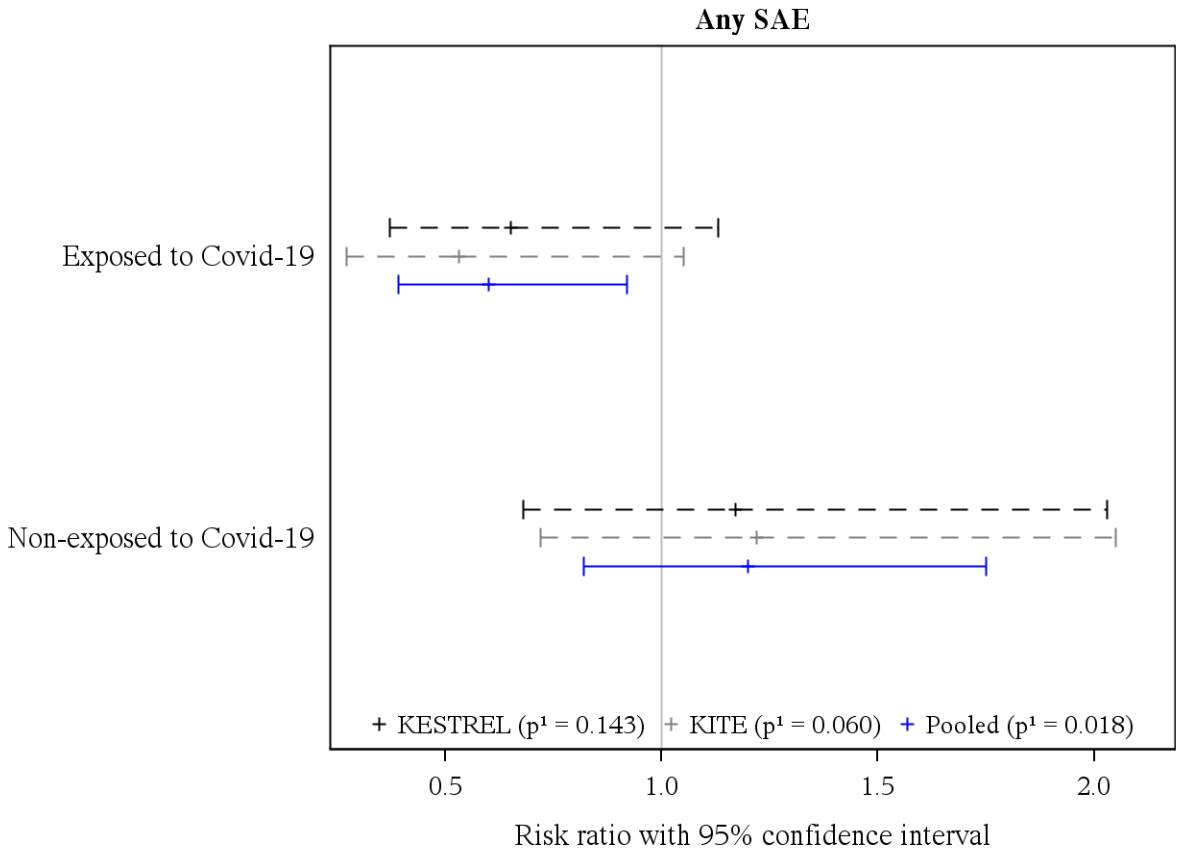
Figure 13.7.1 Any serious adverse event by HbA1c (SAF), forest plot, week 52, any ocular SAE



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: $p_H = 0.096$

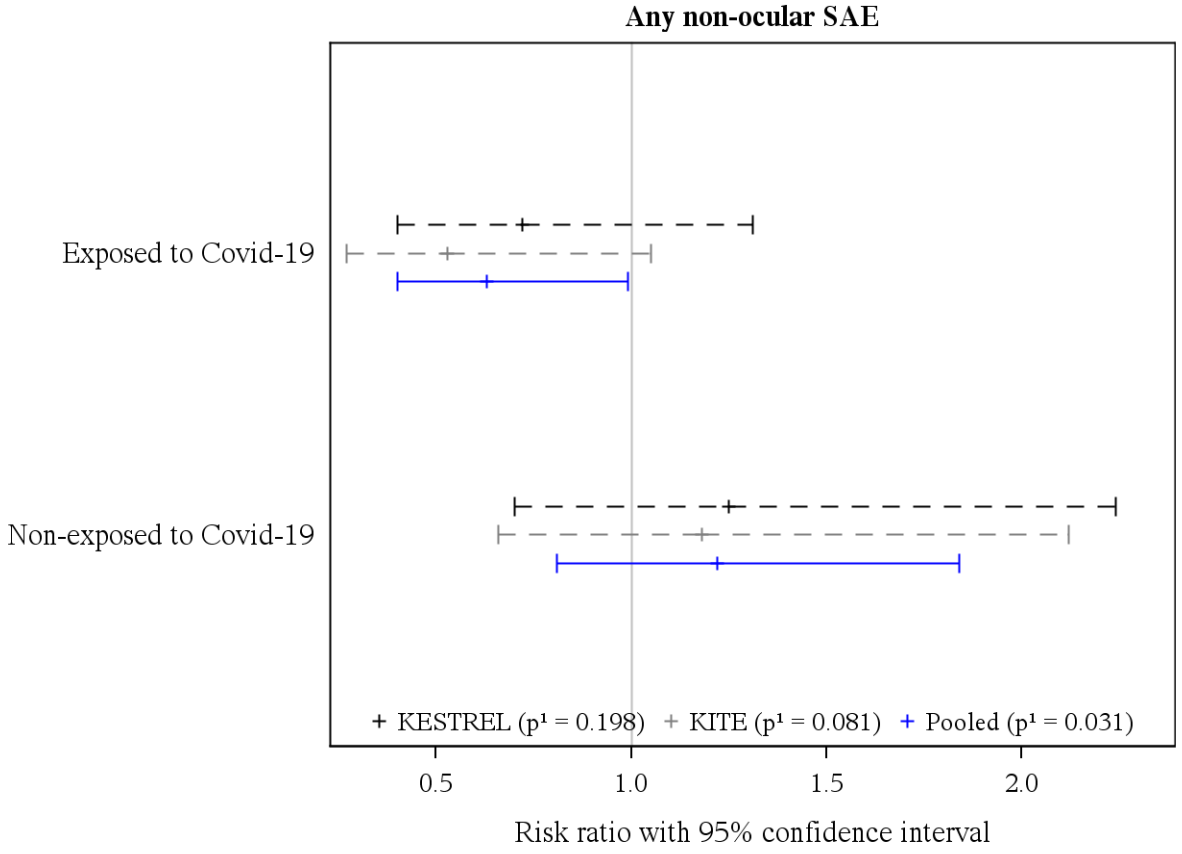
Figure 13.12 Any serious adverse event by exposure (SAF), forest plot, week 52

