Dossier zur Nutzenbewertung gemäß § 35a SGB V

Tezepelumab (Tezspire[®])

AstraZeneca GmbH

Modul 4 A – Anhang 4-G-4

Add-on-Erhaltungstherapie bei Erwachsenen und Jugendlichen ab 12 Jahren mit schwerem Asthma, das trotz hochdosierter inhalativer Kortikosteroide plus eines weiteren Arzneimittels zur Erhaltungstherapie unzureichend kontrolliert ist

> UE-Analysen, ohne Berücksichtigung von erkrankungsbezogenen Ereignissen Biomarker_{low}-Population RCT mit dem zu bewertenden Arzneimittel

> > Stand: 11.11.2022

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Table MT1AA_SBMI0: Incidence of non-disease related TEAEs during study period DSAFB

		Tezepelumab		Placebo	_			
		n (%)		n (%)	RR	OR	RD	_
	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related TEAEs during study period	66	41 (62.1) [49.3, 73.8]	48	32 (66.7) [51.6, 79.6]	0.932 [0.708, 1.227]	0.820 [0.376, 1.788]	-4.5 [-24.1, 15.0	0.694]

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 02FEB2022

Table NT1AA_SBMI0: Incidence of non-disease related TEAEs during study period DSAFB

		Tezepelumab		Placebo	_			
		n (%)		n (%)	RR	OR	RD	
	Ν	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related TEAEs during	55	33 (60.0)	40	27 (67.5)	0.889	0.722	-7.5	0.522
study period		[45.9, 73.0]		[50.9, 81.4]	[0.655, 1.205]	[0.308, 1.696]	[-29.1, 14.1]

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 01FEB2022

Table NT1AA_TBMI0: Incidence of non-disease related TEAEs during study period DSAFB - adult

		Tezepelumab		Placebo				
		n (%)		n (%)	RR	OR	RD	_
	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related TEAEs during	54	33 (61.1)	39	26 (66.7)	0.917	0.786	-5.6	0.665
study period		[46.9, 74.1]		[49.8, 80.9]	[0.674, 1.247]	[0.332, 1.860]	[-27.5, 16.3]]

Note: DSAFB - adult = Dossier Biomarker Safety Set - adult. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 01FEB2022

AstraZeneca Value Dossier Analysis: CD-RI-MEDI9929-1146 Data Cut Date: 06JUN2017

Table PT3AA_SBMI0: Incidence of non-disease related TEAEs during study period DSAFB

		Tezepelumab		Placebo	_			
	N	n (%) [95 % CI]	N	n (%) [95 % CI]		OR [95 % CI]	RD [95 % CI]	p-value
Non-disease related TEAEs during	12	8 (66.7)	9	6 (66.7)	1.000	1.000	0.0	1.000
study period		[34.9, 90.1]		. ,	[0.543, 1.843]	[0.160, 6.255]	[-50.5, 50.5]

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 07FEB2022

AstraZeneca Value Dossier Analysis: D5180C00009 Data Cut Date: 18Nov2020

Table ST1AA_SBMI0: Incidence of non-disease related TEAEs during study period DSAFB

		Tezepelumab		Placebo	_			
	N	n (%) [95 % CI]	N	n (%) [95 % CI]		OR [95 % CI]	RD [95 % CI]	p-value
Non-disease related TEAEs during	12	5 (41.7)	11	6 (54.5)	0.764	0.595	-12.9	0.684
study period	10	[15.2, 72.3]		· · ·	[0.323, 1.805]			

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 07FEB2022

Table DT1AA_UBMI0: Incidence of non-disease related TEAEs during study period DSAFNB - LTE

		Teze+Teze		Pbo+Pbo	_			
		n (%)		n (%)	RR	OR	RD	
	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related TEAEs during study period	45	33 (73.3) [58.1, 85.4]	19	15 (78.9) [54.4, 93.9]	0.929 [0.694, 1.243]	0.733 [0.203, 2.653]	-5.6 [-31.8, 20.6	0.758]

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: aae, created on: 15JUL2022

Table CT1AA_SBMI0: Incidence of non-disease related TEAEs during study period DSAFB

		Tezepelumab		Placebo	_			
	N	n (%) [95 % CI]	N	n (%) [95 % CI]		OR [95 % CI]	RD [95 % CI]	p-value
Non-disease related TEAEs during	4	3 (75.0)	8	7 (87.5)	0.857	0.429	-12.5	1.000
study period		[19.4, 99.4]		[47.3, 99.7]	[0.459, 1.599]	[0.020, 9.364]	[-79.5, 54.5]

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 07FEB2022

	Tezepelumab		Placebo					
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
study period	IN	[]] % []	11	[]] % []	[55 % C1]	[]] % []]	[]] % []]	p varue
Sex								0.339
Male	20	11 (55.0)	8	6 (75.0)	0.733	0.407	-20.0	0.419
		[31.5, 76.9]		[34.9, 96.8]	[0.418, 1.288]	[0.066, 2.531]	[-65.8, 25.8	3]
Female	46	30 (65.2)	40	26 (65.0)	1.003	1.010	0.2	1.000
		[49.8, 78.6]		[48.3, 79.4]	[0.736, 1.368]	[0.415, 2.456]	[-22.3, 22.8	3]
Age								0.293
< 65 years	56	37 (66.1)	39	26 (66.7)	0.991	0.974	-0.6	1.000
-		[52.2, 78.2]		[49.8, 80.9]	[0.741, 1.325]	[0.410, 2.314]	[-22.1, 20.9]
>= 65 years	10	4 (40.0)	9	6 (66.7)	0.600	0.333	-26.7	0.370
-		[12.2, 73.8]		[29.9, 92.5]	[0.247, 1.459]	[0.051, 2.177]	[-80.5, 27.1	.]
Exacerbations in the year before								0.916
study								
<= 2	38	23 (60.5)	31	20 (64.5)	0.938	0.843	-4.0	0.806
		[43.4, 76.0]		[45.4, 80.8]	[0.651, 1.353]	[0.316, 2.252]	[-29.8, 21.9]
> 2	28	18 (64.3)	17	12 (70.6)	0.911	0.750	-6.3	0.752
		[44.1, 81.4]		[44.0, 89.7]	[0.603, 1.376]	[0.205, 2.748]	[-39.0, 26.4]
Race		N<10 any level						NE
White	43	23 (53.5)	36	24 (66.7)				
		[37.7, 68.8]		[49.0, 81.4]				
Black or African American	6	6 (100.0)	4	2 (50.0)				
		[54.1, 100.0]		[6.8, 93.2]				
Asian	15	10 (66.7)	6	4 (66.7)				
		[38.4, 88.2]		[22.3, 95.7]				
Other	2	2 (100.0)	2	2 (100.0)				
		[15.8, 100.0]		[15.8, 100.0]				

Table MT1AA_SBSIK: Incidence of non-disease related TEAEs during study period by key subgroups DSAFB

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup. Source Data: aae, created on: 04APR2022

MT1AA_SBSIK

Table MT1AA_SBSIK:	Incidence c	f non-disease	related T	TEAEs during	study period	by key subgroups
			DSAFB			

		Tezepelumab		Placebo	_			
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Region								0.235
Europe	21	13 (61.9)	15	6 (40.0)	1.548	2.438	21.9	0.311
		[38.4, 81.9]		[16.3, 67.7]	[0.765, 3.131]	[0.627, 9.473]	[-16.2, 60.0]
America	21	12 (57.1)	13	11 (84.6)	0.675	0.242	-27.5	0.140
		[34.0, 78.2]		[54.6, 98.1]	[0.436, 1.045]	[0.043, 1.377]	[-62.6, 7.6]	
Asia/Pacific	13	8 (61.5)	9	7 (77.8)	0.791	0.457	-16.2	0.648
		[31.6, 86.1]		[40.0, 97.2]	[0.455, 1.377]	[0.066, 3.144]	[-63.6, 31.1]
Rest of the world	11	8 (72.7)	11	8 (72.7)	1.000	1.000	0.0	1.000
		[39.0, 94.0]		[39.0, 94.0]	[0.599, 1.668]	[0.153, 6.531]	[-46.3, 46.3]
BMI		N<10 any level						NE
< 18.5 kg/m**2	2	2 (100.0)	0					
-		[15.8, 100.0]						
18.5 - < 25.0 kg/m**2	12	6 (50.0)	11	8 (72.7)				
-		[21.1, 78.9]		[39.0, 94.0]				
25.0 - < 30.0 kg/m**2	24	13 (54.2)	16	12 (75.0)				
2		[32.8, 74.4]		[47.6, 92.7]				
>= 30.0 kg/m**2	28	20 (71.4)	21	12 (57.1)				
-		[51.3, 86.8]		[34.0, 78.2]				
Baseline eosinophils - Low								0.044 i
< 150 cells/uL	37	26 (70.3)	23	13 (56.5)	1.243	1.818	13.7	0.404
		[53.0, 84.1]		[34.5, 76.8]				1
>= 150 cells/uL	29	15 (51.7)	25	19 (76.0)	0.681	0.338	-24.3	0.092
		[32.5, 70.6]		[54.9, 90.6]	[0.449, 1.031]	[0.105, 1.092]	[-52.7, 4.2]	
		- , -		- , -	- , -	. , .	, .	
Baseline specific perennial FEIA								0.790
status								
All negative	39	25 (64.1)	29	19 (65.5)	0.978	0.940	-1.4	1.000
- 3		[47.2, 78.8]		[45.7, 82.1]				
Any positive	24	14 (58.3)	17	11 (64.7)	0.902	0.764	-6.4	0.753
<u> </u>	_	[36.6, 77.9]		· · · ·	[0.554, 1.468]			
		_ ,]		- ,	_ ,		- ,	-

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

		Tezepelumab		Placebo	_			
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Total serum IgE		N<10 any level						NE
Low	61	40 (65.6) [52.3, 77.3]	44	29 (65.9) [50.1, 79.5]				
High	5	1 (20.0) [0.5, 71.6]		3 (75.0) [19.4, 99.4]				
OCS at baseline								0.781
Yes	8	6 (75.0) [34.9, 96.8]	7		0.875 [0.530, 1.445]		-10.7 [-63.8, 42.3	1.000
No	58	35 (60.3) [46.6, 73.0]		26 (63.4) [46.9, 77.9]	0.952 [0.696, 1.301]	0.878 [0.385, 2.003]	-3.1 [-24.5, 18.4	
LAMA use at baseline								0.302
Yes	15	10 (66.7) [38.4, 88.2]	16	· · · ·	1.185 [0.676, 2.077]		10.4 [-30.1, 50.9	0.716
No	51	31 (60.8) [46.1, 74.2]	32	(,	0.846 [0.621, 1.152]		-11.1 [-34.2, 12.0	0.351
Tiotropium use at baseline								0.687
Yes	13	8 (61.5) [31.6, 86.1]	15	- (,	1.026 [0.565, 1.862]		1.5 [-41.9, 45.0	1.000
No	53	33 (62.3) [47.9, 75.2]	33	23 (69.7)		0.717	-7.4	0.642

Table MT1AA_SBSIK: Incidence of non-disease related TEAEs during study period by key subgroups DSAFB

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup. Source Data: aae, created on: 04APR2022

MT1AA_SBSIK

Table MT1AA_SBSIK: Incidence of non-disease related TEAEs during study period by key subgroups DSAFB

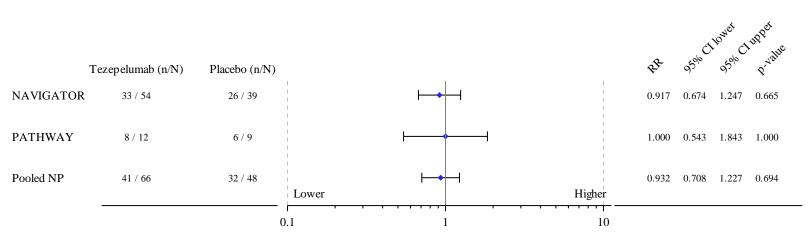
		Tezepelumab		Placebo				
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Montelukast/ Cromoglicic acid use								0.146
at baseline								
Yes	19	14 (73.7)	14	8 (57.1)	1.289	2.100	16.5	0.459
		[48.8, 90.9]		[28.9, 82.3]	[0.761, 2.185]	[0.482, 9.140]	[-22.3, 55.4]
No	47	27 (57.4)	34	24 (70.6)	0.814	0.563	-13.1	0.253
		[42.2, 71.7]		[52.5, 84.9]	[0.586, 1.130]	[0.220, 1.436]	[-36.5, 10.2]

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Figure MF1AA_SBMF0: Forest plot for non-disease related TEAEs during study period **DSAFB**



Test for heterogeneity - p-value: 0.803, I-square: 0.0 %

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of affected patients. RR = relative risk. CI = confidence interval. Heterogeneity was investigated with Cochran Q test. NE = not evaluable.

Source tables: NT1AA_TBMI0, PT3AA_SBMI0, MT1AA_SBMI0

		Tezepelumab		Placebo	_			
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Sex								0.347
Male	19	10 (52.6)	8	6 (75.0)	0.702	0.370	-22.4	0.405
		[28.9, 75.6]		[34.9, 96.8]	[0.391, 1.259]	[0.059, 2.323]	[-68.7, 24.0]
Female	36	23 (63.9)	32	21 (65.6)	0.974	0.927	-1.7	1.000
		[46.2, 79.2]		[46.8, 81.4]	[0.685, 1.383]	[0.342, 2.512]	[-27.4, 24.0]
Age								0.376
< 65 years	46	29 (63.0)	33	22 (66.7)	0.946	0.853	-3.6	0.814
		[47.5, 76.8]		· · · ·	[0.682, 1.312]	[0.333, 2.182]	[-27.5, 20.3]
>= 65 years	9	4 (44.4)	7	5 (71.4)	0.622	0.320	-27.0	0.358
1		[13.7, 78.8]		[29.0, 96.3]	[0.261, 1.482]	[0.039, 2.618]	[-86.3, 32.3	
Exacerbations in the year before study								0.513
<= 2	31	20 (64.5)	27	18 (66.7)	0.968	0.909	-2.2	1.000
	51	[45.4, 80.8]	67	· · · ·	[0.666, 1.406]			
> 2	24	13 (54.2)	13	9 (69.2)		0.525	-15.1	0.491
		[32.8, 74.4]	10	· · ·	[0.467, 1.311]			
Race		N<10 any level						NE
White	34	17 (50.0)	28	19 (67.9)				1111
	01	[32.4, 67.6]	20	[47.6, 84.1]				
Black or African American	4	4 (100.0)	3	1 (33.3)				
		[39.8, 100.0]		[0.8, 90.6]				
Asian	15	10 (66.7)	7	5 (71.4)				
		[38.4, 88.2]		[29.0, 96.3]				
Other	2	2 (100.0)	2	2 (100.0)				
		[15.8, 100.0]		[15.8, 100.0]				

Table NT1AA_SBSIK:	Incidence	of	non-disease	related	TEAEs	during	study	period	by	key	subgroups
				DSAFB							

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup. Source Data: aae, created on: 11APR2022

NT1AA_SBSIK

		Tezepelumab		Placebo	_			
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Region								0.228
Europe	11	7 (63.6)	10	4 (40.0)	1.591	2.625	23.6	0.395
-		[30.8, 89.1]		[12.2, 73.8]	[0.659, 3.839]	[0.450, 15.310]	[-27.5, 74.8]	l
America	20	10 (50.0)	11	9 (81.8)	0.611	0.222	-31.8	0.128
		[27.2, 72.8]		[48.2, 97.7]	[0.364, 1.027]	[0.038, 1.298]	[-70.5, 6.8]	
Asia/Pacific	13	8 (61.5)	10	8 (80.0)	0.769	0.400	-18.5	0.405
		[31.6, 86.1]		[44.4, 97.5]	[0.453, 1.307]	[0.059, 2.702]	[-63.6, 26.6]	l
Rest of the world	11	8 (72.7)	9	6 (66.7)	1.091	1.333	6.1	1.000
		[39.0, 94.0]		[29.9, 92.5]	[0.607, 1.962]	[0.196, 9.083]	[-44.6, 56.7]	
BMI		N<10 any level						NE
< 18.5 kg/m**2	3	2 (66.7)	0					
		[9.4, 99.2]						
18.5 - < 25.0 kg/m**2	11	5 (45.5)	8	6 (75.0)				
		[16.7, 76.6]		[34.9, 96.8]				
25.0 - < 30.0 kg/m**2	20	11 (55.0)	14	10 (71.4)				
		[31.5, 76.9]		[41.9, 91.6]				
>= 30.0 kg/m**2	21	15 (71.4)	18	11 (61.1)				
		[47.8, 88.7]		[35.7, 82.7]				
Baseline eosinophils - Low								0.117
< 150 cells/uL	32	21 (65.6)	22	13 (59.1)	1.111	1.322	6.5	0.775
100 00115/42	01	[46.8, 81.4]			[0.723, 1.705]			
>= 150 cells/uL	23	12 (52.2)	18	14 (77.8)	0.671	0.312	-25.6	0.114
100 00110/ 02	20	[30.6, 73.2]	10	· /	[0.422, 1.065]			0.111
Baseline specific perennial FEIA								0.771
status								
All negative	33	21 (63.6)	25	17 (68.0)	0.936	0.824	-4.4	0.786
	00	[45.1, 79.6]	20	[46.5, 85.1]				
Any positive	22	12 (54.5)	14	9 (64.3)	0.848	0.667	-9.7	0.732
F === 01.0		[32.2, 75.6]		- ()	[0.492, 1.465]			

Table NT1AA_SBSIK: Incidence of non-disease related TEAEs during study period by key subgroups DSAFB

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

		Tezepelumab		Placebo		0.5	22	
Non-disease related TEAEs during	N	n (%)	Ν	n (%)	RR	OR	RD	
study period	IN	[95 % CI]	IN	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Total serum IgE		N<10 any level						NE
Low	50	32 (64.0) [49.2, 77.1]	38	26 (68.4) [51.3, 82.5]				
High	5	1 (20.0) [0.5, 71.6]	2	1 (50.0) [1.3, 98.7]				
OCS at baseline								0.921
Yes	8	6 (75.0) [34.9, 96.8]	7	- (/	0.875 [0.530, 1.445]		-10.7	
No	47	27 (57.4) [42.2, 71.7]		21 (63.6)	0.903 [0.632, 1.289]	0.771	-6.2	0.647
LAMA use at baseline								0.403
Yes	15	10 (66.7) [38.4, 88.2]	16		1.067 [0.633, 1.797]		4.2	1.000
No	40	[38.4, 88.2] 23 (57.5) [40.9, 73.0]		17 (70.8)	0.812	0.557	-13.3	0.424
Tiotropium use at baseline		_ ,]		. ,		_ ,	_ ,	0.876
Yes	13	8 (61.5) [31.6, 86.1]	15	- ()	0.923 [0.528, 1.615]	0.800 [0.170, 3.767]	-5.1 [-47.9, 37.7	1.000 /]
No	42	25 (59.5)	25	17 (68.0)	0.875 [0.607, 1.263]	0.692	-8.5	0.604

Table NT1AA_SBSIK: Incidence of non-disease related TEAEs during study period by key subgroups DSAFB

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup. Source Data: aae, created on: 11APR2022

NT1AA_SBSIK

Table NT1AA_SBSIK: Incidence of non-disease related TEAEs during study period by key subgroups DSAFB

		[ezepelumab		Placebo				
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	Ν	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Montelukast/ Cromoglicic acid use at baseline								0.305
Yes	20	14 (70.0) [45.7, 88.1]	14	9 (64.3) [35.1, 87.2]	1.089 [0.671, 1.768]	1.296 [0.303, 5.540]	5.7 [-32.5, 43.9	1.000]
No	35	19 (54.3) [36.6, 71.2]	26	18 (69.2) [48.2, 85.7]	0.784 [0.527, 1.167]	0.528 [0.182, 1.532]	-14.9 [-42.5, 12.6	0.294]