Figure 13.12.1 Any serious adverse event by exposure (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: $p_H = 0.970$

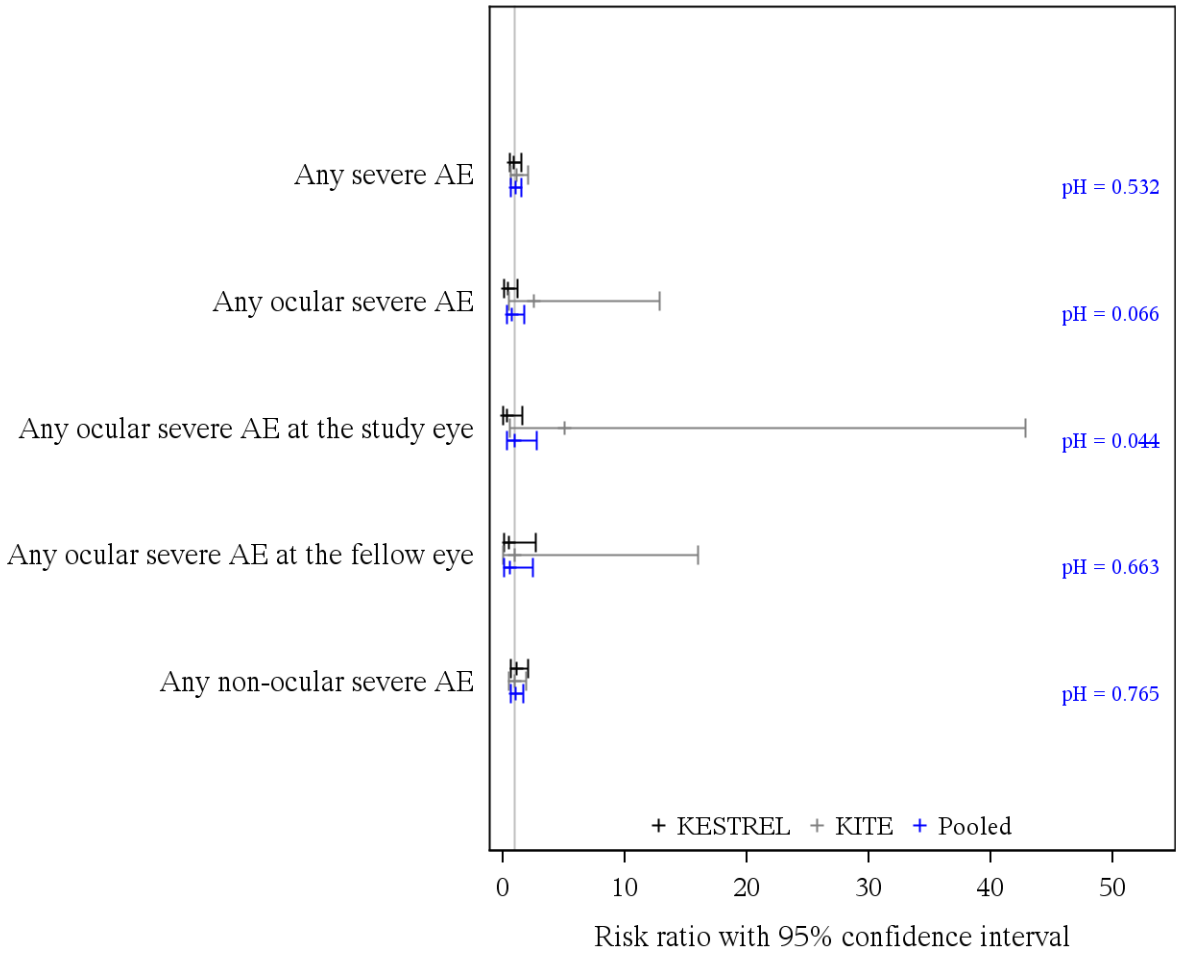
Figure 13.12.2 Any serious adverse event by exposure (SAF), forest plot, week 52, any non-ocular SAE



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: $p_H = 0.668$

14 Safety analysis: Any severe adverse event

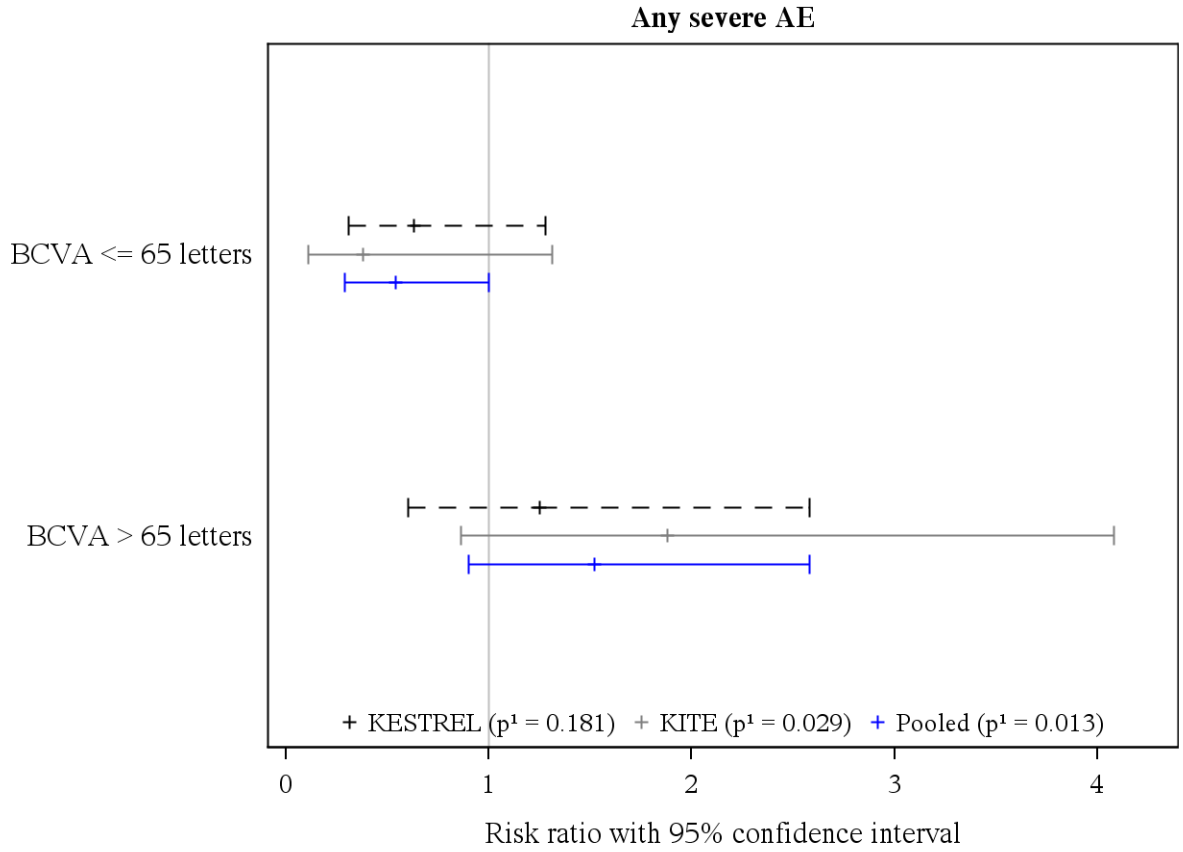
Figure 14.1 Any severe adverse event (SAF), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

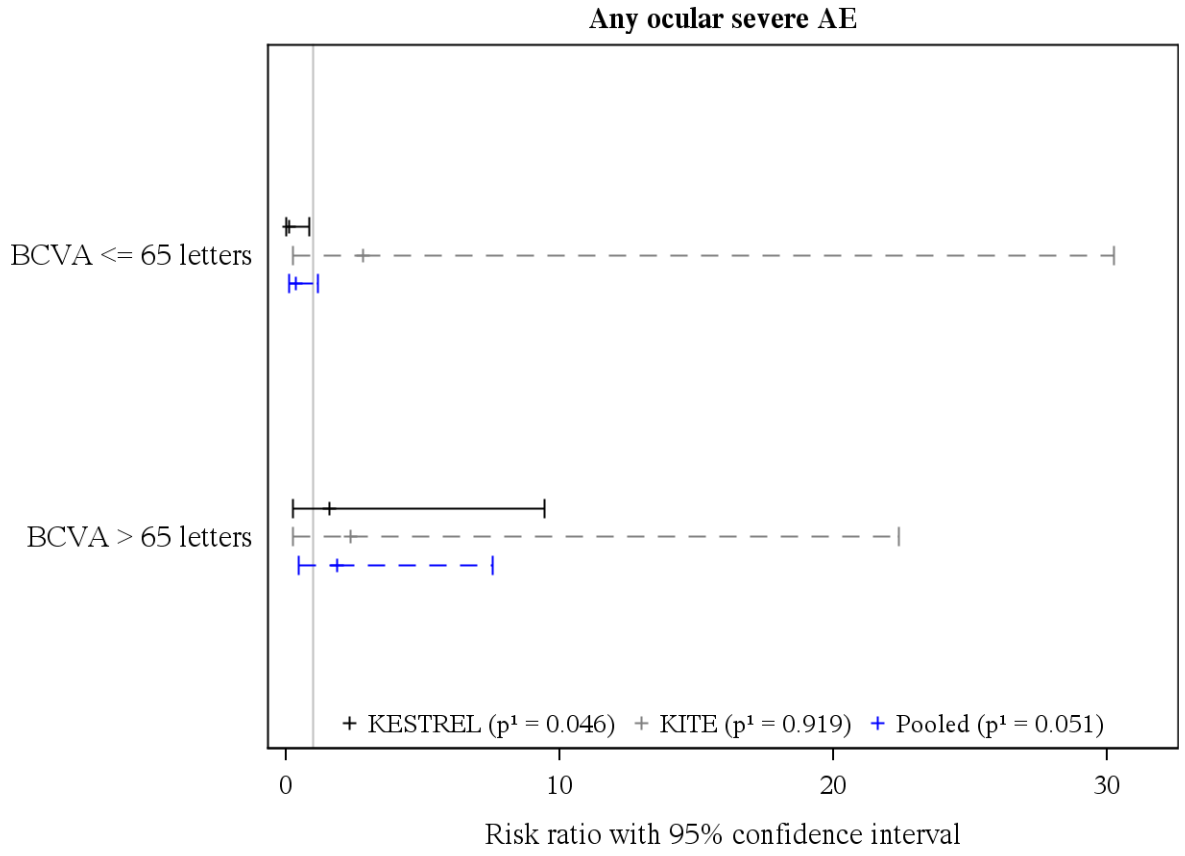
Figure 14.4 Any severe adverse event by BCVA (SAF), forest plot, week 52

Figure 14.4.1 Any severe adverse event by BCVA (SAF), forest plot, week 52, any severe AE