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

		Tezepelumab		Placebo	_			
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Sex								0.539
Male	18	10 (55.6)	7	5 (71.4)	0.778	0.500	-15.9	0.659
	10	[30.8, 78.5]		, ,	[0.416, 1.453]			
Female	36	23 (63.9)	32	21 (65.6)	0.974	0.927	-1.7	1.000
		[46.2, 79.2]		()	[0.685, 1.383]			
Age								0.336
< 65 years	45	29 (64.4)	32	21 (65.6)	0.982	0.949	-1.2	1.000
(05 years	-15	[48.8, 78.1]	52	, ,	[0.705, 1.368]			
>= 65 years	9	4 (44.4)	7	5 (71.4)	0.622	0.320	-27.0	0.358
	2	[13.7, 78.8]	,		[0.261, 1.482]			
Exacerbations in the year before study								0.560
<= 2	31	20 (64.5)	26	17 (65.4)	0.987	0.963	-0.9	1.000
		[45.4, 80.8]		[44.3, 82.8]	[0.673, 1.447]	[0.323, 2.871]	[-29.3, 27.5]
> 2	23	13 (56.5)	13	9 (69.2)	0.816	0.578	-12.7	0.501
		[34.5, 76.8]		[38.6, 90.9]	[0.490, 1.359]	[0.137, 2.433]	[-51.0, 25.6]
Race		N<10 any level						NE
White	33	17 (51.5)	28	19 (67.9)				
		[33.5, 69.2]		[47.6, 84.1]				
Black or African American	4	4 (100.0)	3	1 (33.3)				
		[39.8, 100.0]		[0.8, 90.6]				
Asian	15	10 (66.7)	6	4 (66.7)				
		[38.4, 88.2]		[22.3, 95.7]				
Other	2	2 (100.0)	2	2 (100.0)				
		[15.8, 100.0]		[15.8, 100.0]				

Table NT1AA_TBSIK: Incidence of non-disease related TEAEs during study period by key subgroups DSAFB - adult

Note: DSAFB - adult = Dossier Biomarker Safety Set - adult.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

		Tezepelumab		Placebo				
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Region								0.280
Europe	11	7 (63.6)	10	4 (40.0)	1.591	2.625	23.6	0.395
-		[30.8, 89.1]		[12.2, 73.8]	[0.659, 3.839]	[0.450, 15.310]	[-27.5, 74.8]
America	19	10 (52.6)	11	9 (81.8)	0.643	0.247	-29.2	0.140
		[28.9, 75.6]		[48.2, 97.7]	[0.386, 1.071]	[0.042, 1.460]	[-68.4, 10.0]
Asia/Pacific	13	8 (61.5)	9	7 (77.8)	0.791	0.457	-16.2	0.648
		[31.6, 86.1]		[40.0, 97.2]	[0.455, 1.377]	[0.066, 3.144]	[-63.6, 31.1]
Rest of the world	11	8 (72.7)	9	6 (66.7)	1.091	1.333	6.1	1.000
		[39.0, 94.0]		[29.9, 92.5]	[0.607, 1.962]	[0.196, 9.083]	[-44.6, 56.7]
BMI		N<10 any level						NE
< 18.5 kg/m**2	2	2 (100.0)	0					
5		[15.8, 100.0]						
18.5 - < 25.0 kg/m**2	11	5 (45.5)	7	5 (71.4)				
-		[16.7, 76.6]		[29.0, 96.3]				
25.0 - < 30.0 kg/m**2	20	11 (55.0)	14	10 (71.4)				
-		[31.5, 76.9]		[41.9, 91.6]				
>= 30.0 kg/m**2	21	15 (71.4)	18	11 (61.1)				
2		[47.8, 88.7]		[35.7, 82.7]				
Baseline eosinophils - Low								0.129
< 150 cells/uL	32	21 (65.6)	21	12 (57.1)	1.148	1.432	8.5	0.573
		[46.8, 81.4]		[34.0, 78.2]	[0.734, 1.796]	[0.462, 4.437]	[-22.3, 39.2]
>= 150 cells/uL	22	12 (54.5)	18	14 (77.8)	0.701	0.343	-23.2	0.186
		[32.2, 75.6]		[52.4, 93.6]	[0.445, 1.105]	[0.085, 1.380]	[-56.6, 10.1	1
Baseline specific perennial FEIA								0.661
status								
All negative	32	21 (65.6)	24	16 (66.7)	0.984	0.955	-1.0	1.000
		[46.8, 81.4]		[44.7, 84.4]	[0.674, 1.437]	[0.312, 2.923]	[-29.7, 27.6]
Any positive	22	12 (54.5)	14	9 (64.3)	0.848	0.667	-9.7	0.732
		[32.2, 75.6]		[35.1, 87.2]	[0.492, 1.465]	[0.168, 2.645]	[-48.2, 28.7]

Table NT1AA_TBSIK: Incidence of non-disease related TEAEs during study period by key subgroups DSAFB - adult

Note: DSAFB - adult = Dossier Biomarker Safety Set - adult.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Non-disease related TEAEs during n (%) RR OR RD study period N [95 % CI] N [95 % CI] [95 % CI] [95 % CI] p-valu	ue
study period N [95 % CI] N [95 % CI] [95 % CI] [95 % CI] [95 % CI] p-valu	ue
Total serum IgE N<10 any level NE	
Low 49 32 (65.3) 37 25 (67.6)	
[50.4, 78.3] [50.2, 82.0]	
High 5 1 (20.0) 2 1 (50.0)	
[0.5, 71.6] [1.3, 98.7]	
OCS at baseline 0.823	
Yes 8 6 (75.0) 7 6 (85.7) 0.875 0.500 -10.7 1.000	
[34.9, 96.8] $[42.1, 99.6]$ $[0.530, 1.445]$ $[0.035, 7.104]$ $[-63.8, 42.3]$	
No 46 27 (58.7) 32 20 (62.5) 0.939 0.853 -3.8 0.816	
[43.2, 73.0] $[43.7, 78.9]$ $[0.654, 1.348]$ $[0.338, 2.151]$ $[-28.4, 20.8]$	
LAMA use at baseline 0.390	
Yes 15 10 (66.7) 15 9 (60.0) 1.111 1.333 6.7 1.000	
$[38.4, 88.2] \qquad [32.3, 83.7] [0.643, 1.919] [0.301, 5.915] [-34.4, 47.7]$	
No 39 23 (59.0) 24 17 (70.8) 0.833 0.592 -11.9 0.424	
[42.1, 74.4] $[48.9, 87.4]$ $[0.577, 1.201]$ $[0.200, 1.755]$ $[-39.1, 15.4]$	
Tiotropium use at baseline 0.852	
Yes 13 8 (61.5) 14 9 (64.3) 0.957 0.889 -2.7 1.000	
$[31.6, 86.1] \qquad [35.1, 87.2] [0.536, 1.711] [0.186, 4.244] [-46.6, 41.1]$	
No 41 25 (61.0) 25 17 (68.0) 0.897 0.735 -7.0 0.608	
[44.5, 75.8] $[46.5, 85.1]$ $[0.623, 1.290]$ $[0.258, 2.099]$ $[-33.9, 19.8]$	

Table NT1AA_TBSIK: Incidence of non-disease related TEAEs during study period by key subgroups DSAFB - adult

Note: DSAFB - adult = Dossier Biomarker Safety Set - adult.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table NT1AA_TBSIK: Incidence of non-disease related TEAEs during study period by key subgroups DSAFB - adult

		Tezepelumab		Placebo				
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Montelukast/ Cromoglicic acid use at baseline								0.198
at baseline								
Yes	19	14 (73.7)	13	8 (61.5)	1.197	1.750	12.1	0.699
		[48.8, 90.9]		[31.6, 86.1]	[0.721, 1.988]	[0.385, 7.951]	[-27.4, 51.7]
No	35	19 (54.3)	26	18 (69.2)	0.784	0.528	-14.9	0.294
		[36.6, 71.2]		[48.2, 85.7]	[0.527, 1.167]	[0.182, 1.532]	[-42.5, 12.6]

Note: DSAFB - adult = Dossier Biomarker Safety Set - adult.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

		Teze+Teze		Pbo+Pbo				
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
C								
Sex	1 7	12 (70 ()	2	1 (50.0)	1.412	2 400	20.6	0.554 1.000
Male	17	12 (70.6) [44.0, 89.7]	2	1(50.0)		2.400 [0.124, 46.391]		
Female	28	[44.0, 89.7] 21 (75.0)	17	[1.3, 98.7] 14 (82.4)	0.911	0.643	-7.4	0.719
Female	28	[55.1, 89.3]		· · · ·		[0.142, 2.916]		
		[55.1, 69.5]		[30.0, 90.2]	[0.670, 1.230]	[0.142, 2.916]	[-30.3, 21.0]	
Age								0.329
< 65 years	36	25 (69.4)	16	13 (81.3)	0.855	0.524	-11.8	0.506
1		[51.9, 83.7]				[0.124, 2.218]	[-40.7, 17.0]	
>= 65 years	9	8 (88.9)	3	2 (66.7)	1.333	4.000	22.2	0.455
1		[51.8, 99.7]		[9.4, 99.2]	[0.580, 3.066]	[0.167, 95.756]	[-57.2, 100.0]
Exacerbations in the year before								0.308
study								
<= 2	26	20 (76.9)	11	8 (72.7)		1.250	4.2	1.000
		[56.4, 91.0]				[0.250, 6.255]		
> 2	19	13 (68.4)	8	7 (87.5)	0.782	0.310	-19.1	0.633
		[43.4, 87.4]		[47.3, 99.7]	[0.523, 1.169]	[0.031, 3.111]	[-59.0, 20.8]	
Race		N<10 any level						NE
White	31	20 (64.5)	14	10 (71.4)				
		[45.4, 80.8]		[41.9, 91.6]				
Black or African American	4	4 (100.0)	2	2 (100.0)				
Didon of hilloun hadridan	-	[39.8, 100.0]	-	[15.8, 100.0]				
Asian	8	7 (87.5)	2	2 (100.0)				
	0	[47.3, 99.7]	5	[15.8, 100.0]				
Other	2	2 (100.0)	1	1 (100.0)				
	-	[15.8, 100.0]	-	[2.5, 100.0]				

Table DT1AA_UBSIK: Incidence of non-disease related TEAEs during study period by key subgroups DSAFNB - LTE

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events. LTE = long term extension.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

	Teze+Teze			Pbo+Pbo	_			
Non-disease related TEAEs during study period	N	n (%)	N	n (%)		OR [95 % CI]	RD	p-value
study period	IN	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Region		N<10 any level						NE
Europe	9	8 (88.9)	6	3 (50.0)				
-		[51.8, 99.7]		[11.8, 88.2]				
America	19	10 (52.6)	4	4 (100.0)				
		[28.9, 75.6]		[39.8, 100.0]				
Asia/Pacific	6	5 (83.3)	3	3 (100.0)				
		[35.9, 99.6]		[29.2, 100.0]				
Rest of the world	11	10 (90.9)	6	5 (83.3)				
		[58.7, 99.8]		[35.9, 99.6]				
BMI		N<10 any level						NE
< 18.5 kg/m**2	2	1 (50.0)	0					
5		[1.3, 98.7]						
18.5 - < 25.0 kg/m**2	6	4 (66.7)	3	2 (66.7)				
		[22.3, 95.7]		[9.4, 99.2]				
25.0 - < 30.0 kg/m**2	18	14 (77.8)	7	6 (85.7)				
		[52.4, 93.6]		[42.1, 99.6]				
>= 30.0 kg/m**2	19	14 (73.7)	9	7 (77.8)				
		[48.8, 90.9]		[40.0, 97.2]				
Baseline eosinophils - Low								0.507
< 150 cells/uL	25	18 (72.0)	10	7 (70.0)	1.029	1.102	2.0	1.000
		[50.6, 87.9]		[34.8, 93.3]	[0.640, 1.652]	[0.220, 5.512]	[-38.4, 42.4]	
>= 150 cells/uL	20	15 (75.0)	9	8 (88.9)	0.844	0.375	-13.9	0.633
		[50.9, 91.3]		[51.8, 99.7]	[0.599, 1.189]	[0.037, 3.786]	[-49.9, 22.1]	
Baseline specific perennial FEIA								0.434
status								
All negative	27	20 (74.1)	14	12 (85.7)	0.864	0.476	-11.6	0.692
-		[53.7, 88.9]			[0.634, 1.177]	[0.085, 2.677]	[-41.7, 18.5]	
Any positive	18	13 (72.2)	5	3 (60.0)	1.204	1.733	12.2	0.621
		[46.5, 90.3]		[14.7, 94.7]	[0.557, 2.602][0.220, 13.670]	[-48.2, 72.7]	

Table DT1AA_UBSIK: Incidence of non-disease related TEAEs during study period by key subgroups DSAFNB - LTE

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension. N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup.

Source Data: aae, created on: 11JUL2022

		Teze+Teze		Pbo+Pbo	_			
Non-disease related TEAEs during study period	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Total serum IgE		N<10 any level						NE
Low	40	30 (75.0) [58.8, 87.3]	18	14 (77.8) [52.4, 93.6]				
High	5	3 (60.0) [14.7, 94.7]	1	1 (100.0) [2.5, 100.0]				
OCS at baseline		N<10 any level						NE
Yes	4	3 (75.0) [19.4, 99.4]	1	1 (100.0) [2.5, 100.0]				
No	41	30 (73.2) [57.1, 85.8]	18	14 (77.8) [52.4, 93.6]				
LAMA use at baseline								0.355
Yes	11	9 (81.8) [48.2, 97.7]	7	5 (71.4) [29.0, 96.3]	1.145 [0.664, 1.976]	1.800 [0.191, 16.980]	10.4][-41.8, 62.6	1.000]
No	34	24 (70.6) [52.5, 84.9]	12	10 (83.3) [51.6, 97.9]	0.847 [0.607, 1.182]	0.480 [0.089, 2.596]	-12.7 [-44.4, 19.0	0.472]
Tiotropium use at baseline								0.985
Yes	9	7 (77.8) [40.0, 97.2]	6	5 (83.3) [35.9, 99.6]	0.933 [0.566, 1.539]	0.700 [0.049, 10.014]	-5.6 [-59.8, 48.7]	1.000]
No	36	26 (72.2) [54.8, 85.8]	13	10 (76.9) [46.2, 95.0]	0.939 [0.655, 1.346]	0.780 [0.177, 3.434]	-4.7 [-37.1, 27.7	1.000]

Table DT1AA_UBSIK: Incidence of non-disease related TEAEs during study period by key subgroups DSAFNB - LTE

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events. LTE = long term extension.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table DT1AA_UBSIK: Incidence of non-disease related TEAEs during study period by key subgroups DSAFNB - LTE

		Teze+Teze		Pbo+Pbo	_			
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Montelukast/ Cromoglicic acid use at baseline								0.670
Yes	15	13 (86.7) [59.5, 98.3]	6	6 (100.0) [54.1, 100.0]	0.867 [0.711, 1.057]	0.415 + [0.017, 9.961]	-13.3 [-42.2, 15.5	1.000]
No	30	20 (66.7) [47.2, 82.7]	13	9 (69.2) [38.6, 90.9]	0.963 [0.619, 1.498]	0.889 [0.219, 3.609]	-2.6 [-38.3, 33.2	1.000]

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension. N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup.

Source Data: aae, created on: 11JUL2022

		Tezepelumab		Placebo				
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Region (cat. N)		N<10 any level						NE
Western Europe	11	7 (63.6) [30.8, 89.1]	13	7 (53.8) [25.1, 80.8]				
North America	15	8 (53.3) [26.6, 78.7]	8	6 (75.0) [34.9, 96.8]				
South America	5	2 (40.0) [5.3, 85.3]	3	3 (100.0) [29.2, 100.0]				
Central/Eastern Europe	4	3 (75.0) [19.4, 99.4]	4	2 (50.0) [6.8, 93.2]				
Asia Pacific	13	8 (61.5) [31.6, 86.1]	7	5 (71.4) [29.0, 96.3]				
Rest of the world	7	5 (71.4) [29.0, 96.3]	5	4 (80.0) [28.4, 99.5]				
Baseline eosinophils (cat. N)								0.117
< 150 cells/uL	32	21 (65.6) [46.8, 81.4]	22	13 (59.1) [36.4, 79.3]	1.111 [0.723, 1.705]	1.322 [0.431, 4.051]	6.5 [-23.6, 36.7]	0.775
150 - < 300 cells/uL	23	12 (52.2) [30.6, 73.2]	18	14 (77.8) [52.4, 93.6]	0.671 [0.422, 1.065]	0.312 [0.078, 1.239]	-25.6 [-58.6, 7.4]	0.114
Baseline eosinophils (cat. Q)								0.348
Q1: < 140 cells/uL	28	18 (64.3) [44.1, 81.4]	22	13 (59.1) [36.4, 79.3]	1.088 [0.698, 1.696]	1.246 [0.395, 3.931]	5.2 [-26.0, 36.4]	0.774
Q2: 140 - < 250 cells/uL	23	13 (56.5) [34.5, 76.8]	11	9 (81.8) [48.2, 97.7]	0.691 [0.439, 1.088]	0.289 [0.051, 1.646]	-25.3 [-62.5, 11.9]	0.252
Q3: 250 - < 430 cells/uL	4	2 (50.0) [6.8, 93.2]	7	5 (71.4) [29.0, 96.3]	0.700 [0.236, 2.074]	0.400 [0.031, 5.151]	-21.4 [-100.0, 57.6]	0.576]
Baseline FENO (cat. N) < 25 ppb	55	N<10 any level 33 (60.0) [45.9, 73.0]	40	27 (67.5) [50.9, 81.4]				NE

Table NT1AA_SBSIN: Incidence of non-disease related TEAEs during study period by study specific subgroups DSAFB

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table NT1AA_SBSIN: Incidence of non-disease related TEAEs during study period by study specific subgroups DSAFB

		Tezepelumab		Placebo				
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Baseline FENO (cat. Q)								0.404
Q1: < 16 ppb	31	17 (54.8)	26	18 (69.2)	0.792	0.540	-14.4	0.290
		[36.0, 72.7]		[48.2, 85.7]	[0.526, 1.193]	[0.181, 1.609]] [-42.9, 14.1]]
Q2: 16 - < 30 ppb	24	16 (66.7)	14	9 (64.3)	1.037	1.111	2.4	1.000
		[44.7, 84.4]		[35.1, 87.2]	[0.640, 1.680]	[0.278, 4.434]][-34.7, 39.4]]
Total serum IgE (cat. N)		N<10 any level						NE
Q1: < 53.1 IU/ml	41	29 (70.7)	34	23 (67.6)				
		[54.5, 83.9]		[49.5, 82.6]				
Q2: 53.1 - < 195.6 IU/ml	9	3 (33.3)	4	3 (75.0)				
		[7.5, 70.1]		[19.4, 99.4]				
Q4: >= 572.4 IU/ml	5	1 (20.0)	2	1 (50.0)				
		[0.5, 71.6]		[1.3, 98.7]				
Nasal polyps last 2 years		N<10 any level						NE
Yes	4	2 (50.0)	3	3 (100.0)				
		[6.8, 93.2]		[29.2, 100.0]				
No	51	31 (60.8)	37	24 (64.9)				
		[46.1, 74.2]		[47.5, 79.8]				

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup. Source Data: aae, created on: 09MAR2022

NT1AA_SBSIN

Table NT1AA_TBSIN:	Incidence of non-di	sease related 7	TEAEs during	study period	by study	specific subgroups
		DSAFB -	- adult			