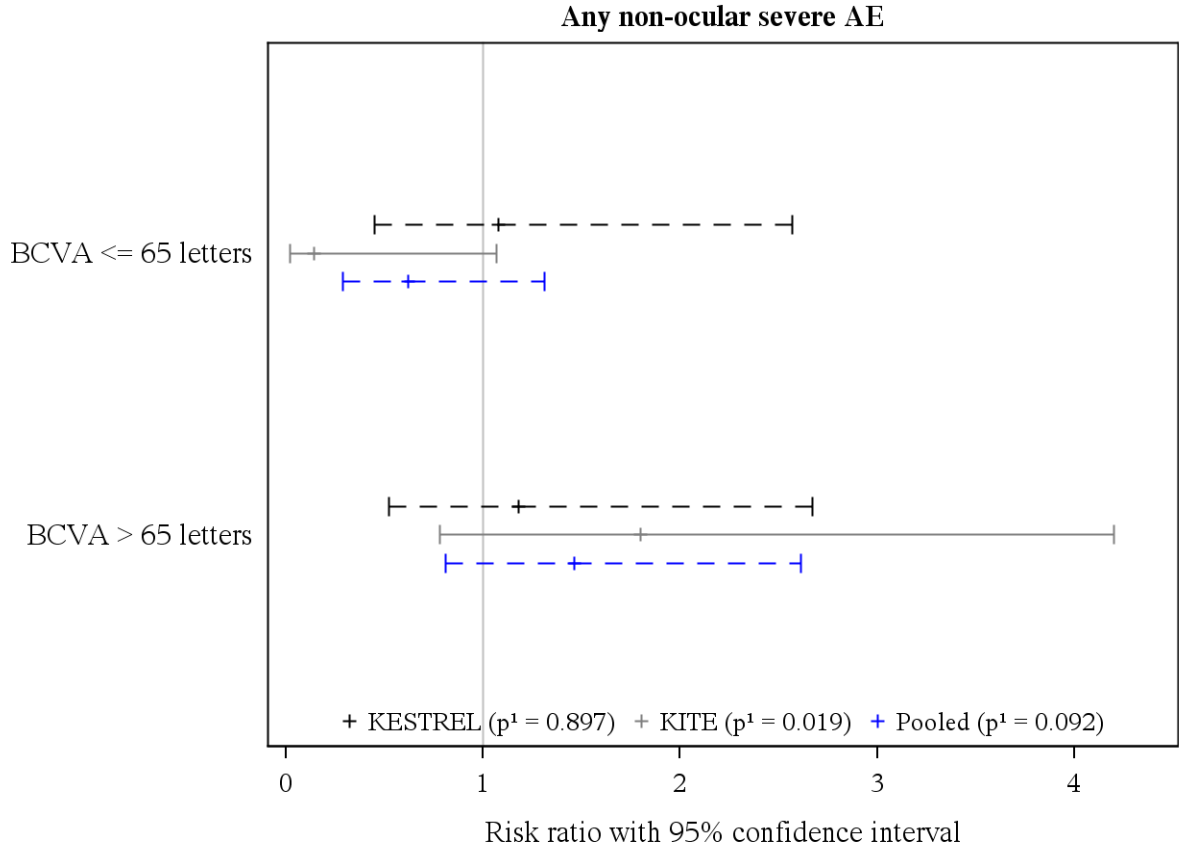
p¹ = p-value of interaction test subgroup*treatment
Dashed line: p¹ >= 0.05
p-value of test of heterogeneity based on study*treatment in the main analysis: $p_H = 0.532$

Figure 14.4.2 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: $p_H = 0.066$

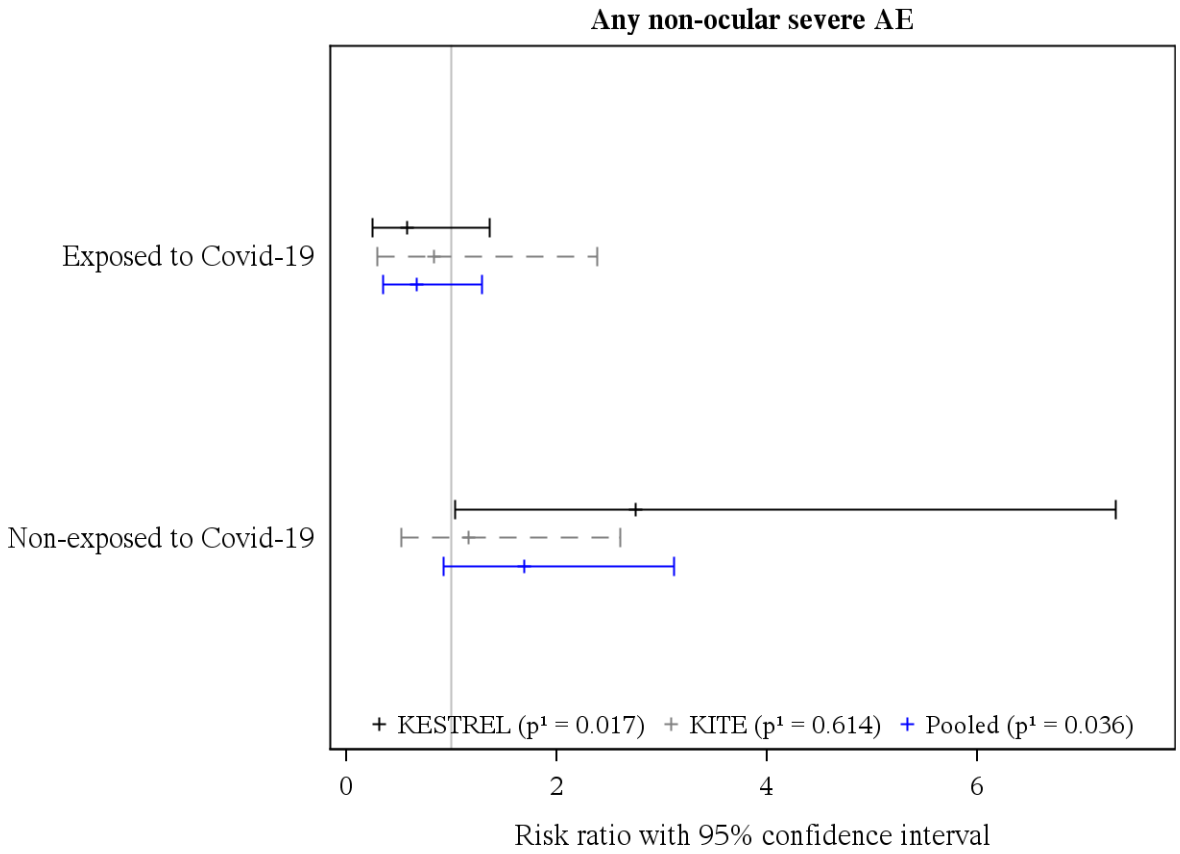
Figure 14.4.3 Any severe adverse event by BCVA (SAF), forest plot, week 52, any non-ocular severe AE



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 14.12 Any severe adverse event by exposure (SAF), forest plot, week 52

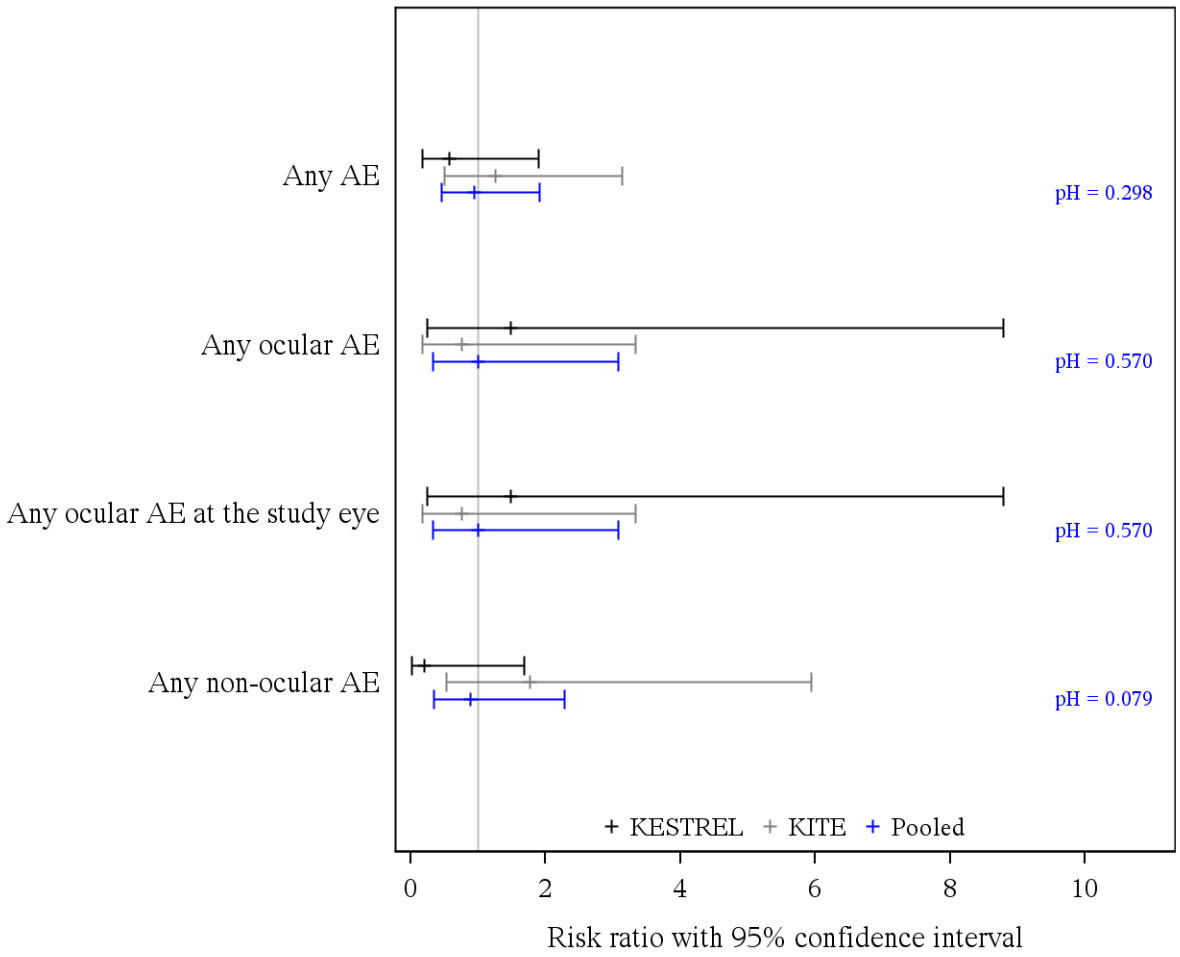
Figure 14.12.1 Any severe adverse event by exposure (SAF), forest plot, week 52, any non-ocular severe AE