			Placebo	_				
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Region (cat. N)		N<10 any level						NE
Western Europe	11	7 (63.6)	13	7 (53.8)				
		[30.8, 89.1]		[25.1, 80.8]				
North America	14	- ()	8	6 (75.0)				
		[28.9, 82.3]		[34.9, 96.8]				
South America	5	2 (40.0)	3	3 (100.0)				
		[5.3, 85.3]		[29.2, 100.0]				
Central/Eastern Europe	4	3 (75.0)	4	2 (50.0)				
		[19.4, 99.4]		[6.8, 93.2]				
Asia Pacific	13	8 (61.5)	6	4 (66.7)				
		[31.6, 86.1]		[22.3, 95.7]				
Rest of the world	7	5 (71.4)	5	4 (80.0)				
		[29.0, 96.3]		[28.4, 99.5]				
Baseline eosinophils (cat. N)								0.129
< 150 cells/uL	32	21 (65.6)	21	12 (57.1)	1.148	1.432	8.5	0.573
< 150 Cells/uL	34	[46.8, 81.4]	21	[34.0, 78.2]	[0.734, 1.796]			
150 - < 300 cells/uL	22	12 (54.5)	18	14 (77.8)	0.701	0.343	-23.2	0.186
150 - < 500 Cerrs/ul	66	[32.2, 75.6]	10	. ,	[0.445, 1.105]			
		[52.2, 75.0]		[52.4, 55.0]	[0.445, 1.105]	[0.005, 1.500]	[50.0, 10.1]	
Baseline eosinophils (cat. Q)								0.366
01: < 140 cells/uL	28	18 (64.3)	21	12 (57.1)	1.125	1.350	7.1	0.768
5		[44.1, 81.4]		[34.0, 78.2]		[0.423, 4.304]	[-24.6, 38.9]	
Q2: 140 - < 250 cells/uL	22	13 (59.1)	11	9 (81.8)	0.722	0.321	-22.7	0.258
5		[36.4, 79.3]		[48.2, 97.7]	[0.463, 1.128]	[0.056, 1.851]	[-60.2, 14.8]	
03: 250 - < 430 cells/uL	4	2 (50.0)	7	5 (71.4)	0.700	0.400	-21.4	0.576
5		[6.8, 93.2]		[29.0, 96.3]	[0.236, 2.074]	[0.031, 5.151]	[-100.0, 57.6]]
Baseline FENO (cat. N)		N<10 any level						NE
< 25 ppb	54	33 (61.1)	39	26 (66.7)				
		[46.9, 74.1]		[49.8, 80.9]				

Note: DSAFB - adult = Dossier Biomarker Safety Set - adult.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table NT1AA_TBSIN: Incidence of non-disease related TEAEs during study period by study specific subgroups DSAFB - adult

		Tezepelumab Placebo						
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Baseline FENO (cat. Q)								0.401
Q1: < 16 ppb	30	17 (56.7) [37.4, 74.5]	26	. ,	0.819 [0.546, 1.227]	0.581 [0.193, 1.750]	-12.6 [-41.2, 16.1]	0.412
Q2: 16 - < 30 ppb	24	16 (66.7) [44.7, 84.4]	13	8 (61.5) [31.6, 86.1]	1.083 [0.648, 1.812]	1.250 [0.307, 5.085]	5.1 [-33.3, 43.5]	1.000
Total serum IgE (cat. N)		N<10 any level						NE
Q1: < 53.1 IU/ml	40	29 (72.5) [56.1, 85.4]	33	22 (66.7) [48.2, 82.0]				
Q2: 53.1 - < 195.6 IU/ml	9	3 (33.3) [7.5, 70.1]	4	3 (75.0) [19.4, 99.4]				
Q4: >= 572.4 IU/ml	5	1 (20.0) [0.5, 71.6]	2	1 (50.0) [1.3, 98.7]				
Nasal polyps last 2 years		N<10 any level						NE
Yes	4	2 (50.0) [6.8, 93.2]	3	3 (100.0) [29.2, 100.0]				
No	50	31 (62.0) [47.2, 75.3]	36	23 (63.9) [46.2, 79.2]				

Note: DSAFB - adult = Dossier Biomarker Safety Set - adult.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

		Teze+Teze		Pbo+Pbo	_		
Non-disease related TEAEs during study period	N	n (%) [95 % CI]	N	n (%) [95 % CI]		OR 95 % CT1	RD [95 % CI]p-value
beady portion		[50 % 01]		[50 % 01]		50 % 01]	[jo w oi]p tuite
Age (cat. N)		N<10 any level					NE
< 18 years	1	0 (0.0) [0.0, 97.5]	0				
18 - < 65 years	35	25 (71.4) [53.7, 85.4]	16	13 (81.3) [54.4, 96.0]			
>= 65 years	9	8 (88.9) [51.8, 99.7]	3	2 (66.7) [9.4, 99.2]			
Region (cat. N)		N<10 any level					NE
Western Europe	9	8 (88.9) [51.8, 99.7]	7	4 (57.1) [18.4, 90.1]			
North America	14	8 (57.1) [28.9, 82.3]	3	3 (100.0) [29.2, 100.0]			
South America	5	2 (40.0) [5.3, 85.3]	1	1 (100.0) [2.5, 100.0]			
Central/Eastern Europe	4	3 (75.0) [19.4, 99.4]	4	3 (75.0) [19.4, 99.4]			
Asia Pacific	6	5 (83.3) [35.9, 99.6]	2	2 (100.0) [15.8, 100.0]			
Rest of the world	7	7 (100.0) [59.0, 100.0]	2	2 (100.0) [15.8, 100.0]			

Table DT1AA_UBSIN: Incidence of non-disease related TEAEs during study period by study specific subgroups DSAFNB - LTE

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension.

N = total number of patients in analysis set. n = number of patients with response. TEAE = treatment emergent adverse events. LTE = long term extension.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table DT1AA_UBSIN: Incidence of non-disease related TEAEs during study period by study specific subgroups DSAFNB - LTE

		Teze+Teze	eze+Teze		Pbo+Pbo		_			
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD			
study period	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value		
Baseline eosinophils (cat. N)								0.507		
< 150 cells/uL	25	18 (72.0)	10	7 (70.0)	1.029	1.102	2.0	1.000		
		[50.6, 87.9]		[34.8, 93.3]	[0.640, 1.652]	[0.220, 5.512]	[-38.4, 42.4]		
150 - < 300 cells/uL	20	15 (75.0)	9	8 (88.9)	0.844	0.375	-13.9	0.633		
		[50.9, 91.3]		[51.8, 99.7]	[0.599, 1.189]	[0.037, 3.786]	[-49.9, 22.1]		
Baseline eosinophils (cat. Q)		N<10 any level						NE		
01: < 140 cells/uL	21	-	10	7 (70.0)						
g1. 110 00110, d2		[43.0, 85.4]	10	[34.8, 93.3]						
Q2: 140 - < 250 cells/uL	21	17 (81.0)	7	7 (100.0)						
		[58.1, 94.6]		[59.0, 100.0]						
Q3: 250 - < 430 cells/uL	3	2 (66.7)	2	1 (50.0)						
		[9.4, 99.2]		[1.3, 98.7]						

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension.

N = total number of patients in analysis set. n = number of patients with response. TEAE = treatment emergent adverse events. LTE = long term extension.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table DT1AA_UBSIN: Incidence of non-disease related TEAEs during study period by study specific subgroups DSAFNB - LTE

		Teze+Teze		Pbo+Pbo				
Non-disease related TEAEs during study period	N	n (%) [95 % CI]	N	n (%) [95 % CI]		OR [95 % CI]	RD [95 % CI]	p-value
<u></u>		. [00 0 0-]		[]	[]	[00 0 00]	[]	P
Baseline FENO (cat. N)		N<10 any level						NE
< 25 ppb	45	33 (73.3) [58.1, 85.4]	19	15 (78.9) [54.4, 93.9]				
Baseline FENO (cat. Q)								0.605
Q1: < 16 ppb	23	17 (73.9) [51.6, 89.8]	12	9 (75.0) [42.8, 94.5]	0.986 [0.656, 1.481]	0.944 [0.190, 4.698]	-1.1 [-37.8, 35.6	1.000]
Q2: 16 - < 30 ppb	22	16 (72.7) [49.8, 89.3]	7	6 (85.7) [42.1, 99.6]	0.848 [0.571, 1.261]	0.444 [0.044, 4.503]	-13.0 [-54.3, 28.3	0.646]

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension.

N = total number of patients in analysis set. n = number of patients with response. TEAE = treatment emergent adverse events. LTE = long term extension.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table DT1AA_UBSIN: Incidence of non-disease related TEAEs during study period by study specific subgroups DSAFNB - LTE

		Teze+Teze		Pbo+Pbo			
Non-disease related TEAEs during study period	N	n (%) [95 % CI]	N	n (%) [95 % CI]		OR [95 % CI][RD 95 % CI]p-value
Total serum IgE (cat. N)		N<10 any level					NE
Q1: < 53.1 IU/ml	34	27 (79.4)	16	13 (81.3)			
		[62.1, 91.3]		[54.4, 96.0]			
Q2: 53.1 - < 195.6 IU/ml	6	3 (50.0)	2	1 (50.0)			
		[11.8, 88.2]		[1.3, 98.7]			
Q4: >= 572.4 IU/ml	5	3 (60.0)	1	1 (100.0)			
		[14.7, 94.7]		[2.5, 100.0]			
Nasal polyps last 2 years		N<10 any level					NE
Yes	4	4 (100.0)	1	1 (100.0)			
		[39.8, 100.0]		[2.5, 100.0]			
No	41	29 (70.7)	18	14 (77.8)			
		[54.5, 83.9]		[52.4, 93.6]			

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension.

N = total number of patients in analysis set. n = number of patients with response. TEAE = treatment emergent adverse events. LTE = long term extension.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table MT1AAN_SBMI0: Incidence of non-disease related non-severe TEAEs during study period DSAFB

		Tezepelumab		Placebo				
		n (%)		n (%)	RR	OR	RD	7
	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related non-severe TEAEs during study period	66	39 (59.1) [46.3, 71.0]	48	31 (64.6) [49.5, 77.8]	0.915 [0.685, 1.223]	0.792 [0.367, 1.708]	-5.5 [-25.3, 14.3	0.566]

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 02FEB2022

Table NT1AAN_SBMI0: Incidence of non-disease related non-severe TEAEs during study period DSAFB

		Tezepelumab		Placebo	_			
		n (%)		n (%)		OR	RD	
	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related non-severe TEAEs during study period	55	32 (58.2) [44.1, 71.3]	40	26 (65.0) [48.3, 79.4]	0.895 [0.650, 1.232]	0.749 [0.323, 1.739]	-6.8 [-28.7, 15.0	0.530

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 01FEB2022

Table NT1AAN_TBMI0: Incidence of non-disease related non-severe TEAEs during study period DSAFB - adult

		Tezepelumab		Placebo	_			
		n (%)		n (%)	RR	OR	RD	
	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related non-severe	54	32 (59.3)	39	25 (64.1)	0.924	0.815	-4.8	0.672
TEAEs during study period		[45.0, 72.4]		[47.2, 78.8]	[0.670, 1.276]	[0.348, 1.906]	[-27.0, 17.3]

Note: DSAFB - adult = Dossier Biomarker Safety Set - adult. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 01FEB2022

AstraZeneca Value Dossier Analysis: CD-RI-MEDI9929-1146 Data Cut Date: 06JUN2017

Table PT3AAN_SBMI0: Incidence of non-disease related non-severe TEAEs during study period DSAFB

		Tezepelumab		Placebo	_			
	N	n (%) [95 % CI]	N	n (%) [95 % CI]		OR [95 % CI]	RD [95 % CI]	p-value
Non-disease related non-severe	12	7 (58.3)	9	6 (66.7)	0.875	0.700	-8.3	1.000
TEAEs during study period	12	[27.7, 84.8]	2	[29.9, 92.5]	[0.450, 1.701]			

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 07FEB2022

Table ST1AAN_SBMI0: Incidence of non-disease related non-severe TEAEs during study period DSAFB

		Tezepelumab		Placebo	_			
	N	n (%) [95 % CI]	N	n (%) [95 % CI]		OR [95 % CI]	RD [95 % CI]	p-value
	10		11					
Non-disease related non-severe TEAEs during study period	12	5 (41.7) [15.2, 72.3]	11	6 (54.5) [23.4, 83.3]	0.764 [0.323, 1.805]	0.595 [0.114, 3.102]	-12.9 [-62.1, 36.4	0.684

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 07FEB2022

Table DT1AAN_UBMI0: Incidence of non-disease related non-severe TEAEs during study period DSAFNB - LTE

		Teze+Teze		Pbo+Pbo	_			
		n (%)		n (%)	RR	OR	RD	
	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related non-severe TEAEs during	45	33 (73.3)	19	15 (78.9)	0.929	0.733	-5.6	0.758
study period		[58.1, 85.4]		[54.4, 93.9]	[0.694, 1.243]	[0.203, 2.653]	[-31.8, 20.6]

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: aae, created on: 15JUL2022

Table CT1AAN_SBMI0: Incidence of non-disease related non-severe TEAEs during study period DSAFB

		Tezepelumab		Placebo				
	N	n (%) [95 % CI]	N	n (%) [95 % CI]		OR [95 % CI]	RD [95 % CI]	p-value
Non-disease related non-severe TEAEs during study period	4	3 (75.0) [19.4, 99.4]	8	7 (87.5) [47.3, 99.7]	0.857 [0.459, 1.599]	0.429 [0.020, 9.364]	-12.5 [-79.5, 54.5	1.000

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 07FEB2022

Table MT1AAN_SBSIK:	Incidence of non-	-disease related	d non-severe	TEAEs (during	study	period l	by key	subgroups
		D	SAFB						

	Tezepelumab Placebo							
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Sex								0.396
Male	20	11 (55.0)	8	- (/	0.733	0.407	-20.0	0.419
		[31.5, 76.9]			[0.418, 1.288]			-
Female	46	28 (60.9)	40	(,,,		0.933	-1.6	1.000
		[45.4, 74.9]		[45.8, 77.3]	[0.698, 1.360]	[0.390, 2.232]	[-24.6, 21.3]
Age								0.312
< 65 years	56	35 (62.5)	39	25 (64.1)	0.975	0.933	-1.6	1.000
(US Years	50	[48.5, 75.1]	55	· · · ·	[0.715, 1.330]			
>= 65 years	10	4 (40.0)	9		0.600	0.333	-26.7	0.370
, oo years	10	()	2	- (/	[0.247, 1.459]			
		[,]		[,]	[.1
Exacerbations in the year before								0.751
study								
<= 2	38	22 (57.9)	31	- (/		0.868	-3.4	0.810
		[40.8, 73.7]			[0.640, 1.395]		[-29.6, 22.8	-
> 2	28	17 (60.7)	17	(,		0.644	-9.9	0.541
		[40.6, 78.5]		[44.0, 89.7]	[0.561, 1.319]	[0.177, 2.339]	[-42.8, 23.1	.]
Race		N<10 any level						NE
White	43	21 (48.8)	36	24 (66.7)				
		[33.3, 64.5]		[49.0, 81.4]				
Black or African American	6	6 (100.0)	4	2 (50.0)				
brach of million imorroun	U	[54.1, 100.0]	-	[6.8, 93.2]				
Asian	15	10 (66.7)	6	3 (50.0)				
	10	[38.4, 88.2]	Ŭ	[11.8, 88.2]				
Other	2	2 (100.0)	2	2 (100.0)				
0 0101		[15.8, 100.0]		[15.8, 100.0]				
		,		,				

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table MT1AAN_SBSIK:	Incidence of non-	-disease related	d non-severe	TEAEs (during	study	period l	by key	subgroups
		D	SAFB						

	Tezepelumab		Placebo					
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Region								0.428
Europe	21	11 (52.4)	15	6 (40.0)	1.310	1.650	12.4	0.516
		[29.8, 74.3]		[16.3, 67.7]	[0.624, 2.750]	[0.431, 6.313]	[-26.1, 50.8]
America	21	12 (57.1)	13	11 (84.6)	0.675	0.242	-27.5	0.140
		[34.0, 78.2]		[54.6, 98.1]	[0.436, 1.045]	[0.043, 1.377]	[-62.6, 7.6]]
Asia/Pacific	13	8 (61.5)	9	6 (66.7)	0.923	0.800	-5.1	1.000
		[31.6, 86.1]		[29.9, 92.5]	[0.491, 1.735]	[0.135, 4.745]	[-55.1, 44.9]
Rest of the world	11	8 (72.7)	11	8 (72.7)	1.000	1.000	0.0	1.000
		[39.0, 94.0]		[39.0, 94.0]	[0.599, 1.668]	[0.153, 6.531]	[-46.3, 46.3]
BMI		N<10 any level						NE
< 18.5 kg/m**2	2	2 (100.0)	0					
		[15.8, 100.0]						
18.5 - < 25.0 kg/m**2	12	6 (50.0)	11	7 (63.6)				
		[21.1, 78.9]		[30.8, 89.1]				
25.0 - < 30.0 kg/m**2	24	12 (50.0)	16	12 (75.0)				
		[29.1, 70.9]		[47.6, 92.7]				
>= 30.0 kg/m**2	28	19 (67.9)	21	12 (57.1)				
		[47.6, 84.1]		[34.0, 78.2]				
Baseline eosinophils - Low								0.026 i
< 150 cells/uL	37	25 (67.6)	23	12 (52.2)	1.295	1.910	15.4	0.281
		[50.2, 82.0]		[30.6, 73.2]	[0.825, 2.032]	[0.656, 5.563]	[-13.5, 44.3]
>= 150 cells/uL	29	14 (48.3)	25	19 (76.0)	0.635	0.295	-27.7	0.052
		[29.4, 67.5]		[54.9, 90.6]	[0.411, 0.983]	[0.091, 0.951]	[-56.2, 0.7]]
Baseline specific perennial FEIA								0.869
status								
All negative	39	23 (59.0)	29	18 (62.1)	0.950	0.878	-3.1	1.000
		[42.1, 74.4]		[42.3, 79.3]				
Any positive	24	14 (58.3)	17	11 (64.7)	0.902	0.764	-6.4	0.753
		[36.6, 77.9]		[38.3, 85.8]	[0.554, 1.468]	[0.212, 2.757]	[-41.5, 28.7]

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup. Source Data: aae, created on: 04APR2022

MT1AAN_SBSIK

Table MT1AAN_SBSIK:	Incidence of non-disease	related non-severe	TEAEs during	study	period by key subgr	oups
		DSAFB				

		Tezepelumab		Placebo	_			
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Total serum IgE		N<10 any level						NE
Low	61	38 (62.3)	44	28 (63.6)				
		[49.0, 74.4]		[47.8, 77.6]				
High	5	1 (20.0)	4	3 (75.0)				
		[0.5, 71.6]		[19.4, 99.4]				
OCS at baseline								0.437
Yes	8	5 (62.5)	7	6 (85.7)	0.729	0.278	-23.2	0.569
		[24.5, 91.5]		[42.1, 99.6]	[0.394, 1.350]	[0.022, 3.577]	[-79.0, 32.6]
No	58	34 (58.6)	41	25 (61.0)		0.907	-2.4	
		[44.9, 71.4]		[44.5, 75.8]	[0.693, 1.333]	[0.401, 2.052]	[-24.0, 19.3]
LAMA use at baseline								0.294
Yes	15	9 (60.0)	16	- (,			10.0	0.722
		[32.3, 83.7]			[0.632, 2.278]			
No	51	30 (58.8)		- (-)	0.818			
		[44.2, 72.4]		[53.3, 86.3]	[0.597, 1.122]	[0.216, 1.447]	[-36.2, 10.1]
Tiotropium use at baseline								0.692
Yes	13	7 (53.8)	15	0 (52 2)	1.010	1.021	0.5	1.000
165	13	[25.1, 80.8]	10	()	[0.506, 2.015]			
No	53	32 (60.4)	33	23 (69.7)		0.663	-9.3	0.490
10	55	[46.0, 73.5]	55	· · · ·	[0.633, 1.185]			
		[=0.0, /3.3]		[51.5, 64.4]	[0.035, 1.105]	[0.205, 1.009]	[52.5, 15.0	1

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table MT1AAN_SBSIK: Incidence of non-disease related non-severe TEAEs during study period by key subgroups DSAFB

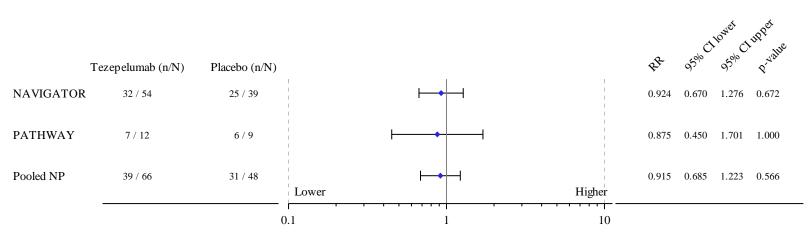
		[ezepelumab		Placebo	_			
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Montelukast/ Cromoglicic acid use at baseline								0.248
Yes	19	13 (68.4)	14	8 (57.1)	1.197	1.625	11.3	0.716
		[43.4, 87.4]		[28.9, 82.3]	[0.693, 2.069]	[0.387, 6.817]	[-28.2, 50.8]
No	47	26 (55.3) [40.1, 69.8]	34	23 (67.6) [49.5, 82.6]	0.818 [0.578, 1.156]	0.592 [0.236, 1.486]	-12.3 [-36.1, 11.4	0.357]

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Figure MF1AAN_SBMF0: Forest plot for non-disease related non-severe TEAEs during study period **DSAFB**



Test for heterogeneity - p-value: 0.884, I-square: 0.0 %

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of affected patients. RR = relative risk. CI = confidence interval. Heterogeneity was investigated with Cochran Q test. NE = not evaluable.