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: $p_H = 0.765$

15 Safety analysis: Any adverse event leading to study drug discontinuation

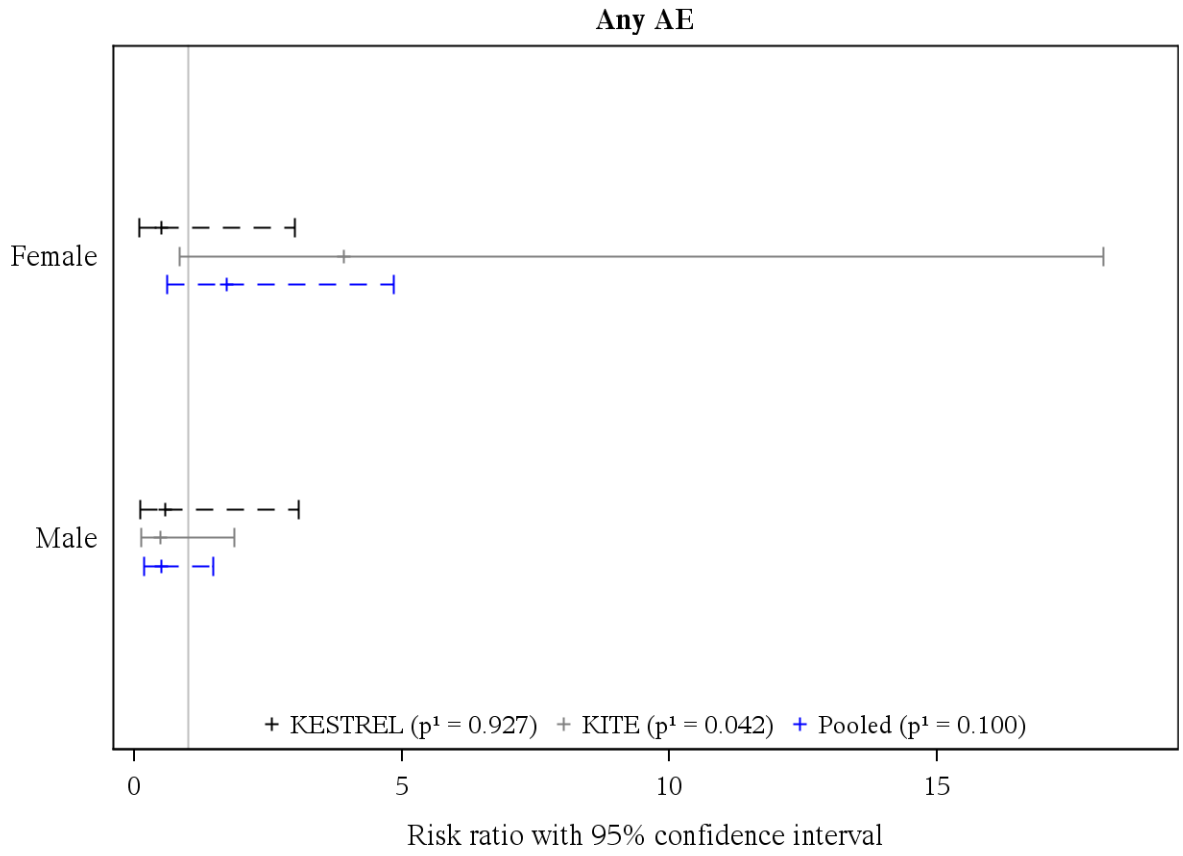
Figure 15.1 Any adverse event leading to study drug discontinuation (SAF), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

Figure 15.3 Any adverse event leading to study drug discontinuation by gender (SAF), forest plot, week 52

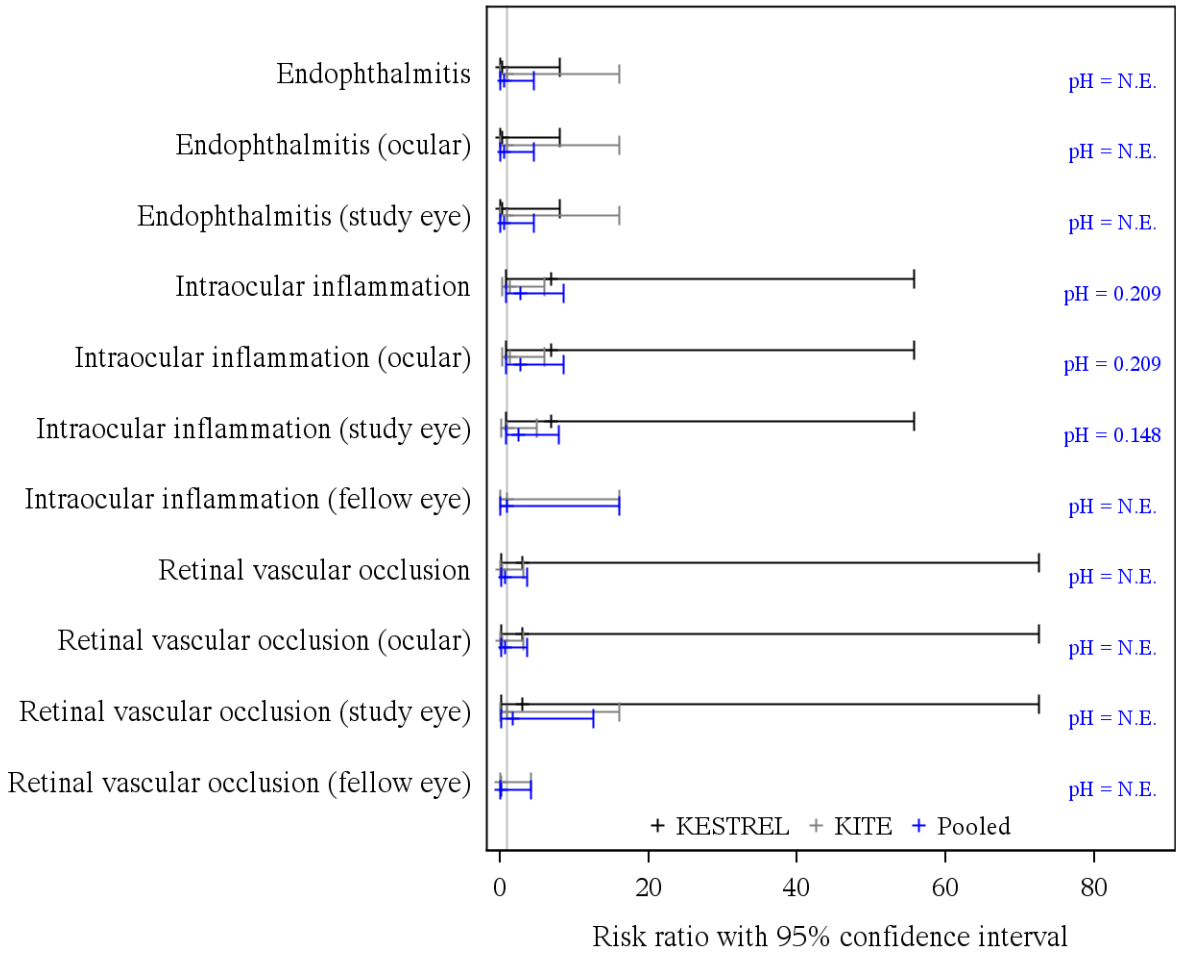
Figure 15.3.1 Any adverse event leading to study drug discontinuation by gender (SAF), forest plot, week 52, any AE



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: $p_H = 0.298$

20 Safety analysis: Any adverse event of special interest

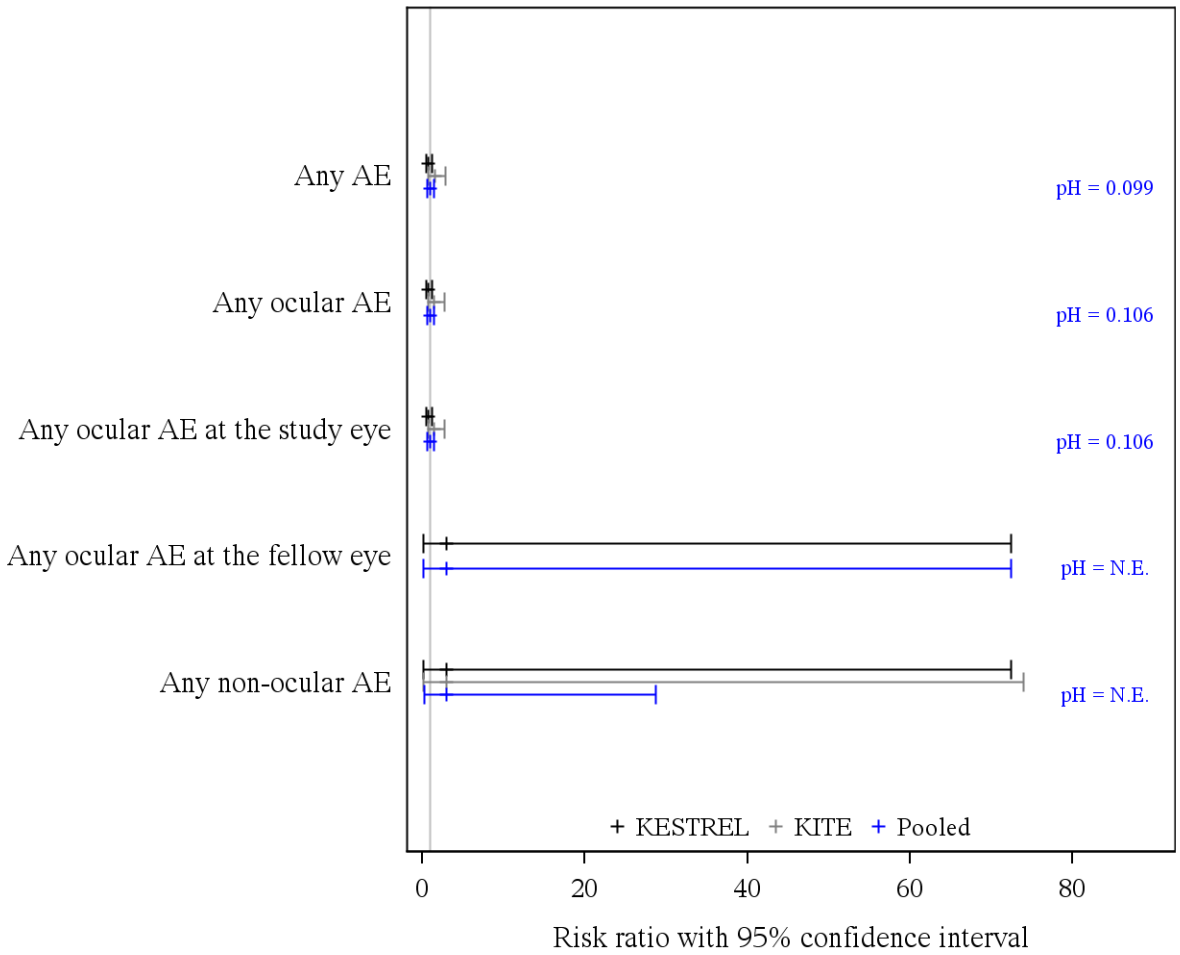
Figure 20.1 Any adverse event of special interest (SAF), forest plot, week 52



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

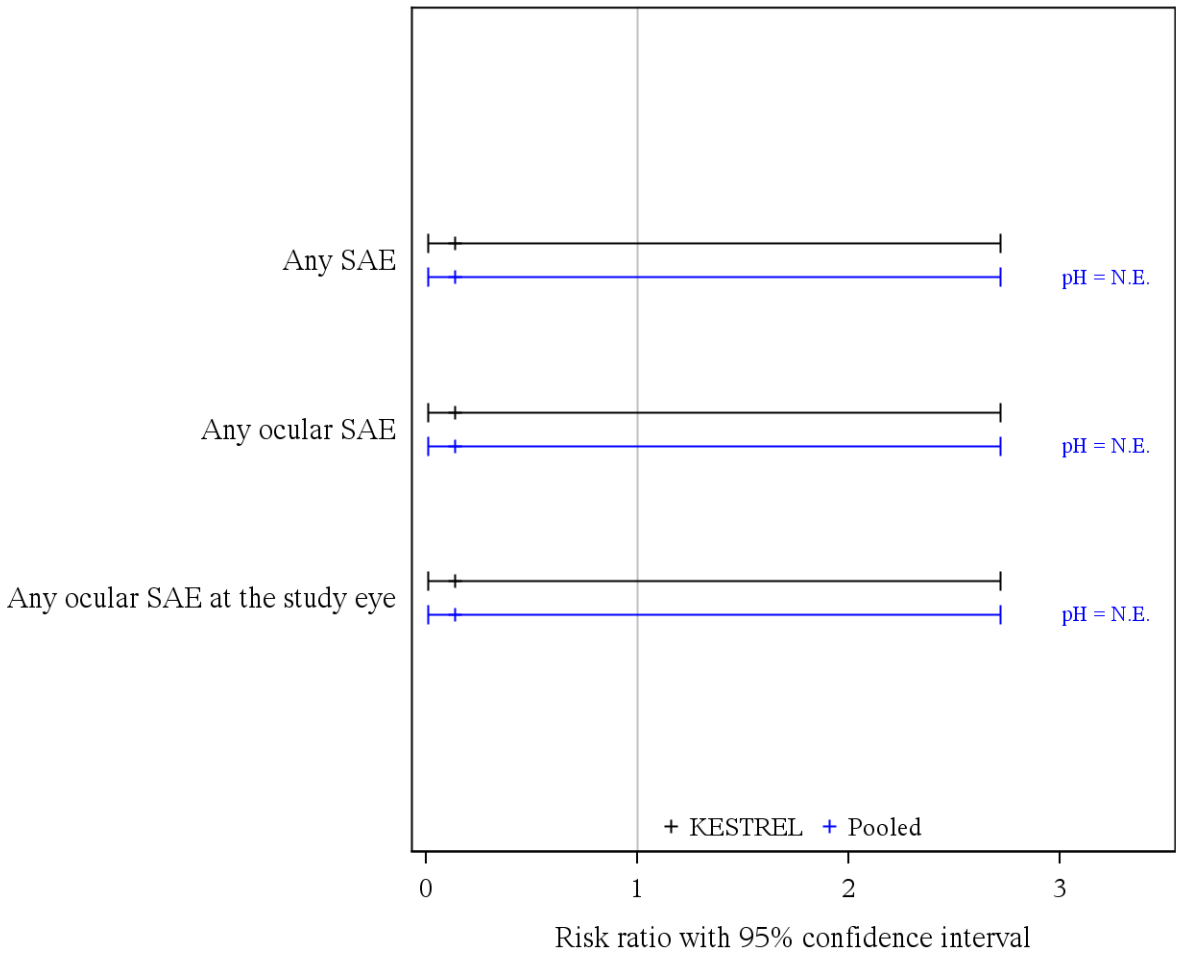
Figure 21.1 Any adverse event of potential relevance to intravitreal anti-VEGF injection (SAF), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