Source tables: NT1AAN_TBMI0, PT3AAN_SBMI0, MT1AAN_SBMI0

Table NT1AAN_SBSIK:	Incidence c	f non-disease	related n	non-severe	TEAEs d	during	study	period	by key	subgroups	
			DSA	AFB							

		Tezepelumab		Placebo	_			
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Sex								0.349
Male	19	10 (52.6)	8	6 (75.0)	0.702	0.370	-22.4	0.405
Male	19	[28.9, 75.6]	0	()	[0.391, 1.259]			
Female	36	22 (61.1)	32	20 (62.5)	0.978	0.943	-1.4	1.000
remare	50	[43.5, 76.9]	52	· · · ·	[0.673, 1.421]			
		[13.3, 70.5]		[13.7, 70.9]	[0.075, 1.181]	[0.001, 0.010]	[17.5, 11.7	1
Age								0.367
< 65 years	46	28 (60.9)	33	21 (63.6)	0.957	0.889	-2.8	0.819
-		[45.4, 74.9]		[45.1, 79.6]	[0.676, 1.353]	[0.353, 2.239]	[-27.0, 21.5]
>= 65 years	9	4 (44.4)	7	5 (71.4)	0.622	0.320	-27.0	0.358
-		[13.7, 78.8]		[29.0, 96.3]	[0.261, 1.482]	[0.039, 2.618]	[-86.3, 32.3]
Exacerbations in the year before study								0.513
<= 2	31	19 (61.3)	27	17 (63.0)	0.973	0.931	-1.7	1.000
		[42.2, 78.2]		[42.4, 80.6]	[0.651, 1.456]	[0.321, 2.699]	[-30.2, 26.8]
> 2	24	13 (54.2)	13	9 (69.2)	0.782	0.525	-15.1	0.491
		[32.8, 74.4]		[38.6, 90.9]	[0.467, 1.311]	[0.126, 2.185]	[-53.0, 22.9]
Race		N<10 any level						NE
White	34	16 (47.1)	28	19 (67.9)				
		[29.8, 64.9]		[47.6, 84.1]				
Black or African American	4	4 (100.0)	3	1 (33.3)				
		[39.8, 100.0]		[0.8, 90.6]				
Asian	15	10 (66.7)	7	4 (57.1)				
		[38.4, 88.2]		[18.4, 90.1]				
Other	2	2 (100.0)	2	2 (100.0)				
		[15.8, 100.0]		[15.8, 100.0]				

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup. Source Data: aae, created on: 11APR2022

NT1AAN_SBSIK

Table NT1AAN_SBSIK:	Incidence	of non-disease	related non-severe	TEAEs during	study	period by key	subgroups
			DSAFB				

		Tezepelumab		Placebo				
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Region								0.356
Europe	11	6 (54.5)	10	4 (40.0)	1.364	1.800	14.5	0.670
-		[23.4, 83.3]		[12.2, 73.8]	[0.537, 3.460]	[0.318, 10.201]	[-37.3, 66.4	·]
America	20	10 (50.0)	11	9 (81.8)	0.611	0.222	-31.8	0.128
		[27.2, 72.8]		[48.2, 97.7]	[0.364, 1.027]	[0.038, 1.298]	[-70.5, 6.8]]
Asia/Pacific	13	8 (61.5)	10	7 (70.0)	0.879	0.686	-8.5	1.000
		[31.6, 86.1]		[34.8, 93.3]	[0.487, 1.588]	[0.119, 3.963]	[-56.1, 39.2	2]
Rest of the world	11	8 (72.7)	9	6 (66.7)	1.091	1.333	6.1	1.000
		[39.0, 94.0]		[29.9, 92.5]	[0.607, 1.962]	[0.196, 9.083]	[-44.6, 56.7	']
BMI		N<10 any level						NE
< 18.5 kg/m**2	3	2 (66.7)	0					
5		[9.4, 99.2]						
18.5 - < 25.0 kg/m**2	11	5 (45.5)	8	5 (62.5)				
2		[16.7, 76.6]		[24.5, 91.5]				
25.0 - < 30.0 kg/m**2	20	10 (50.0)	14	10 (71.4)				
2		[27.2, 72.8]		[41.9, 91.6]				
>= 30.0 kg/m**2	21	15 (71.4)	18	11 (61.1)				
2		[47.8, 88.7]		[35.7, 82.7]				
Baseline eosinophils - Low								0.050
< 150 cells/uL	32	21 (65.6)	22	12 (54.5)	1.203	1.591	11.1	0.571
		[46.8, 81.4]		[32.2, 75.6]	[0.762, 1.899]	[0.523, 4.837]	[-19.3, 41.4	·]
>= 150 cells/uL	23	11 (47.8)	18	14 (77.8)	0.615	0.262	-30.0	0.063
		[26.8, 69.4]		[52.4, 93.6]	[0.376, 1.007]	[0.066, 1.041]	[-62.9, 3.0]]
Baseline specific perennial FEIA								0.751
status								
All negative	33	20 (60.6)	25	16 (64.0)	0.947	0.865	-3.4	1.000
		[42.1, 77.1]		[42.5, 82.0]	[0.633, 1.416]	[0.296, 2.534]	[-32.0, 25.3	3]
Any positive	22	12 (54.5)	14	9 (64.3)	0.848	0.667	-9.7	0.732
		[32.2, 75.6]		[35.1, 87.2]	[0.492, 1.465]	[0.168, 2.645]	[-48.2, 28.7]

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup. Source Data: aae, created on: 11APR2022

NT1AAN_SBSIK

		Tezepelumab		Placebo				
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Total serum IgE		N<10 any level						NE
Low	50	31 (62.0) [47.2, 75.3]	38	25 (65.8) [48.6, 80.4]				
High	5	1 (20.0) [0.5, 71.6]	2	1 (50.0) [1.3, 98.7]				
OCS at baseline								0.474
Yes	8	5 (62.5) [24.5, 91.5]	7	- ()	0.729 [0.394, 1.350]		-23.2 [-79.0, 32.6	0.569 5]
No	47	27 (57.4) [42.2, 71.7]	33	_ (,	0.948 [0.655, 1.371]		-3.2 [-27.6, 21.3	0.821 8]
LAMA use at baseline								0.447
Yes	15	9 (60.0) [32.3, 83.7]			1.067 [0.587, 1.939]		3.8 [-37.4, 44.9	1.000 9]
No	40	23 (57.5) [40.9, 73.0]	24	17 (70.8) [48.9, 87.4]	0.812 [0.561, 1.175]	0.557 [0.189, 1.641]		0.424 8]
Tiotropium use at baseline								0.948
Yes	13	7 (53.8) [25.1, 80.8]	15	- (/	0.897 [0.468, 1.721]			1.000 3]
No	42	25 (59.5) [43.3, 74.4]	25	17 (68.0) [46.5, 85.1]	0.875 [0.607, 1.263]		-8.5 [-35.2, 18.3	0.604 3]

Table NT1AAN_SBSIK: Incidence of non-disease related non-severe TEAEs during study period by key subgroups DSAFB

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table NT1AAN_SBSIK: Incidence of non-disease related non-severe TEAEs during study period by key subgroups DSAFB

		[ezepelumab		Placebo				
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Montelukast/ Cromoglicic acid use at baseline								0.554
Yes	20	13 (65.0) [40.8, 84.6]	14	9 (64.3) [35.1, 87.2]	1.011 [0.610, 1.677]	1.032 [0.247. 4.303]	0.7	1.000
No	35	19 (54.3) [36.6, 71.2]	26	17 (65.4) [44.3, 82.8]	0.830 [0.549, 1.255]	0.629	-11.1	0.438

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table NT1AAN_TBSIK: Incidence of non-disease related non-severe TEAEs during study period by key subgroups DSAFB - adult

		Tezepelumab		Placebo	_			
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Sex								0.538
Male	18	10 (55.6)	7	5 (71.4)	0.778	0.500	-15.9	0.659
		[30.8, 78.5]		[29.0, 96.3]	[0.416, 1.453]	[0.076, 3.293]	[-66.4, 34.6	5]
Female	36	22 (61.1)	32	20 (62.5)	0.978	0.943	-1.4	1.000
		[43.5, 76.9]		[43.7, 78.9]	[0.673, 1.421]	[0.354, 2.513]	[-27.5, 24.7	']
Age								0.325
< 65 years	45	28 (62.2)	32	20 (62.5)	0.996	0.988	-0.3	1.000
-		[46.5, 76.2]		[43.7, 78.9]	[0.700, 1.415]	[0.388, 2.519]	[-24.9, 24.4	£]
>= 65 years	9	4 (44.4)	7	5 (71.4)	0.622	0.320	-27.0	0.358
-		[13.7, 78.8]		[29.0, 96.3]	[0.261, 1.482]	[0.039, 2.618]	[-86.3, 32.3	3]
Exacerbations in the year before study								0.553
<= 2	31	19 (61.3)	26	16 (61.5)	0.996	0.990	-0.2	1.000
		[42.2, 78.2]		[40.6, 79.8]	[0.659, 1.505]	[0.339, 2.887]	[-29.2, 28.7]
> 2	23	13 (56.5)	13	9 (69.2)	0.816	0.578	-12.7	0.501
		[34.5, 76.8]		[38.6, 90.9]	[0.490, 1.359]	[0.137, 2.433]	[-51.0, 25.6	5]
Race		N<10 any level						NE
White	33	16 (48.5)	28	19 (67.9)				
		[30.8, 66.5]		[47.6, 84.1]				
Black or African American	4	4 (100.0)	3	1 (33.3)				
		[39.8, 100.0]		[0.8, 90.6]				
Asian	15	10 (66.7)	6	3 (50.0)				
		[38.4, 88.2]		[11.8, 88.2]				
Other	2	2 (100.0)	2	2 (100.0)				
		[15.8, 100.0]		[15.8, 100.0]				

Note: DSAFB - adult = Dossier Biomarker Safety Set - adult.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table NT1AAN_TBSIK:	Incidence of	non-disease	related	non-severe	TEAEs	during	study	period k	by key	subgroups	
			DSAFB	- adult							

		Tezepelumab		Placebo	_			
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Region								0.417
Europe	11	6 (54.5)	10	4 (40.0)	1.364	1.800	14.5	0.670
		[23.4, 83.3]		[12.2, 73.8]		[0.318, 10.201]	·	-
America	19	10 (52.6)	11	9 (81.8)	0.643	0.247	-29.2	0.140
		[28.9, 75.6]		[48.2, 97.7]		[0.042, 1.460]		-
Asia/Pacific	13	8 (61.5)	9	6 (66.7)	0.923	0.800	-5.1	1.000
		[31.6, 86.1]			[0.491, 1.735]			
Rest of the world	11	8 (72.7)	9	6 (66.7)	1.091	1.333	6.1	1.000
		[39.0, 94.0]		[29.9, 92.5]	[0.607, 1.962]	[0.196, 9.083]	[-44.6, 56.7]
BMI		N<10 any level						NE
< 18.5 kg/m**2	2	2 (100.0)	0					
		[15.8, 100.0]						
18.5 - < 25.0 kg/m**2	11	5 (45.5)	7	4 (57.1)				
		[16.7, 76.6]		[18.4, 90.1]				
25.0 - < 30.0 kg/m**2	20	10 (50.0)	14	10 (71.4)				
		[27.2, 72.8]		[41.9, 91.6]				
>= 30.0 kg/m**2	21	15 (71.4)	18	11 (61.1)				
		[47.8, 88.7]		[35.7, 82.7]				
Baseline eosinophils - Low								0.055
< 150 cells/uL	32	21 (65.6)	21	11 (52.4)	1.253	1.736	13.2	0.397
		[46.8, 81.4]			[0.776, 2.022]			
>= 150 cells/uL	22	11 (50.0)	18	14 (77.8)	0.643	0.286	-27.8	0.104
		[28.2, 71.8]		[52.4, 93.6]	[0.396, 1.045]	[0.071, 1.148]	[-61.2, 5.7]	
Baseline specific perennial FEIA status								0.637
All negative	32	20 (62.5)	24	15 (62.5)	1.000	1.000	0.0	1.000
		[43.7, 78.9]		[40.6, 81.2]	[0.664, 1.507]	[0.335, 2.984]	[-29.3, 29.3]
Any positive	22	12 (54.5)	14	9 (64.3)	0.848	0.667	-9.7	0.732
		[32.2, 75.6]		[35.1, 87.2]	[0.492, 1.465]	[0.168, 2.645]	[-48.2, 28.7]

Note: DSAFB - adult = Dossier Biomarker Safety Set - adult.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table NT1AAN_TBSIK:	Incidence	of	non-disease	related	non-severe	TEAEs	during	study	period k	by ke	y s	subgroups
					- adult							

		Tezepelumab	_	Placebo				
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Total serum IgE		N<10 any level						NE
Low	49	31 (63.3)	37	24 (64.9)				
		[48.3, 76.6]		[47.5, 79.8]				
High	5	1 (20.0)	2	1 (50.0)				
		[0.5, 71.6]		[1.3, 98.7]				
OCS at baseline								0.408
Yes	8	5 (62.5)	7	6 (85.7)	0.729	0.278	-23.2	0.569
		[24.5, 91.5]		[42.1, 99.6]	[0.394, 1.350]	[0.022, 3.577]	[-79.0, 32.6]
No	46	27 (58.7)	32	19 (59.4)	0.989	0.972	-0.7	1.000
		[43.2, 73.0]		[40.6, 76.3]	[0.679, 1.439]	[0.388, 2.434]	[-25.5, 24.2]
LAMA use at baseline								0.417
Yes	15	9 (60.0)	15	8 (53.3)	1.125		6.7	1.000
		[32.3, 83.7]			[0.600, 2.109]			
No	39	23 (59.0)	24	17 (70.8)		0.592	-11.9	0.424
		[42.1, 74.4]		[48.9, 87.4]	[0.577, 1.201]	[0.200, 1.755]	[-39.1, 15.4	:]
Tiotropium use at baseline	10	F (FO 0)		0 (55 4)	0.040	0.075		0.899
Yes	13	7 (53.8)	14	8 (57.1)	0.942	0.875	-3.3	1.000
		[25.1, 80.8]	~ -		[0.479, 1.855]			
No	41	25 (61.0)	25	17 (68.0)	0.897	0.735	-7.0	0.608
		[44.5, 75.8]		[46.5, 85.1]	[0.623, 1.290]	[0.258, 2.099]	[-33.9, 19.8]

Note: DSAFB - adult = Dossier Biomarker Safety Set - adult.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table NT1AAN_TBSIK: Incidence of non-disease related non-severe TEAEs during study period by key subgroups DSAFB - adult

		Tezepelumab		Placebo				
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Montelukast/ Cromoglicic acid use at baseline								0.393
Yes	19	13 (68.4) [43.4, 87.4]	13	8 (61.5) [31.6, 86.1]	1.112 [0.656, 1.884]	1.354 [0.309, 5.936]	6.9 [-33.3, 47.1	0.721]
No	35	19 (54.3) [36.6, 71.2]	26	17 (65.4) [44.3, 82.8]	0.830 [0.549, 1.255]	0.629 [0.221, 1.790]	-11.1 [-39.1, 16.9	0.438]

Note: DSAFB - adult = Dossier Biomarker Safety Set - adult.

N = total number of patients	in analysis set.	. n = number of patients	with response. O	DCS = oral	corticosteroids.	TEAE = treatment
emergent adverse events.						

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table DT1AAN_UBSIK:	Incidence of	non-disease	related	non-severe	TEAEs	during	study	period b	by key	subgroups	

	Teze+Teze Pbo+Pbo		_					
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Sex								0.554
Male	17	12 (70.6)	2	1 (50.0)	1.412	2.400	20.6	1.000
		[44.0, 89.7]				[0.124, 46.391]	[-80.0, 100.0]	
Female	28	21 (75.0)	17	14 (82.4)	0.911	0.643	-7.4	0.719
		[55.1, 89.3]		[56.6, 96.2]	[0.670, 1.238]	[0.142, 2.916]	[-36.3, 21.6]	
Age								0.329
< 65 years	36	25 (69.4)	16	13 (81.3)	0.855	0.524	-11.8	0.506
-		[51.9, 83.7]		[54.4, 96.0]	[0.621, 1.177]	[0.124, 2.218]	[-40.7, 17.0]	
>= 65 years	9	8 (88.9)	3	2 (66.7)	1.333	4.000	22.2	0.455
		[51.8, 99.7]		[9.4, 99.2]	[0.580, 3.066]	[0.167, 95.756]	[-57.2, 100.0]	
Exacerbations in the year before study								0.308
<= 2	26	20 (76.9)	11	8 (72.7)	1.058	1.250	4.2	1.000
		[56.4, 91.0]		[39.0, 94.0]	[0.696, 1.608]	[0.250, 6.255]	[-33.2, 41.6]	
> 2	19	13 (68.4)	8	7 (87.5)	0.782	0.310	-19.1	0.633
		[43.4, 87.4]		[47.3, 99.7]	[0.523, 1.169]	[0.031, 3.111]	[-59.0, 20.8]	
Race		N<10 any level						NE
White	31	20 (64.5)	14	10 (71.4)				
		[45.4, 80.8]		[41.9, 91.6]				
Black or African American	4	4 (100.0)	2	2 (100.0)				
		[39.8, 100.0]		[15.8, 100.0]				
Asian	8	7 (87.5)	2	2 (100.0)				
		[47.3, 99.7]		[15.8, 100.0]				
Other	2	2 (100.0)	1	1 (100.0)				
		[15.8, 100.0]		[2.5, 100.0]				

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events. LTE = long term extension.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

		Teze+Teze	Pbo+Pbo		_			
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Region		N<10 any level						NE
Europe	9	8 (88.9)	6	3 (50.0)				NE
Lurope)	[51.8, 99.7]	0	[11.8, 88.2]				
America	19	10 (52.6)	4	4 (100.0)				
		[28.9, 75.6]		[39.8, 100.0]				
Asia/Pacific	6	5 (83.3)	3	3 (100.0)				
		[35.9, 99.6]		[29.2, 100.0]				
Rest of the world	11	10 (90.9)	6	5 (83.3)				
		[58.7, 99.8]		[35.9, 99.6]				
BMI	_	N<10 any level						NE
< 18.5 kg/m**2	2	1 (50.0) [1.3, 98.7]	0					
18.5 - < 25.0 kg/m**2	6	4 (66.7)	3	2 (66.7)				
		[22.3, 95.7]		[9.4, 99.2]				
25.0 - < 30.0 kg/m**2	18	14 (77.8)	7	6 (85.7)				
		[52.4, 93.6]		[42.1, 99.6]				
>= 30.0 kg/m**2	19	14 (73.7)	9	7 (77.8)				
		[48.8, 90.9]		[40.0, 97.2]				
Baseline eosinophils - Low								0.507
< 150 cells/uL	25	18 (72.0)	10	7 (70.0)	1.029	1.102	2.0	1.000
		[50.6, 87.9]		· · · ·	[0.640, 1.652]			
>= 150 cells/uL	20	15 (75.0)	9	8 (88.9)	0.844	0.375	-13.9	0.633
		[50.9, 91.3]		[51.8, 99.7]	[0.599, 1.189]	[0.037, 3.786]	[-49.9, 22.1]]
Baseline specific perennial FEIA status								0.434
All negative	27	20 (74.1)	14	12 (85.7)	0.864	0.476	-11.6	0.692
		[53.7, 88.9]			[0.634, 1.177]			
Any positive	18	13 (72.2)	5	3 (60.0)	1.204	1.733	12.2	0.621
		[46.5, 90.3]		[14.7, 94.7]	[0.557, 2.602]	[0.220, 13.670]	[-48.2, 72.7]]

Table DT1AAN_UBSIK: Incidence of non-disease related non-severe TEAEs during study period by key subgroups DSAFNB - LTE

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension. N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup.