22 Safety analysis: Any serious adverse event of potential relevance to intravitreal anti-VEGF injection

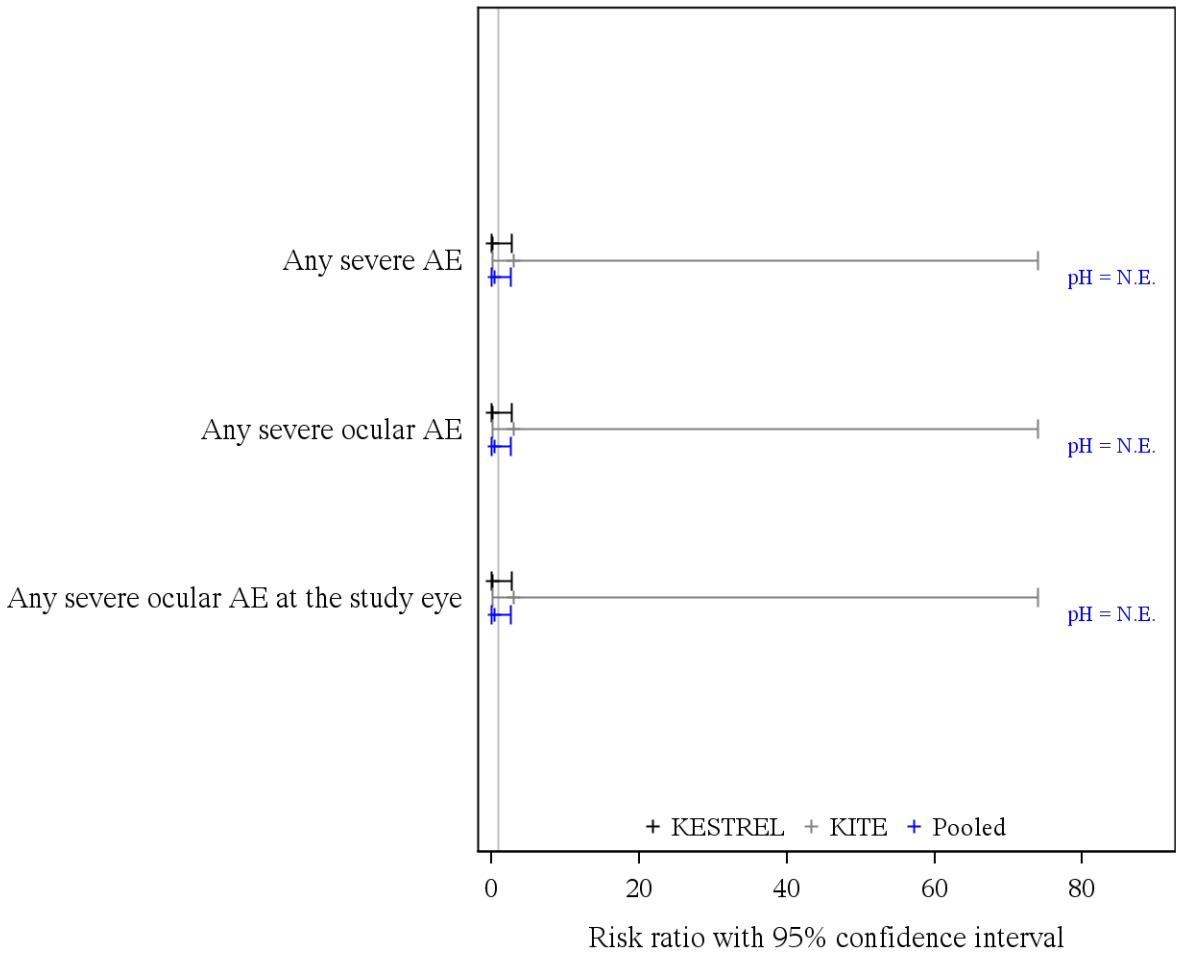
Figure 22.1 Any serious adverse event of potential relevance to intravitreal anti-VEGF injection (SAF), forest plot, week 52



p_H: p-value of test of heterogeneity based on study*treatment in the main analysis.

23 Safety analysis: Any severe adverse event of potential relevance to intravitreal anti-VEGF injection

Figure 23.1 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.