Source Data: aae, created on: 11JUL2022

	Teze+Teze			Pbo+Pbo				
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Total serum IgE		N<10 any level						NE
Low	40	30 (75.0)	18	14 (77.8)				NL
FOM	40	[58.8, 87.3]	10	[52.4, 93.6]				
High	5	3 (60.0)	1	1 (100.0)				
nign	J	[14.7, 94.7]	т	[2.5, 100.0]				
		[14./, 94./]		[2.3, 100.0]				
OCS at baseline		N<10 any level						NE
Yes	4	3 (75.0)	1	1 (100.0)				
		[19.4, 99.4]		[2.5, 100.0]				
No	41	30 (73.2)	18	14 (77.8)				
		[57.1, 85.8]		[52.4, 93.6]				
LAMA use at baseline								0.355
Yes	11	9 (81.8)	7	5 (71.4)	1.145	1.800	10.4	1.000
165	11	[48.2, 97.7]	,	- (-)	[0.664, 1.976]			
No	34	24 (70.6)	12	10 (83.3)	0.847	0.480	-12.7	0.472
NO	54	()	12	- (,				
		[52.5, 84.9]		[51.6, 97.9]	[0.607, 1.182]	[0.089, 2.596]	[-44.4, 19.0]
Tiotropium use at baseline								0.985
Yes	9	7 (77.8)	6	5 (83.3)	0.933	0.700	-5.6	1.000
		[40.0, 97.2]		[35.9, 99.6]	[0.566, 1.539]	[0.049, 10.014]] [-59.8, 48.7]
No	36	26 (72.2)	13	10 (76.9)	0.939	0.780	-4.7	1.000
		[54.8, 85.8]		[46.2, 95.0]	[0.655, 1.346]	[0.177, 3.434]	[-37.1, 27.7	1
		[,]		,		,		-

Table DT1AAN_UBSIK: Incidence of non-disease related non-severe TEAEs during study period by key subgroups DSAFNB - LTE

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events. LTE = long term extension.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table DT1AAN UBSIK: Incidence of non-disease related non-severe TEAEs during study period by key subgroups DSAFNB - LTE

	Teze+Teze		Pbo+Pbo		_			
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Montelukast/ Cromoglicic acid use at baseline								0.670
Yes	15	13 (86.7) [59.5, 98.3]	6	6 (100.0) [54.1, 100.0]	0.867 [0.711, 1.057]	0.415 + [0.017, 9.961]	-13.3 [-42.2, 15.5	1.000]
No	30	20 (66.7) [47.2, 82.7]	13	9 (69.2) [38.6, 90.9]	0.963 [0.619, 1.498]	0.889 [0.219, 3.609]	-2.6 [-38.3, 33.2	1.000]

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension. N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup.

Source Data: aae, created on: 11JUL2022

		Tezepelumab	Placebo						
Non-disease related non-severe		n (%)		n (%)	RR	OR	OR RD		
TEAEs during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
Region (cat. N)		N<10 any level						NE	
Western Europe	11	6 (54.5)	13	7 (53.8)					
		[23.4, 83.3]		[25.1, 80.8]					
North America	15	8 (53.3)	8	6 (75.0)					
		[26.6, 78.7]		[34.9, 96.8]					
South America	5	2 (40.0)	3	3 (100.0)					
		[5.3, 85.3]		[29.2, 100.0]					
Central/Eastern Europe	4	3 (75.0)	4	2 (50.0)					
-		[19.4, 99.4]		[6.8, 93.2]					
Asia Pacific	13	8 (61.5)	7	4 (57.1)					
		[31.6, 86.1]		[18.4, 90.1]					
Rest of the world	7	5 (71.4)	5	4 (80.0)					
		[29.0, 96.3]		[28.4, 99.5]					
Baseline eosinophils (cat. N)								0.050	
< 150 cells/uL	32	21 (65.6)	22	12 (54.5)	1.203	1.591	11.1	0.571	
		[46.8, 81.4]		[32.2, 75.6]	[0.762, 1.899]	[0.523, 4.837]	[-19.3, 41.4]		
150 - < 300 cells/uL	23	11 (47.8)	18	14 (77.8)	0.615	0.262	-30.0	0.063	
		[26.8, 69.4]		[52.4, 93.6]	[0.376, 1.007]	[0.066, 1.041]	[-62.9, 3.0]		
Baseline eosinophils (cat. Q)								0.188	
01: < 140 cells/uL	28	18 (64.3)	22	12 (54.5)	1.179	1.500	9.7	0.567	
		[44.1, 81.4]		[32.2, 75.6]	[0.736, 1.887]	[0.479, 4.695]	[-21.7, 41.1]		
Q2: 140 - < 250 cells/uL	23	12 (52.2)	11	9 (81.8)	0.638	0.242	-29.6	0.140	
2		[30.6, 73.2]		[48.2, 97.7]	[0.394, 1.031]	[0.043, 1.377]	[-67.0, 7.7]		
03: 250 - < 430 cells/uL	4	2 (50.0)	7	5 (71.4)	0.700	0.400	-21.4	0.576	
2		[6.8, 93.2]		· · ·	[0.236, 2.074]	[0.031, 5.151]	[-100.0, 57.6		
Baseline FENO (cat. N)		N<10 any level						NE	
< 25 ppb	55	32 (58.2)	40	26 (65.0)					
rr-		[44.1, 71.3]	10	[48.3, 79.4]					
		,		[

Table NT1AAN_SBSIN: Incidence of non-disease related non-severe TEAEs during study period by study specific subgroups DSAFB

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table NT1AAN_SBSIN: Incidence of non-disease related non-severe TEAEs during study period by study specific subgroups DSAFB

	Tezepelumab		Placebo					
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Baseline FENO (cat. Q)								0.658
Q1: < 16 ppb	31	17 (54.8) [36.0, 72.7]	26	· · ·	0.839 [0.549, 1.282]	0.643 [0.220, 1.881]	-10.5	0.588]
Q2: 16 - < 30 ppb	24	15 (62.5) [40.6, 81.2]	14	. ,	0.972 [0.591, 1.600]	0.926 [0.235, 3.645]	-1.8 [-39.1, 35.6]	1.000]
Total serum IgE (cat. N)		N<10 any level						NE
Q1: < 53.1 IU/ml	41	29 (70.7) [54.5, 83.9]	34	22 (64.7) [46.5, 80.3]				
Q2: 53.1 - < 195.6 IU/ml	9	2 (22.2) [2.8, 60.0]	4	3 (75.0) [19.4, 99.4]				
Q4: >= 572.4 IU/ml	5	1 (20.0) [0.5, 71.6]	2	1 (50.0) [1.3, 98.7]				
Nasal polyps last 2 years		N<10 any level						NE
Yes	4	2 (50.0) [6.8, 93.2]	3	3 (100.0) [29.2, 100.0]				
No	51	30 (58.8) [44.2, 72.4]	37	23 (62.2) [44.8, 77.5]				

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

		Tezepelumab		Placebo				
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Region (cat. N)		N<10 any level						NE
Western Europe	11	6 (54.5) [23.4, 83.3]	13	7 (53.8) [25.1, 80.8]				
North America	14	8 (57.1) [28.9, 82.3]	8	6 (75.0) [34.9, 96.8]				
South America	5	2 (40.0) [5.3, 85.3]	3	3 (100.0) [29.2, 100.0]				
Central/Eastern Europe	4	3 (75.0) [19.4, 99.4]	4	2 (50.0) [6.8, 93.2]				
Asia Pacific	13	8 (61.5) [31.6, 86.1]	6	3 (50.0) [11.8, 88.2]				
Rest of the world	7	5 (71.4) [29.0, 96.3]	5	4 (80.0) [28.4, 99.5]				
Baseline eosinophils (cat. N)								0.055
< 150 cells/uL	32	21 (65.6) [46.8, 81.4]	21	11 (52.4) [29.8, 74.3]	1.253 [0.776, 2.022]	1.736 [0.563, 5.346]	13.2 [-17.7, 44.2]	0.397
150 - < 300 cells/uL	22	11 (50.0) [28.2, 71.8]	18	14 (77.8) [52.4, 93.6]	0.643 [0.396, 1.045]	0.286 [0.071, 1.148]	-27.8 [-61.2, 5.7]	0.104
Baseline eosinophils (cat. Q)								0.197
Q1: < 140 cells/uL	28	18 (64.3) [44.1, 81.4]	21	11 (52.4) [29.8, 74.3]	1.227 [0.750, 2.008]	1.636 [0.516, 5.187]	11.9 [-20.0, 43.8]	0.558
Q2: 140 - < 250 cells/uL	22	12 (54.5) [32.2, 75.6]	11	9 (81.8) [48.2, 97.7]	0.667 [0.416, 1.069]	0.267 [0.046, 1.530]	-27.3 [-65.0, 10.4]	0.249
Q3: 250 - < 430 cells/uL	4	2 (50.0) [6.8, 93.2]	7	5 (71.4) [29.0, 96.3]	0.700 [0.236, 2.074]	0.400 [0.031, 5.151]	-21.4 [-100.0, 57.6]	0.576
Baseline FENO (cat. N)		N<10 any level						NE
< 25 ppb	54	32 (59.3) [45.0, 72.4]	39	25 (64.1) [47.2, 78.8]				

Table NT1AAN_TBSIN: Incidence of non-disease related non-severe TEAEs during study period by study specific subgroups DSAFB - adult

Note: DSAFB - adult = Dossier Biomarker Safety Set - adult.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table NT1AAN_TBSIN: Incidence of non-disease related non-severe TEAEs during study period by study specific subgroups DSAFB - adult

	Tezepelumab		Placebo					
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Baseline FENO (cat. Q)								0.646
Q1: < 16 ppb	30	17 (56.7) [37.4, 74.5]	26	17 (65.4) [44.3. 82.8]	0.867 [0.570, 1.319]	0.692	-8.7	0.589 1
Q2: 16 - < 30 ppb	24		13	8 (61.5)		1.042	1.0	1.000
Total serum IgE (cat. N)		N<10 any level						NE
Q1: < 53.1 IU/ml	40	29 (72.5) [56.1, 85.4]	33	21 (63.6) [45.1, 79.6]				
Q2: 53.1 - < 195.6 IU/ml	9	2 (22.2) [2.8, 60.0]	4	3 (75.0) [19.4, 99.4]				
Q4: >= 572.4 IU/ml	5	1 (20.0) [0.5, 71.6]	2	1 (50.0) [1.3, 98.7]				
Nasal polyps last 2 years		N<10 any level						NE
Yes	4	2 (50.0) [6.8, 93.2]	3	3 (100.0) [29.2, 100.0]				
No	50		36	22 (61.1) [43.5, 76.9]				

Note: DSAFB - adult = Dossier Biomarker Safety Set - adult.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup. Source Data: aae, created on: 09MAR2022

NT1AAN_TBSIN

Table DT1AAN_UBSIN:	Incidence of	non-disease	related	non-severe	TEAEs	during	study	period	by	study	specific	subgroups	5
				DSAFNB - LT	Ε								

		Teze+Teze		Pbo+Pbo				
Non-disease related non-severe		n (%)		n (%)	RR		OR	RD
TEAEs during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % C	I][95	% CI][9	95 % CI]p-value
h = (a + N)		N<10 any level						NE
Age (cat. N)	1	-	0					NE
< 18 years	1	0 (0.0) [0.0, 97.5]	0					
18 - < 65 years	35	25 (71.4)	16	13 (81.3)				
		[53.7, 85.4]		[54.4, 96.0]				
>= 65 years	9	8 (88.9)	3	2 (66.7)				
		[51.8, 99.7]		[9.4, 99.2]				
Region (cat. N)		N<10 any level						NE
Western Europe	9	8 (88.9)	7	4 (57.1)				
		[51.8, 99.7]		[18.4, 90.1]				
North America	14	8 (57.1)	3	3 (100.0)				
		[28.9, 82.3]		[29.2, 100.0]				
South America	5	2 (40.0)	1	1 (100.0)				
		[5.3, 85.3]		[2.5, 100.0]				
Central/Eastern Europe	4	3 (75.0)	4	3 (75.0)				
		[19.4, 99.4]		[19.4, 99.4]				
Asia Pacific	6	5 (83.3)	2	2 (100.0)				
		[35.9, 99.6]		[15.8, 100.0]				
Rest of the world	7	7 (100.0)	2	2 (100.0)				
		[59.0, 100.0]		[15.8, 100.0]				

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension.

N = total number of patients in analysis set. n = number of patients with response. TEAE = treatment emergent adverse events. LTE = long term extension.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table DT1AAN_UBSIN: Incidence of non-disease related non-severe TEAEs during study period by study specific subgroups DSAFNB - LTE

		Teze+Teze		Pbo+Pbo	_			
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Baseline eosinophils (cat. N)								0.507
< 150 cells/uL	25	18 (72.0)	10	7 (70.0)	1.029	1.102	2.0	1.000
		[50.6, 87.9]		[34.8, 93.3]	[0.640, 1.652]	[0.220, 5.512]	[-38.4, 42.4]
150 - < 300 cells/uL	20	15 (75.0)	9	8 (88.9)	0.844	0.375	-13.9	0.633
		[50.9, 91.3]		[51.8, 99.7]	[0.599, 1.189]	[0.037, 3.786]	[-49.9, 22.1]
		N (10]]						
Baseline eosinophils (cat. Q)		N<10 any level						NE
Q1: < 140 cells/uL	21	14 (66.7)	10	7 (70.0)				
		[43.0, 85.4]		[34.8, 93.3]				
Q2: 140 - < 250 cells/uL	21	17 (81.0)	7	7 (100.0)				
		[58.1, 94.6]		[59.0, 100.0]				
Q3: 250 - < 430 cells/uL	3	2 (66.7)	2	1 (50.0)				
		[9.4, 99.2]		[1.3, 98.7]				

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension.

N = total number of patients in analysis set. n = number of patients with response. TEAE = treatment emergent adverse events. LTE = long term extension.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table DT1AAN_UBSIN: Incidence of non-disease related non-severe TEAEs during study period by study specific subgroups DSAFNB - LTE

		Teze+Teze		Pbo+Pbo				
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Baseline FENO (cat. N)		N<10 any level						NE
< 25 ppb	45	33 (73.3) [58.1, 85.4]	19	15 (78.9) [54.4, 93.9]				
Baseline FENO (cat. Q)								0.605
Q1: < 16 ppb	23	17 (73.9) [51.6, 89.8]	12	9 (75.0) [42.8, 94.5]	0.986 [0.656, 1.481]	0.944 [0.190, 4.698]	-1.1 [-37.8, 35.6	1.000
Q2: 16 - < 30 ppb	22	16 (72.7) [49.8, 89.3]	7	6 (85.7) [42.1, 99.6]	0.848 [0.571, 1.261]	0.444 [0.044, 4.503]	-13.0 [-54.3, 28.3	0.646

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension.

N = total number of patients in analysis set. n = number of patients with response. TEAE = treatment emergent adverse events. LTE = long term extension.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table DT1AAN_UBSIN: Incidence of non-disease related non-severe TEAEs during study period by study specific subgroups DSAFNB - LTE

	Teze+Teze		Pbo+Pbo				
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD
TEAEs during study period	N	[95 % CI]	Ν	[95 % CI]	[95 % CI][95 % CI][95 % CI]p-value
Tatal source Tat (ast N)		NK10 and land					NIT
Total serum IgE (cat. N)		N<10 any level					NE
Q1: < 53.1 IU/ml	34	27 (79.4)	16	13 (81.3)			
		[62.1, 91.3]		[54.4, 96.0]			
Q2: 53.1 - < 195.6 IU/ml	6	3 (50.0)	2	1 (50.0)			
		[11.8, 88.2]		[1.3, 98.7]			
Q4: >= 572.4 IU/ml	5	3 (60.0)	1	1 (100.0)			
		[14.7, 94.7]		[2.5, 100.0]			
Nasal polyps last 2 years		N<10 any level					NE
Yes	4	4 (100.0)	1	1 (100.0)			
		[39.8, 100.0]		[2.5, 100.0]			
No	41	29 (70.7)	18	14 (77.8)			
		[54.5, 83.9]		[52.4, 93.6]			

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension.

N = total number of patients in analysis set. n = number of patients with response. TEAE = treatment emergent adverse events. LTE = long term extension.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table MT1AAC_SBMI0: Incidence of non-disease related severe TEAEs during study period DSAFB

		Tezepelumab		Placebo				
		n (%)		n (%)	RR	OR	RD	
	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related severe TEAEs	66	7 (10.6)	48	4 (8.3)	1.273	1.305	2.3	0.758
during study period		[4.4, 20.6]		[2.3, 20.0]	[0.395, 4.104]		[-10.3, 14.9]

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 02FEB2022

Table NT1AAC_SBMI0: Incidence of non-disease related severe TEAEs during study period DSAFB

		Tezepelumab		Placebo				
		n (%)		n (%)	RR	OR	RD	
	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related severe TEAEs	55	4 (7.3)	40	4 (10.0)	0.727	0.706	-2.7	0.717
during study period		[2.0, 17.6]		[2.8, 23.7]	[0.193, 2.735]	[0.166, 3.010]	[-16.4, 11.0]

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 01FEB2022

Table NT1AAC_TBMI0: Incidence of non-disease related severe TEAEs during study period DSAFB - adult

	1	Tezepelumab		Placebo				
		n (%)		n (%)	RR	OR	RD	
	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related severe TEAEs	54	4 (7.4)	39	4 (10.3)	0.722	0.700	-2.8	0.716
during study period		[2.1, 17.9]		[2.9, 24.2]	[0.192, 2.712]	[0.164, 2.969]	[-10.9, 11.2]

Note: DSAFB - adult = Dossier Biomarker Safety Set - adult. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 01FEB2022

AstraZeneca Value Dossier Analysis: CD-RI-MEDI9929-1146 Data Cut Date: 06JUN2017

Table PT3AAC_SBMI0: Incidence of non-disease related severe TEAEs during study period DSAFB

	1	Tezepelumab		Placebo				
	N	n (%) [95 % CI]	N	n (%) [95 % CI]		OR [95 % CI]	RD [95 % CI]	n voluo
	IN	[93 % CI]	IN	[93 % [1]	[90 % CI]	[93 % CI]	[93 % CI]	p-value
Non-disease related severe TEAEs during study period	12	3 (25.0) [5.5, 57.2]	9	0 (0.0) [0.0, 33.6]	5.385 + [0.313, 92.735]	7.000 + [0.316, 154.865]	25.0 [-9.2, 59.2	0.229]

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 07FEB2022

Table ST1AAC_SBMI0: Incidence of non-disease related severe TEAEs during study period DSAFB

	1	Tezepelumab		Placebo					
	N	n (%)	N	n (%)		OR	RD		
	IN	[95 % CI]	IN	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
Non-disease related severe TEAEs during study period	12	2 (16.7) [2.1, 48.4]	11	1 (9.1) [0.2, 41.3]	1.833 [0.192, 17.512]	2.000 [0.155, 25.755]	7.6 [-28.2, 43.4	1.000	

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 07FEB2022

Table DT1AAC_UBMI0: Incidence of non-disease related severe TEAEs during study period DSAFNB - LTE

		Teze+Teze		Pbo+Pbo				
	N	n (%) [95 % CI]	N	n (%) [95 % CI]		OR [95 % CI]	RD [95 % CI]	p-value
	45		10					
Non-disease related severe TEAEs during study period	45	5 (11.1) [3.7, 24.1]	19	3 (15.8) [3.4, 39.6]	0.704 [0.187, 2.653]	0.667 [0.142, 3.123]	-4.7 [-27.2, 17.9	0.685

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: aae, created on: 15JUL2022

Table CT1AAC_SBMI0: Incidence of non-disease related severe TEAEs during study period DSAFB

	1	Tezepelumab		Placebo				
		n (%)		n (%)	RR	OR	RD	-
	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related severe TEAEs during study period	4	0 (0.0) [0.0, 60.2]	8	2 (25.0) [3.2, 65.1]	0.360 + [0.021, 6.117]	0.289 + [0.011, 7.568]	-25.0 [-73.8, 23.8	0.515]

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 07FEB2022

Table MT1AAC_SBSIK: Incidence of non-disease related severe TEAEs during study period by key subgroups DSAFB

	1	ſezepelumab		Placebo				
Non-disease related severe TEAEs		n (%)		n (%)	RR	OR	RD	
during study period	Ν	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Sex								0.993
Male	20	1 (5.0)	8	0 (0.0)	1.286 +	1.308 +	5.0	1.000
		[0.1, 24.9]		[0.0, 36.9]	[0.058, 28.651]	[0.048, 35.470]	[-13.3, 23.3]
Female	46	6 (13.0)	40	4 (10.0)	1.304	1.350	3.0	0.745
		[4.9, 26.3]		[2.8, 23.7]	[0.396, 4.296]	[0.352, 5.171]	[-12.8, 18.8]
Age		n<10 all						NE
		levels						
< 65 years	56	6 (10.7)	39	3 (7.7)				
		[4.0, 21.9]		[1.6, 20.9]				
>= 65 years	10	1 (10.0)	9	1 (11.1)				
		[0.3, 44.5]		[0.3, 48.2]				
Exacerbations in the year before		n<10 all						NE
study		levels						
<= 2	38	4 (10.5)	31	4 (12.9)				
		[2.9, 24.8]		[3.6, 29.8]				
> 2	28	3 (10.7)	17	0 (0.0)				
		[2.3, 28.2]		[0.0, 19.5]				

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

		Tezepelumab		Placebo	_		
Non-disease related severe TEAEs		n (%)		n (%)	RR	OR	RD
during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI][9	5 % CI][95	5 % CI]p-value
Race		N<10 any level					NE
White	43	4 (9.3)	36	2 (5.6)			
		[2.6, 22.1]		[0.7, 18.7]			
Black or African American	6	2 (33.3)	4	0 (0.0)			
		[4.3, 77.7]		[0.0, 60.2]			
Asian	15	1 (6.7)	6	1 (16.7)			
		[0.2, 31.9]		[0.4, 64.1]			
Other	2	0 (0.0)	2	1 (50.0)			
		[0.0, 84.2]		[1.3, 98.7]			
Region		n<10 all					NE
		levels					
Europe	21	4 (19.0)	15	2 (13.3)			
-		[5.4, 41.9]		[1.7, 40.5]			
America	21	2 (9.5)	13	0 (0.0)			
		[1.2, 30.4]		[0.0, 24.7]			
Asia/Pacific	13	1 (7.7)	9	1 (11.1)			
		[0.2, 36.0]		[0.3, 48.2]			
Rest of the world	11	0 (0.0)	11	1 (9.1)			
		[0.0, 28.5]		[0.2, 41.3]			
BMI		N<10 any level					NE
< 18.5 kg/m**2	2	0 (0.0)	0				
		[0.0, 84.2]					
18.5 - < 25.0 kg/m**2	12	2 (16.7)	11	1 (9.1)			
		[2.1, 48.4]		[0.2, 41.3]			
25.0 - < 30.0 kg/m**2	24	3 (12.5)	16	1 (6.3)			
		[2.7, 32.4]		[0.2, 30.2]			
>= 30.0 kg/m**2	28	2 (7.1)	21	2 (9.5)			
		[0.9, 23.5]		[1.2, 30.4]			

Table MT1AAC_SBSIK: Incidence of non-disease related severe TEAEs during study period by key subgroups DSAFB

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

		[ezepelumab		Placebo				
Non-disease related severe TEAEs		n (%)		n (%)	RR	OR	RD	
during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Baseline eosinophils - Low		n<10 all levels						NE
< 150 cells/uL	37	5 (13.5)	23	2 (8.7)				
		[4.5, 28.8]		[1.1, 28.0]				
>= 150 cells/uL	29	2 (6.9)	25	2 (8.0)				
		[0.8, 22.8]		[1.0, 26.0]				
Baseline specific perennial FEIA								0.832
status								
All negative	39	6 (15.4)	29	4 (13.8)	1.115	1.136	1.6	1.000
		[5.9, 30.5]		[3.9, 31.7]	[0.346, 3.595]	[0.289, 4.462]	[-18.3, 21.5]]
Any positive	24	0 (0.0)	17	0 (0.0)	0.720 +	0.714 +	-0.8 +	NE
		[0.0, 14.2]		[0.0, 19.5]	[0.015, 34.616]	[0.014, 37.757]	[-14.9, 13.4]]
Total serum IgE		N<10 any level						NE
Low	61	7 (11.5)	44	4 (9.1)				
		[4.7, 22.2]		[2.5, 21.7]				
High	5	0 (0.0)	4	0 (0.0)				
		[0.0, 52.2]		[0.0, 60.2]				

Table MT1AAC_SBSIK: Incidence of non-disease related severe TEAEs during study period by key subgroups DSAFB

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table MT1AAC_SBSIK: Incidence of non-disease related severe TEAEs during study period by key subgroups DSAFB

	1	ſezepelumab		Placebo				
Non-disease related severe TEAEs		n (%)		n (%)	RR	OR	RD	
during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
OCS at baseline								0.582
Yes	8	1 (12.5)	7	0 (0.0)	2.667 +	3.000 +	12.5	1.000
		[0.3, 52.7]		[0.0, 41.0]	[0.126, 56.626]][0.105, 86.094]	[-23.8, 48.8]]
No	58	6 (10.3)	41	4 (9.8)	1.060	1.067	0.6	1.000
		[3.9, 21.2]		[2.7, 23.1]	[0.319, 3.521]	[0.281, 4.050]	[-13.5, 14.7]
LAMA use at baseline		n<10 all						NE
		levels						
Yes	15	1 (6.7)	16	2 (12.5)				
		[0.2, 31.9]		[1.6, 38.3]				
No	51	6 (11.8)	32	2 (6.3)				
NO	51	[4.4, 23.9]	52	[0.8, 20.8]				
		[1.1, 23.7]		[0.0, 20.0]				
Tistussium uss at beseling								NE
Tiotropium use at baseline		n<10 all						NE
		levels						
Yes	13	1 (7.7)	15	2 (13.3)				
		[0.2, 36.0]		[1.7, 40.5]				
No	53	6 (11.3)	33	2 (6.1)				
		[4.3, 23.0]		[0.7, 20.2]				

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table MT1AAC_SBSIK: Incidence of non-disease related severe TEAEs during study period by key subgroups DSAFB

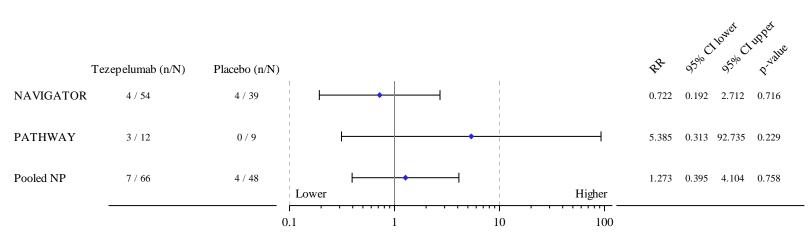
]	ſezepelumab		Placebo			
Non-disease related severe TEAEs		n (%)		n (%)	RR	OR R	
during study period	N	[95 % CI]	N	[95 % CI]	[95 % CI][95	% CI][95 %	6 CI]p-value
Montelukast/ Cromoglicic acid use at baseline		n<10 all levels					NE
Yes	19	2 (10.5) [1.3, 33.1]	14	0 (0.0) [0.0, 23.2]			
No	47	5 (10.6) [3.5, 23.1]	34	4 (11.8) [3.3, 27.5]			

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Figure MF1AAC_SBMF0: Forest plot for non-disease related severe TEAEs during study period DSAFB



Test for heterogeneity - p-value: 0.210, I-square: 36.5 %

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of affected patients. RR = relative risk. CI = confidence interval. Heterogeneity was investigated with Cochran Q test. NE = not evaluable.

Source tables: NT1AAC_TBMI0, PT3AAC_SBMI0, MT1AAC_SBMI0

Table MT1AAS_SBMI0: Incidence of non-disease related serious TEAEs during study period DSAFB

	1	Tezepelumab		Placebo			
		n (%)		n (%)	RR	OR	RD
	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI] p-value
Non-disease related serious TEAEs	66	5 (7.6)	48	5 (10.4)	0.727	0.705	-2.8 0.740
during study period		[2.5, 16.8]		[3.5, 22.7]	[0.223, 2.373]	[0.192, 2.585]	[-15.4, 9.7]

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 02FEB2022

Table NT1AAS_SBMI0: Incidence of non-disease related serious TEAEs during study period DSAFB

		Tezepelumab		Placebo				
		n (%)		n (%)		OR	RD	1 .
	N	[95 % CI]	IN	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related serious TEAEs	55	3 (5.5)	40	4 (10.0)	0.545	0.519	-4.5	0.450
during study period		[1.1, 15.1]		[2.8, 23.7]	[0.129, 2.303]	[0.110, 2.461]	[-17.8, 8.7]]

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 01FEB2022

Table NT1AAS_TBMI0: Incidence of non-disease related serious TEAEs during study period DSAFB - adult

	1	Tezepelumab		Placebo				
		n (%)		n (%)	RR	OR	RD	
	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related serious TEAEs during study period	54	3 (5.6) [1.2, 15.4]	39	4 (10.3) [2.9, 24.2]	0.542 [0.128, 2.284]	0.515 [0.108, 2.443]	-4.7 [-18.2, 8.8]	0.448

Note: DSAFB - adult = Dossier Biomarker Safety Set - adult. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 01FEB2022

AstraZeneca Value Dossier Analysis: CD-RI-MEDI9929-1146 Data Cut Date: 06JUN2017

Table PT3AAS_SBMI0: Incidence of non-disease related serious TEAEs during study period DSAFB

	1	Tezepelumab		Placebo	_			
	N	n (%) [95 % CI]	N	n (%)		OR	RD	
	IN	[95 % CI]	IN	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related serious TEAEs during study period	12	2 (16.7) [2.1, 48.4]	9	1 (11.1) [0.3, 48.2]	1.500 [0.160, 14.083]	1.600 [0.122, 20.993]	5.6 [-33.6, 44.7	1.000]

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 07FEB2022

AstraZeneca Value Dossier Analysis: D5180C00009 Data Cut Date: 18Nov2020

Table ST1AAS_SBMI0: Incidence of non-disease related serious TEAEs during study period DSAFB

	Г	Tezepelumab		Placebo				
		n (%)		n (%)	RR	OR	RD	
	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related serious TEAEs during study period	12	1 (8.3) [0.2, 38.5]	11	3 (27.3) [6.0, 61.0]	0.306 [0.037, 2.521]	0.242	-18.9	0.317

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 07FEB2022

Table DT1AAS_UBMI0: Incidence of non-disease related serious TEAEs during study period DSAFNB - LTE

		Teze+Teze		Pbo+Pbo	_			
		n (%)		n (%)	RR	OR	RD	2
	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related serious TEAEs during study	45	6 (13.3)	19	1 (5.3)	2.533	2.769	8.1	0.664
period		[5.1, 26.8]		[0.1, 26.0]	[0.327, 19.639]	[0.310, 24.730]][-9.8, 25.9]

Note: DSAFNB - LTE = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: aae, created on: 15JUL2022

Table CT1AAS_SBMI0: Incidence of non-disease related serious TEAEs during study period DSAFB

		Tezepelumab		Placebo				
		n (%)		n (%)	RR	OR	RD	7
	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related serious TEAEs during study period	4	0 (0.0) [0.0, 60.2]	8	1 (12.5) [0.3, 52.7]	0.600 + [0.030, 12.150]	0.556 + [0.018, 16.769]	-12.5 [-54.2, 29.2	1.000]

Note: DSAFB = Dossier Biomarker Safety Set. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: AAE, created on: 07FEB2022

		ſezepelumab		Placebo			
Non-disease related serious TEAEs		n (%)		n (%)	RR	OR	RD
during study period	Ν	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % Cl][95 % CI]p-value
Sex		n<10 all levels					NE
Male	20	2 (10.0)	8	1 (12.5)			
		[1.2, 31.7]		[0.3, 52.7]			
Female	46	3 (6.5)	40	4 (10.0)			
		[1.4, 17.9]		[2.8, 23.7]			
Age		n<10 all levels					NE
< 65 years	56	4 (7.1)	39	4 (10.3)			
		[2.0, 17.3]		[2.9, 24.2]			
>= 65 years	10	1 (10.0)	9	1 (11.1)			
		[0.3, 44.5]		[0.3, 48.2]			
Exacerbations in the year before		n<10 all					NE
study		levels	~ .				
<= 2	38	3 (7.9)	31	3 (9.7)			
× 2	20	[1.7, 21.4]	4 1	[2.0, 25.8]			
> 2	28	2 (7.1)	17	2 (11.8)			
		[0.9, 23.5]		[1.5, 36.4]			

Table MT1AAS_SBSIK: Incidence of non-disease related serious TEAEs during study period by key subgroups DSAFB

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

		Tezepelumab		Placebo	_		
Non-disease related serious TEAEs		n (%)		n (%)	RR	OR	RD
during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI][95	6 % CI][95	5 % CI]p-value
Race		N<10 any level					NE
White	43	3 (7.0)	36	4 (11.1)			
		[1.5, 19.1]		[3.1, 26.1]			
Black or African American	6	1 (16.7)	4	0 (0.0)			
		[0.4, 64.1]		[0.0, 60.2]			
Asian	15	1 (6.7)	6	1 (16.7)			
		[0.2, 31.9]		[0.4, 64.1]			
Other	2	0 (0.0)	2	0 (0.0)			
		[0.0, 84.2]		[0.0, 84.2]			
Region		n<10 all					NE
		levels					
Europe	21	4 (19.0)	15	1 (6.7)			
		[5.4, 41.9]		[0.2, 31.9]			
America	21	0 (0.0)	13	1 (7.7)			
		[0.0, 16.1]		[0.2, 36.0]			
Asia/Pacific	13	1 (7.7)	9	2 (22.2)			
		[0.2, 36.0]		[2.8, 60.0]			
Rest of the world	11	0 (0.0)	11	1 (9.1)			
		[0.0, 28.5]		[0.2, 41.3]			
BMI		N<10 any level					NE
< 18.5 kg/m**2	2	0 (0.0)	0				
		[0.0, 84.2]					
18.5 - < 25.0 kg/m**2	12	2 (16.7)	11	1 (9.1)			
		[2.1, 48.4]		[0.2, 41.3]			
25.0 - < 30.0 kg/m**2	24	1 (4.2)	16	2 (12.5)			
		[0.1, 21.1]		[1.6, 38.3]			
>= 30.0 kg/m**2	28	2 (7.1)	21	2 (9.5)			
		[0.9, 23.5]		[1.2, 30.4]			

Table MT1AAS_SBSIK: Incidence of non-disease related serious TEAEs during study period by key subgroups DSAFB

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Non-disease related serious TEAEs	Tezepelumab n (%)		Placebo n (%)		RR	OR	RD
during study period	Ν	[95 % CI]	Ν	[95 % CI]][95 % CI]p-value
		[00 % 01]		[20 10 22]	[55 10 52]	[
Baseline eosinophils - Low		n<10 all					NE
L		levels					
< 150 cells/uL	37	3 (8.1)	23	3 (13.0)			
		[1.7, 21.9]		[2.8, 33.6]			
>= 150 cells/uL	29	2 (6.9)	25	2 (8.0)			
		[0.8, 22.8]		[1.0, 26.0]			
Baseline specific perennial FEIA		n<10 all					NE
status		levels					
All negative	39	4 (10.3)	29	3 (10.3)			
		[2.9, 24.2]		[2.2, 27.4]			
Any positive	24	1 (4.2)	17	2 (11.8)			
		[0.1, 21.1]		[1.5, 36.4]			
_							
Total serum IgE		N<10 any level					NE
Low	61	5 (8.2)	44	5 (11.4)			
		[2.7, 18.1]		[3.8, 24.6]			
High	5	0 (0.0)	4	0 (0.0)			
		[0.0, 52.2]		[0.0, 60.2]			

Table MT1AAS_SBSIK: Incidence of non-disease related serious TEAEs during study period by key subgroups DSAFB

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Non-disease related serious TEAEs during study period	 N	Cezepelumab n (%) [95 % CI]	N	Placebo n (%) [95 % CI]	 OR [95 % C]	RD [][95 % CI]p-value
OCS at baseline		n<10 all levels				NE
Yes	8	1 (12.5) [0.3, 52.7]	7	1 (14.3) [0.4, 57.9]		
No	58	4 (6.9) [1.9, 16.7]	41	4 (9.8) [2.7, 23.1]		
LAMA use at baseline		n<10 all levels				NE
Yes	15	1 (6.7) [0.2, 31.9]	16	2 (12.5) [1.6, 38.3]		
No	51	4 (7.8) [2.2, 18.9]	32	3 (9.4) [2.0, 25.0]		
Tiotropium use at baseline		n<10 all levels				NE
Yes	13	1 (7.7) [0.2, 36.0]	15	2 (13.3) [1.7, 40.5]		
No	53	4 (7.5) [2.1, 18.2]	33	3 (9.1) [1.9, 24.3]		

Table MT1AAS_SBSIK: Incidence of non-disease related serious TEAEs during study period by key subgroups DSAFB

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Table MT1AAS_SBSIK: Incidence of non-disease related serious TEAEs during study period by key subgroups DSAFB

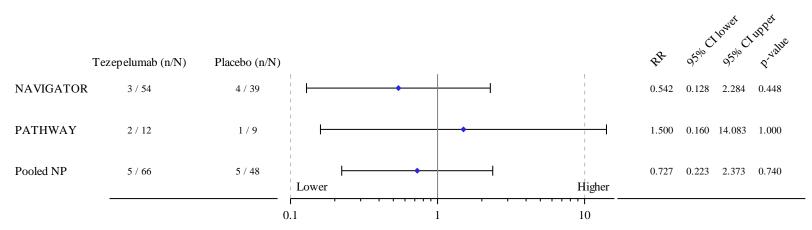
	Tezepelumab		Placebo				
Non-disease related serious TEAEs during study period	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI][9	OR 5 % CI][9	RD 5 % CI]p-value
Montelukast/ Cromoglicic acid use at baseline		n<10 all levels					NE
Yes	19	2 (10.5) [1.3, 33.1]	14	1 (7.1) [0.2, 33.9]			
No	47	3 (6.4) [1.3, 17.5]	34	4 (11.8) [3.3, 27.5]			

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events.

95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Figure MF1AAS_SBMF0: Forest plot for non-disease related serious TEAEs during study period DSAFB



Test for heterogeneity - p-value: 0.453, I-square: 0.0 %

Note: DSAFB = Dossier Biomarker Safety Set.

N = total number of patients in analysis set. n = number of affected patients. RR = relative risk. CI = confidence interval. Heterogeneity was investigated with Cochran Q test. NE = not evaluable.

Source tables: NT1AAS_TBMI0, PT3AAS_SBMI0, MT1AAS_SBMI0

Table DT1AA_LBMI0: Incidence of non-disease related TEAEs during study period DSAFNB - LTE - adult

		Teze+Teze		Pbo+Pbo	_			
		n (%)		n (%)	RR	OR	RD	
	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related TEAEs during study period	44	33 (75.0)	19	15 (78.9)	0.950	0.800	-3.9	1.000
		[59.7, 86.8]		[54.4, 93.9]	[0.712, 1.267]	[0.219, 2.927]	[-30.1, 22.2]

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: aae, created on: 15JUL2022

Table DT1AA_LBSIK:	Incidence	of	non-disease	related	TEAEs	during	study	period	by	key	subgroups	
			DSAFNB	- LTE -	adult							

		Teze+Teze		Pbo+Pbo	_				
Non-disease related TEAEs during study period	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Sex								0.499	
Male	16	12 (75.0) [47.6, 92.7]	2	1 (50.0) [1.3, 98.7]	1.500 [0.365, 6.172]	3.000 [0.150, 59.890]	25.0 [-75.6, 100.0]	0.490	
Female	28	21 (75.0) [55.1, 89.3]	17	14 (82.4)	0.911	0.643 [0.142, 2.916]	-7.4	0.719	
Age								0.359	
< 65 years	35	25 (71.4) [53.7, 85.4]	16	13 (81.3) [54.4, 96.0]	0.879 [0.641, 1.205]	0.577 [0.135, 2.469]	-9.8 [-38.7, 19.0]	0.730	
>= 65 years	9	8 (88.9) [51.8, 99.7]	3	2 (66.7) [9.4, 99.2]	1.333 [0.580, 3.066]	4.000 [0.167, 95.756]	22.2 [-57.2, 100.0]	0.455	
Exacerbations in the year before study								0.395	
<= 2	26	20 (76.9) [56.4, 91.0]	11	8 (72.7) [39.0, 94.0]	1.058 [0.696, 1.608]	1.250 [0.250, 6.255]	4.2 [-33.2, 41.6]	1.000	
> 2	18	13 (72.2) [46.5, 90.3]	8	7 (87.5) [47.3, 99.7]	0.825 [0.560, 1.217]	0.371 [0.036, 3.838]	-15.3 [-55.2, 24.6]	0.628	
Race		N<10 any level						NE	
White	30	20 (66.7) [47.2, 82.7]	14	10 (71.4) [41.9, 91.6]					
Black or African American	4	4 (100.0) [39.8, 100.0]	2	2 (100.0) [15.8, 100.0]					
Asian	8	7 (87.5) [47.3, 99.7]	2	2 (100.0) [15.8, 100.0]					
Other	2	2 (100.0) [15.8, 100.0]	1	1 (100.0) [2.5, 100.0]					

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q.

RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup. Source Data: aae, created on: 11JUL2022

		Teze+Teze		Pbo+Pbo	_			
Non-disease related TEAEs during		n (%)		n (%)	RR RR	OR	RD	
study period	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Region		N<10 any level						NE
Europe	9	8 (88.9)	6	3 (50.0)				
		[51.8, 99.7]		[11.8, 88.2]				
America	18	10 (55.6)	4	4 (100.0)				
		[30.8, 78.5]		[39.8, 100.0]				
Asia/Pacific	6	5 (83.3)	3	3 (100.0)				
		[35.9, 99.6]		[29.2, 100.0]				
Rest of the world	11	10 (90.9)	6	5 (83.3)				
		[58.7, 99.8]		[35.9, 99.6]				
BMI		N<10 any level						NE
< 18.5 kg/m**2	1	1 (100.0)	0					
5		[2.5, 100.0]						
18.5 - < 25.0 kg/m**2	6	4 (66.7)	3	2 (66.7)				
		[22.3, 95.7]		[9.4, 99.2]				
25.0 - < 30.0 kg/m**2	18	14 (77.8)	7	6 (85.7)				
		[52.4, 93.6]		[42.1, 99.6]				
>= 30.0 kg/m**2	19	14 (73.7)	9	7 (77.8)				
		[48.8, 90.9]		[40.0, 97.2]				
Baseline eosinophils - Low								0.617
< 150 cells/uL	25	18 (72.0)	10	7 (70.0)	1.029	1.102	2.0	1.000
		[50.6, 87.9]		[34.8, 93.3]	[0.640, 1.652]	[0.220, 5.512]	[-38.4, 42.4]
>= 150 cells/uL	19	15 (78.9)	9	8 (88.9)	0.888	0.469	-9.9	1.000
		[54.4, 93.9]		[51.8, 99.7]	[0.640, 1.232]	[0.045, 4.931]	[-45.7, 25.8]
Baseline specific perennial FEIA								0.487
status								0.107
All negative	26	20 (76.9)	14	12 (85.7)	0.897	0.556	-8.8	0.689
5		[56.4, 91.0]		[57.2, 98.2]	[0.665, 1.212]			
Any positive	18	13 (72.2)	5	3 (60.0)	1.204	1.733	12.2	0.621
		[46.5, 90.3]		[14.7, 94.7]	[0.557, 2.602]	[0.220, 13.670]	[-48.2, 72.7]

Table DT1AA_LBSIK: Incidence of non-disease related TEAEs during study period by key subgroups DSAFNB - LTE - adult

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

		Teze+Teze		Pbo+Pbo	_			
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Total serum IgE		N<10 any level						NE
Low	39	30 (76.9)	18	14 (77.8)				
		[60.7, 88.9]		[52.4, 93.6]				
High	5	3 (60.0)	1	1 (100.0)				
		[14.7, 94.7]		[2.5, 100.0]				
OCS at baseline		N<10 any level						NE
Yes	4	3 (75.0)	1	1 (100.0)				
		[19.4, 99.4]		[2.5, 100.0]				
No	40	30 (75.0)	18	14 (77.8)				
		[58.8, 87.3]		[52.4, 93.6]				
LAMA use at baseline								0.402
Yes	11	9 (81.8)	7	. ,	1.145		10.4	1.000
		[48.2, 97.7]			[0.664, 1.976]			
No	33	24 (72.7)	12	, ,	0.873		-10.6	0.699
		[54.5, 86.7]		[51.6, 97.9]	[0.629, 1.212]	[0.097, 2.921]	[-42.3, 21.1]
Tiotropium use at baseline								0.913
Yes	9	7 (77.8)	6	5 (83.3)	0.933	0.700	-5.6	1.000
		[40.0, 97.2]			[0.566, 1.539]			=
No	35	26 (74.3)	13	10 (76.9)	0.966	0.867	-2.6	1.000
		[56.7, 87.5]		[46.2, 95.0]	[0.677, 1.378]	[0.194, 3.870]	[-35.0, 29.7]

Table DT1AA_LBSIK: Incidence of non-disease related TEAEs during study period by key subgroups DSAFNB - LTE - adult

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup. Source Data: aae, created on: 11JUL2022

Table DT1AA_LBSIK: Incidence of non-disease related TEAEs during study period by key subgroups DSAFNB - LTE - adult

		Teze+Teze		Pbo+Pbo	_			
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Montelukast/ Cromoglicic acid use at baseline								0.878
Yes	14	13 (92.9) [66.1, 99.8]	6	6 (100.0) [54.1, 100.0]	0.929 [0.803, 1.074]	0.692 + [0.025, 19.431]	-7.1 [-32.5, 18.3	1.000]
No	30	20 (66.7) [47.2, 82.7]	13	9 (69.2) [38.6, 90.9]	0.963 [0.619, 1.498]	0.889 [0.219, 3.609]	-2.6 [-38.3, 33.2	1.000]

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup. Source Data: aae, created on: 11JUL2022 Table DT1AA_LBSIN: Incidence of non-disease related TEAEs during study period by study specific subgroups DSAFNB - LTE - adult

	Teze+Teze		Pbo+Pbo					
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Region (cat. N)		N<10 any level						NE
Western Europe	9	8 (88.9)	7	4 (57.1)				
		[51.8, 99.7]		[18.4, 90.1]				
North America	13	8 (61.5)	3	3 (100.0)				
		[31.6, 86.1]		[29.2, 100.0]				
South America	5	2 (40.0)	1	1 (100.0)				
		[5.3, 85.3]		[2.5, 100.0]				
Central/Eastern Europe	4	3 (75.0)	4	3 (75.0)				
1		[19.4, 99.4]		[19.4, 99.4]				
Asia Pacific	6	5 (83.3)	2	2 (100.0)				
		[35.9, 99.6]		[15.8, 100.0]				
Rest of the world	7	7 (100.0)	2	2 (100.0)				
		[59.0, 100.0]	-	[15.8, 100.0]				
		[,]		[,]				
Baseline eosinophils (cat. N)								0.617
< 150 cells/uL	25	18 (72.0)	10	7 (70.0)	1.029	1.102	2.0	1.000
· 100 CC115/01	20	[50.6, 87.9]	10	· ,	[0.640, 1.652] [0			
150 - < 300 cells/uL	19	15 (78.9)	9	8 (88.9)	0.888	0.469	-9.9	1.000
150 - < 500 Cerrs/uL	19	· · ·	9	· ,				
		[54.4, 93.9]		[51.8, 99.7]	[0.640, 1.232][0	1.045, 4.931]	[-43./, 25.8]

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with response. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup.

Table DT1AA_LBSIN: Incidence of non-disease related TEAEs during study period by study specific subgroups DSAFNB - LTE - adult

	Teze+Teze		Pbo+Pbo		_	
Non-disease related TEAEs during study period	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR OR RD [95 % CI][95 % CI][95 % CI]	p-value
Baseline eosinophils (cat. Q)		N<10 any level				NE
Q1: < 140 cells/uL	21	14 (66.7) [43.0, 85.4]	10	7 (70.0) [34.8, 93.3]		
Q2: 140 - < 250 cells/uL	20	17 (85.0) [62.1, 96.8]	7	7 (100.0) [59.0, 100.0]		
Q3: 250 - < 430 cells/uL	3	2 (66.7) [9.4, 99.2]	2	1 (50.0) [1.3, 98.7]		
Baseline FENO (cat. N)		N<10 any level				NE
< 25 ppb	44	33 (75.0) [59.7, 86.8]	19	15 (78.9) [54.4, 93.9]		

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with response. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup.

Table DT1AA LBSIN: Incidence of non-disease related TEAEs during study period by study specific subgroups DSAFNB - LTE - adult

		Teze+Teze Pbo+1		Pbo+Pbo	_			
Non-disease related TEAEs during		n (%)		n (%)	RR	OR	RD	
study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Baseline FENO (cat. Q)								0.498
Q1: < 16 ppb	22	17 (77.3)	12	9 (75.0)	1.030	1.133	2.3	1.000
		[54.6, 92.2]		[42.8, 94.5]	[0.692, 1.533]	[0.219, 5.864]	[-34.3, 38.8]
Q2: 16 - < 30 ppb	22	16 (72.7)	7	6 (85.7)	0.848	0.444	-13.0	0.646
		[49.8, 89.3]		[42.1, 99.6]	[0.571, 1.261]	[0.044, 4.503]	[-54.3, 28.3]
Total serum IgE (cat. N)		N<10 any level						NE
Q1: < 53.1 IU/ml	33	27 (81.8)	16	13 (81.3)				
		[64.5, 93.0]		[54.4, 96.0]				
Q2: 53.1 - < 195.6 IU/ml	6	3 (50.0)	2	1 (50.0)				
		[11.8, 88.2]		[1.3, 98.7]				
Q4: >= 572.4 IU/ml	5	3 (60.0)	1	1 (100.0)				
		[14.7, 94.7]		[2.5, 100.0]				

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with response. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup. Source Data: aae, created on: 02AUG2022

Table DT1AA_LBSIN: Incidence of non-disease related TEAEs during study period by study specific subgroups DSAFNB - LTE - adult

		Teze+Teze		Pbo+Pbo	_		
Non-disease related TEAEs during study period	N	n (%) [95 % CI]	N	n (%) [95 % CI]		OR 95 % CI]	RD [95 % CI]p-value
Nasal polyps last 2 years		N<10 any level					NE
Yes	4	4 (100.0) [39.8, 100.0]	1	1 (100.0) [2.5, 100.0]			
No	40	29 (72.5) [56.1, 85.4]	18	14 (77.8) [52.4, 93.6]			

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with response. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup.

Table DT1AAN_LBMI0: Incidence of non-disease related non-severe TEAEs during study period DSAFNB - LTE - adult

	Teze+Teze		Pbo+Pbo		_			
		n (%)		n (%)	RR	OR	RD	
	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related non-severe TEAEs during	44	33 (75.0)	19	15 (78.9)	0.950	0.800	-3.9	1.000
study period		[59.7, 86.8]		[54.4, 93.9]	[0.712, 1.267]	[0.219, 2.927]	[-30.1, 22.2]

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: aae, created on: 15JUL2022

Table DT1AAN_LBSIK:	Incidence of non-disease	e related non-severe	TEAEs during	study period by k	ey subgroups
		DSAFNB - LTE - adult			

		Teze+Teze	Pbo+Pbo		_			
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Sex								0.499
	10	40 (85 0)	2	4 (50.0)	1 500	2 000	25 0	
Male	16	12 (75.0)	2	1 (50.0)	1.500	3.000	25.0	0.490
Female	20	[47.6, 92.7]	1 17	[1.3, 98.7]		[0.150, 59.890]		-
Female	28	21 (75.0)	17	14 (82.4)	0.911	0.643	-7.4	0.719
		[55.1, 89.3]		[56.6, 96.2]	[0.670, 1.238]	[0.142, 2.916]	[-36.3, 21.6]	
Age								0.359
< 65 years	35	25 (71.4)	16	13 (81.3)	0.879	0.577	-9.8	0.730
		[53.7, 85.4]		[54.4, 96.0]		[0.135, 2.469]		
>= 65 years	9	8 (88.9)	3	2 (66.7)	1.333	4.000	22.2	0.455
	-	[51.8, 99.7]	-	()		[0.167, 95.756]		
		2 , 3		2 / 3	- / -	- , -	2 ,	-
Exacerbations in the year before study								0.395
<= 2	26	20 (76.9)	11	8 (72.7)	1.058	1.250	4.2	1.000
		[56.4, 91.0]		[39.0, 94.0]	[0.696, 1.608]	[0.250, 6.255]	[-33.2, 41.6]	
> 2	18	13 (72.2)	8	7 (87.5)	0.825	0.371	-15.3	0.628
		[46.5, 90.3]		[47.3, 99.7]	[0.560, 1.217]	[0.036, 3.838]	[-55.2, 24.6]	
Race		N<10 any level						NE
White	30	20 (66.7)	14	10 (71.4)				
		[47.2, 82.7]		[41.9, 91.6]				
Black or African American	4	4 (100.0)	2	2 (100.0)				
		[39.8, 100.0]		[15.8, 100.0]				
Asian	8	7 (87.5)	2	2 (100.0)				
		[47.3, 99.7]		[15.8, 100.0]				
Other	2	2 (100.0)	1	1 (100.0)				
		[15.8, 100.0]		[2.5, 100.0]				

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and

risk measures are only calculated if there are at least 10 patients with events in a subgroup. Source Data: aae, created on: 11JUL2022

DT1AAN_LBSIK

Non-disease related non-severen (%)n (%)RRORRDTEAEs during study periodN95 % CI(95 % CI(95 % CI(95 % CI(95 % CI $95 % CI$) $p-value$ RegionN<10 any level(11.8, 88.2)(11.8, 88.2)NENEAmerica1810 (55.6)4 (100.0)(11.8, 88.2)NEAsia/Pacific65 (83.3)3 (100.0)(35.9, 99.6)(29.2, 100.0)Rest of the world1110 (90.9)6 (58.7, 99.8)(35.9, 99.6)NEPMIN<10 any levelNENE< 18.5 kg/m**211 (1000)0NE18.5 - < 25.0 kg/m**264 (66.7)3 (266.7)NE25.0 - < 30.0 kg/m**21814 (77.8)7 6 (85.7)(42.1, 99.6)>= 30.0 kg/m**21914 (77.8)7 6 (85.7)(48.8, 90.9)(40.0, 97.2)Baseline eosinophils - Low2518 (72.0)107 (70.0)1.0291.1022.0< 150 cells/uL2518 (72.0)107 (70.0)1.0291.0021.000> = 150 cells/uL1915 (78.9)9(51.8, 99.7)(0.640, 1.652)(0.220, 5.512)(-36.4, 42.4)>= 150 cells/uL2620 (76.9)1412 (85.7)0.8970.556-8.80.689All negative2620 (76.9)1412 (85.7)0.6970.556-9.91.000Any positive1813 (72.2)53 (60.0)1.2041.733 <th></th> <th></th> <th>Teze+Teze</th> <th></th> <th>Pbo+Pbo</th> <th>_</th> <th></th> <th></th> <th></th>			Teze+Teze		Pbo+Pbo	_			
RegionN<10 any level									
Europe98889.96333 (50.0) America1810 (55.6) 4 (100.0) Asia/Pacific65 (83.3) 3 (10.0) Asis/Pacific65 (83.3) 3 (100.0) Rest of the world11 10 (90.9) (9.9) $(55.7, 99.6)$ $(29.2, 100.0)$ BMIN<10 any levelNE< 18.5 r25.0 kg/m**21 1 (100.0) $(25, 100.0)$ $18.5 - < 25.0 kg/m**2$ 18 14 (77.8) 7 6 (85.7) $[25.4, 93.6]$ $[42.1, 99.6]$ $[42.1, 99.6]$ $(40.0, 97.2)$ $(40.0, 97.2)$ Baseline eosinophils - Low25 18 (72.0) (70.0) 1.029 1.102 2.0 < 150 cells/uL25 18 (72.0) $(24.4, 93.3)$ $(0.640, 1.652)$ $(0.220, 5.512)$ $(-8.4, 4.2.4)$ $> = 150$ cells/uL19 15 (78.9) 9 8 (88.9) 0.888 0.469 -9.9 1.000 $> = 150$ cells/uL26 20 (76.9) 14 12 (85.7) $(0.667, 1.232)$ $(0.467, 4.331)$ $(-487, 7.25.8)$ Baseline specific perennial FEIA 26 20 (76.9) 14 12 (85.7) $(.687, 0.556, -8.8, 0.689)$ Any positive18 13 12.2 5 3 $(0.00, 1.224)$ $(0.266, 1.212)$ $(0.266, 1.212)$ $(0.266, 1.226)$ $25.0 - 26.0$	TEAEs during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Europe98889.96333 (50.0) America1810 (55.6) 4 (100.0) Asia/Pacific65 (83.3) 3 (10.0) Asis/Pacific65 (83.3) 3 (100.0) Rest of the world11 10 (90.9) (9.9) $(55.7, 99.6)$ $(29.2, 100.0)$ BMIN<10 any level									
America $[51, 8, 99, 7]$ $[11, 8, 86, 2]$ America1810 (55.6)44 (100.0) $[30, 8, 78.5]$ $[39.8, 100.0]$ Asia/Pacific65 (83.3)3Rest of the world1110 (90.9)6 $[58.7, 99.6]$ $[58.7, 99.6]$ $[29.2, 100.0]$ PMIN<10 any level	Region		-						NE
America18 $10 (55, 6)$ 4 $4 (100, 0)$ Asia/Pacific65 (83.3)33 (100.0)Rest of the world11 $10 (90.9)$ 65 (83.3)BMIN<10 any level	Europe	9	· · · ·	6	· ,				
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Asia/Pacific65 (83.3)33 (100.0) (25.9, 99.6]7Rest of the world1110 (90.9) (58.7, 99.8]65 (83.3) (35.9, 99.6]8EMIN<10 any level	America	18	· /	4	· /				
Rest of the world $\begin{bmatrix} [35.9, 99.6] \\ 10 (90.9) \\ [58.7, 99.8] \end{bmatrix}$ $\begin{bmatrix} [29.2, 100.0] \\ 5 (83.3) \\ [35.9, 99.6] \end{bmatrix}$ BMIN<10 any levelNE< 18.5 kg/m**2									
Rest of the world1110 (90.9) (58.7, 99.8]65 (83.3) (35.9, 99.6]EMIN<10 any levelNE< 18.5 kg/m**2	Asia/Pacific	6	· · ·	3	· /				
$ \begin{bmatrix} 58.7, 99.8 \end{bmatrix} = \begin{bmatrix} 35.9, 99.6 \end{bmatrix} $ $ \begin{bmatrix} 84.8, 7, 99.8 \end{bmatrix} = \begin{bmatrix} 35.9, 99.6 \end{bmatrix} $ $ \begin{bmatrix} 84.8, 8, 90.0 \end{bmatrix} $ $ \begin{bmatrix} 1 & 1 & (100.0) & 0 \\ [2.5, 100.0] \\ [2$									
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	Rest of the world	11	· /	6	· ,				
<pre>< 18.5 kg/m**2 1 1 (10.0) 0 [2.5, 100.0] 18.5 - < 25.0 kg/m**2 6 4 (66.7) [22.3, 95.7] [9.4, 99.2] 25.0 - < 30.0 kg/m**2 18 14 (77.8) 7 6 (85.7) [52.4, 93.6] [42.1, 99.6] >= 30.0 kg/m**2 19 14 (73.7) 9 7 (77.8) [48.8, 90.9] [40.0, 97.2] Baseline eosinophils - Low 0.617 < 150 cells/uL 25 18 (72.0) 10 7 (70.0) 1.029 1.102 2.0 1.000 [50.6, 87.9] 9 8 (88.9) 0.888 0.469 -9.9 1.000 [54.4, 93.9] [0.640, 1.652] [0.220, 5.512] [-38.4, 42.4] >= 150 cells/uL 19 15 (78.9) 9 8 (88.9) 0.888 0.469 -9.9 1.000 [54.4, 93.9] [51.8, 99.7] [0.640, 1.232] [0.045, 4.931] [-45.7, 25.8]</pre>			[58.7, 99.8]		[35.9, 99.6]				
<pre>< 18.5 kg/m**2 1 1 (10.0) 0 [2.5, 100.0] 18.5 - < 25.0 kg/m**2 6 4 (66.7) [22.3, 95.7] [9.4, 99.2] 25.0 - < 30.0 kg/m**2 18 14 (77.8) 7 6 (85.7) [52.4, 93.6] [42.1, 99.6] >= 30.0 kg/m**2 19 14 (73.7) 9 7 (77.8) [48.8, 90.9] [40.0, 97.2] Baseline eosinophils - Low 0.617 < 150 cells/uL 25 18 (72.0) 10 7 (70.0) 1.029 1.102 2.0 1.000 [50.6, 87.9] 9 8 (88.9) 0.888 0.469 -9.9 1.000 [54.4, 93.9] [0.640, 1.652] [0.220, 5.512] [-38.4, 42.4] >= 150 cells/uL 19 15 (78.9) 9 8 (88.9) 0.888 0.469 -9.9 1.000 [54.4, 93.9] [51.8, 99.7] [0.640, 1.232] [0.045, 4.931] [-45.7, 25.8]</pre>	BMT		N<10 any level						NE
$ \begin{bmatrix} 2.5, 100.0 \\ 4 & (66.7) & 3 & 2 & (66.7) \\ [22.3, 95.7] & [9.4, 99.2] \\ 25.0 & - & 30.0 & kg/m^{**}2 & 18 & 14 & (77.8) \\ [52.4, 93.6] & [42.1, 99.6] \\ >= & 30.0 & kg/m^{**}2 & 19 & 14 & (73.7) & 9 & 7 & (77.8) \\ [48.8, 90.9] & [48.8, 90.9] & [40.0, 97.2] \\ \end{bmatrix} $ Baseline eosinophils - Low $& & & & & & & & & & & & & & & & & & &$		1	-	0					
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		-	. ,	Ũ					
$ \begin{bmatrix} 22.3, 95.7 \end{bmatrix} & \begin{bmatrix} 9.4, 99.2 \end{bmatrix} \\ \begin{bmatrix} 9.4, 99.2 \end{bmatrix} \\ \begin{bmatrix} 25.0 - \langle 30.0 \text{ kg/m}^{*2} 2 \end{bmatrix} \\ \begin{bmatrix} 18 & 14 & (77.8) \\ [52.4, 93.6] \end{bmatrix} & \begin{bmatrix} 42.1, 99.6 \end{bmatrix} \\ \begin{bmatrix} 42.0, 97.2 \end{bmatrix} \\ \begin{bmatrix} 40.0, 97.2 \end{bmatrix} \\ \begin{bmatrix} 53.4, 93.3 \end{bmatrix} \begin{bmatrix} 0.640, 1.652 \end{bmatrix} \begin{bmatrix} 0.220, 5.512 \end{bmatrix} \begin{bmatrix} -38.4, 42.4 \end{bmatrix} \\ \begin{bmatrix} -38.4, 42.4 \end{bmatrix} \\ \begin{bmatrix} 54.4, 93.9 \end{bmatrix} \\ \begin{bmatrix} 51.8, 99.7 \end{bmatrix} \begin{bmatrix} 0.640, 1.232 \end{bmatrix} \begin{bmatrix} 0.045, 4.931 \end{bmatrix} \begin{bmatrix} -45.7, 25.8 \end{bmatrix} \\ \begin{bmatrix} 0.487 \\ 411 \\ 19 \\ 15 \\ (51.4, 91.0] \\ \begin{bmatrix} 57.2, 98.2 \end{bmatrix} \begin{bmatrix} 0.665, 1.212 \end{bmatrix} \begin{bmatrix} 0.096, 3.207 \end{bmatrix} \begin{bmatrix} -38.7, 21.2 \end{bmatrix} \\ \begin{bmatrix} -38.7, 21.2 \end{bmatrix} \\ \begin{bmatrix} 18 & 13 \\ (72.2 \end{bmatrix} \\ \begin{bmatrix} 51.8, 60.0 \\ 1.204 \\ 1.733 \\ 12.2 \\ 0.621 \end{bmatrix} \end{bmatrix} $	18.5 - < 25.0 kg/m**2	6		3	2 (66.7)				
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	5								
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	25.0 - < 30.0 kg/m**2	18	14 (77.8)	7	6 (85.7)				
$ \begin{bmatrix} 48.8, 90.9 \end{bmatrix} \begin{bmatrix} 40.0, 97.2 \end{bmatrix} $ Baseline eosinophils - Low < 150 cells/uL 25 18 (72.0) 10 7 (70.0) 1.029 1.102 2.0 1.000 [50.6, 87.9] 9 8 (88.9) 0.888 0.469 -9.9 1.000 [54.4, 93.9] 9 [51.8, 99.7] [0.640, 1.652] [0.220, 5.512] [-38.4, 42.4] Baseline specific perennial FEIA status All negative 26 20 (76.9) 14 12 (85.7) 0.897 0.556 -8.8 0.689 [56.4, 91.0] [57.2, 98.2] [0.665, 1.212] [0.096, 3.207] [-38.7, 21.2] Any positive 18 13 (72.2) 5 3 (60.0) 1.204 1.733 12.2 0.621			[52.4, 93.6]		[42.1, 99.6]				
Baseline eosinophils - Low0.617< 150 cells/uL	>= 30.0 kg/m**2	19	14 (73.7)	9	7 (77.8)				
<pre>< 150 cells/uL 25 18 (72.0) 10 7 (70.0) 1.029 1.102 2.0 1.000 [50.6, 87.9] 9 8 (88.9) 0.888 0.469 -9.9 1.000 [54.4, 93.9] 9 8 (88.9) 0.888 0.469 -9.9 1.000 [54.4, 93.9] 9 [51.8, 99.7] [0.640, 1.232] [0.045, 4.931] [-45.7, 25.8] Baseline specific perennial FEIA All negative 26 20 (76.9) 14 12 (85.7) 0.897 0.556 -8.8 0.689 [56.4, 91.0] [57.2, 98.2] [0.665, 1.212] [0.096, 3.207] [-38.7, 21.2] Any positive 18 13 (72.2) 5 3 (60.0) 1.204 1.733 12.2 0.621</pre>			[48.8, 90.9]		[40.0, 97.2]				
<pre>< 150 cells/uL 25 18 (72.0) 10 7 (70.0) 1.029 1.102 2.0 1.000 [50.6, 87.9] 9 8 (88.9) 0.888 0.469 -9.9 1.000 [54.4, 93.9] 9 8 (88.9) 0.888 0.469 -9.9 1.000 [54.4, 93.9] 9 [51.8, 99.7] [0.640, 1.232] [0.045, 4.931] [-45.7, 25.8] Baseline specific perennial FEIA All negative 26 20 (76.9) 14 12 (85.7) 0.897 0.556 -8.8 0.689 [56.4, 91.0] [57.2, 98.2] [0.665, 1.212] [0.096, 3.207] [-38.7, 21.2] Any positive 18 13 (72.2) 5 3 (60.0) 1.204 1.733 12.2 0.621</pre>	Pageline ecginephila Lev								0 617
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	-	25	10 (72 0)	10	7 (70 0)	1 020	1 102	2 0	
<pre>>= 150 cells/uL 19 15 (78.9) 9 8 (88.9) 0.888 0.469 -9.9 1.000 Baseline specific perennial FEIA status All negative 26 20 (76.9) 14 12 (85.7) 0.897 0.556 -8.8 0.689 [56.4, 91.0] [57.2, 98.2] [0.665, 1.212] [0.096, 3.207] [-38.7, 21.2] Any positive 18 13 (72.2) 5 3 (60.0) 1.204 1.733 12.2 0.621</pre>	< 150 Certs/uL	20		10	· ,				
[54.4, 93.9] [51.8, 99.7] [0.640, 1.232] [0.045, 4.931] [-45.7, 25.8] Baseline specific perennial FEIA status 0.487 All negative 26 20 (76.9) 14 12 (85.7) 0.897 0.556 -8.8 0.689 [56.4, 91.0] [57.2, 98.2] [0.665, 1.212] [0.096, 3.207] [-38.7, 21.2] Any positive 18 13 (72.2) 5 3 (60.0) 1.204 1.733 12.2 0.621	>= 150 colle/uI	10		a					
Baseline specific perennial FEIA status 0.487 All negative 26 20 (76.9) 14 12 (85.7) 0.897 0.556 -8.8 0.689 [56.4, 91.0] [57.2, 98.2] [0.665, 1.212] [0.096, 3.207] [-38.7, 21.2] Any positive 18 13 (72.2) 5 3 (60.0) 1.204 1.733 12.2 0.621	>= 150 certs/dl	1)	· /)	- (/				
status All negative 26 20 (76.9) 14 12 (85.7) 0.897 0.556 -8.8 0.689 [56.4, 91.0] [57.2, 98.2] [0.665, 1.212] [0.096, 3.207] [-38.7, 21.2] Any positive 18 13 (72.2) 5 3 (60.0) 1.204 1.733 12.2 0.621			[51.1, 55.5]		[31.0, 33.7]	[0.010, 1.808]	[0.013, 1.931]	[13.7, 13.0	1
All negative 26 20 (76.9) 14 12 (85.7) 0.897 0.556 -8.8 0.689 [56.4, 91.0] [57.2, 98.2] [0.665, 1.212] [0.096, 3.207] [-38.7, 21.2] Any positive 18 13 (72.2) 5 3 (60.0) 1.204 1.733 12.2 0.621									0.487
[56.4, 91.0][57.2, 98.2][0.665, 1.212][0.096, 3.207][-38.7, 21.2]Any positive1813 (72.2)53 (60.0)1.2041.73312.20.621		26	20 (76.9)	14	12 (85.7)	0.897	0.556	-8.8	0.689
Any positive 18 13 (72.2) 5 3 (60.0) 1.204 1.733 12.2 0.621		_ 0							
	Any positive	18		5					
	<u> </u>		· /		· /	[0.557, 2.602][0.220, 13.670]	[-48.2, 72.7]	

Table DT1AAN_LBSIK: Incidence of non-disease related non-severe TEAEs during study period by key subgroups DSAFNB - LTE - adult

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).

Non-disease related non-severe TEAEs during study period	N	Teze+Teze n (%) [95 % CI]	 N	Pbo+Pbo n (%) [95 % CI]		OR [95 % CI]	RD [95 % CI]	p-value
Thinb during beauty period		[]]] []]]	11	[]]]]]]	[]]] []]	[55 % 61]	[]]]]]	p varae
Total serum IgE		N<10 any level						NE
Low	39	30 (76.9)	18	14 (77.8)				
	-	[60.7, 88.9]		[52.4, 93.6]				
High	5	3 (60.0)	1	1 (100.0)				
		[14.7, 94.7]		[2.5, 100.0]				
OCS at baseline		N<10 any level						NE
Yes	4	3 (75.0)	1	1 (100.0)				
		[19.4, 99.4]		[2.5, 100.0]				
No	40	30 (75.0)	18	14 (77.8)				
		[58.8, 87.3]		[52.4, 93.6]				
		. , .		. , .				
LAMA use at baseline								0.402
Yes	11	9 (81.8)	7	5 (71.4)	1.145	1.800	10.4	1.000
		[48.2, 97.7]		[29.0, 96.3]	[0.664, 1.976]	[0.191, 16.980]	[-41.8, 62.6]
No	33	24 (72.7)	12	10 (83.3)	0.873	0.533	-10.6	0.699
		[54.5, 86.7]		[51.6, 97.9]	[0.629, 1.212]	[0.097, 2.921]	[-42.3, 21.1]
Tiotropium use at baseline								0.913
Yes	9	7 (77.8)	6	5 (83.3)	0.933	0.700	-5.6	1.000
		[40.0, 97.2]		[35.9, 99.6]	[0.566, 1.539]	[0.049, 10.014]	[-59.8, 48.7]
No	35	26 (74.3)	13	10 (76.9)	0.966	0.867	-2.6	1.000
		[56.7, 87.5]		[46.2, 95.0]	[0.677, 1.378]	[0.194, 3.870]	[-35.0, 29.7]

Table DT1AAN_LBSIK: Incidence of non-disease related non-severe TEAEs during study period by key subgroups DSAFNB - LTE - adult

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup. Source Data: aae, created on: 11JUL2022

DT1AAN_LBSIK

Table DT1AAN_LBSIK: Incidence of non-disease related non-severe TEAEs during study period by key subgroups DSAFNB - LTE - adult

		Teze+Teze		Pbo+Pbo	_			
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Montelukast/ Cromoglicic acid use at baseline								0.878
Yes	14	13 (92.9)	6	6 (100.0)	0.929	0.692 +	-7.1	1.000
		[66.1, 99.8]		[54.1, 100.0]	[0.803, 1.074]	[0.025, 19.431]	[-32.5, 18.3]
No	30	20 (66.7) [47.2, 82.7]	13	9 (69.2) [38.6, 90.9]	0.963 [0.619, 1.498]	0.889 [0.219, 3.609]	-2.6 [-38.3, 33.2	1.000

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with response. OCS = oral corticosteroids. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup. Source Data: aae, created on: 11JUL2022

Table DT1AAN_LBSIN: Incidence of non-disease related non-severe TEAEs during study period by study specific subgroups DSAFNB - LTE - adult

	Teze+Teze			Pbo+Pbo				
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Region (cat. N)		N<10 any level						NE
Western Europe	9	8 (88.9)	7	4 (57.1)				
		[51.8, 99.7]		[18.4, 90.1]				
North America	13	8 (61.5)	3	3 (100.0)				
		[31.6, 86.1]		[29.2, 100.0]				
South America	5	2 (40.0)	1	1 (100.0)				
		[5.3, 85.3]		[2.5, 100.0]				
Central/Eastern Europe	4	3 (75.0)	4	3 (75.0)				
-		[19.4, 99.4]		[19.4, 99.4]				
Asia Pacific	6	5 (83.3)	2	2 (100.0)				
		[35.9, 99.6]		[15.8, 100.0]				
Rest of the world	7	7 (100.0)	2	2 (100.0)				
		[59.0, 100.0]		[15.8, 100.0]				
Baseline eosinophils (cat. N)								0.617
< 150 cells/uL	25	18 (72.0)	10	7 (70.0)	1.029	1.102	2.0	1.000
		[50.6, 87.9]		[34.8, 93.3]	[0.640, 1.652]			
150 - < 300 cells/uL	19	15 (78.9)	9	8 (88.9)	0.888	0.469	-9.9	1.000
		[54.4, 93.9]		· · ·	[0.640, 1.232]			
		- ,		- ,	- ,	- ,	- ,	-

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with response. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup.

Table DT1AAN_LBSIN: Incidence of non-disease related non-severe TEAEs during study period by study specific subgroups DSAFNB - LTE - adult

		Teze+Teze	Pbo+Pbo		_		
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD
TEAEs during study period	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]p-value
Baseline eosinophils (cat. Q)		N<10 any level					NE
Q1: < 140 cells/uL	21	14 (66.7) [43.0, 85.4]	10	7 (70.0) [34.8, 93.3]			
Q2: 140 - < 250 cells/uL	20	17 (85.0) [62.1, 96.8]	7	7 (100.0) [59.0, 100.0]			
Q3: 250 - < 430 cells/uL	3	2 (66.7) [9.4, 99.2]	2	1 (50.0) [1.3, 98.7]			
Baseline FENO (cat. N)		N<10 any level					NE
< 25 ppb	44	33 (75.0) [59.7, 86.8]	19	15 (78.9) [54.4, 93.9]			

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with response. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup.

Table DT1AAN_LBSIN: Incidence of non-disease related non-severe TEAEs during study period by study specific subgroups DSAFNB - LTE - adult

		Teze+Teze	e+Teze					
Non-disease related non-severe		n (%)		n (%)	RR	OR	RD	
TEAEs during study period	Ν	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Baseline FENO (cat. Q)								0.498
Q1: < 16 ppb	22	17 (77.3)	12	9 (75.0)	1.030	1.133	2.3	1.000
		[54.6, 92.2]		[42.8, 94.5]	[0.692, 1.533]	[0.219, 5.864]	[-34.3, 38.8]
Q2: 16 - < 30 ppb	22	16 (72.7)	7	6 (85.7)	0.848	0.444	-13.0	0.646
		[49.8, 89.3]		[42.1, 99.6]	[0.571, 1.261]	[0.044, 4.503]	[-54.3, 28.3]
Total serum IgE (cat. N)		N<10 any level						NE
Q1: < 53.1 IU/ml	33	27 (81.8)	16	13 (81.3)				
		[64.5, 93.0]		[54.4, 96.0]				
Q2: 53.1 - < 195.6 IU/ml	6	3 (50.0)	2	1 (50.0)				
		[11.8, 88.2]		[1.3, 98.7]				
Q4: >= 572.4 IU/ml	5	3 (60.0)	1	1 (100.0)				
		[14.7, 94.7]		[2.5, 100.0]				

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with response. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup.

Table DT1AAN_LBSIN: Incidence of non-disease related non-severe TEAEs during study period by study specific subgroups DSAFNB - LTE - adult

		Teze+Teze H		Pbo+Pbo	_		
Non-disease related non-severe TEAEs during study period	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI][95	OR 5 % CI][9	RD 5 % CI]p-value
Nasal polyps last 2 years		N<10 any level					NE
Yes	4	4 (100.0) [39.8, 100.0]	1	1 (100.0) [2.5, 100.0]			
No	40	29 (72.5) [56.1, 85.4]	18	14 (77.8) [52.4, 93.6]			

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with response. TEAE = treatment emergent adverse events. LTE = long term extension. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = Cochran Q test for heterogeneity / exact test of Fisher. * = significant treatment effect. i = significant Cochran Q. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test and risk measures are only calculated if there are at least 10 patients with events in a subgroup.

Table DT1AAC_LBMI0: Incidence of non-disease related severe TEAEs during study period DSAFNB - LTE - adult

	Teze+Teze		Pbo+Pbo		_			
		n (%)		n (%)	RR	OR	RD	
	N	[95 % CI]	Ν	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
Non-disease related severe TEAEs during study	44	5 (11.4)	19	3 (15.8)	0.720	0.684	-4.4	0.688
period		[3.8, 24.6]		[3.4, 39.6]	[0.191, 2.711]	[0.146, 3.206]	[-27.1, 18.2]

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: aae, created on: 15JUL2022

Table DT1AAS_LBMI0: Incidence of non-disease related serious TEAEs during study period DSAFNB - LTE - adult

	Teze+Teze		Pbo+Pbo		_			
	N	n (%) [95 % CI]	N	n (%) [95 % CI]		OR [95 % CI]	RD [95 % CI]	p-value
Non-disease related serious TEAEs during study	44	6 (13.6)	19	1 (5.3)	2.591	2.842	8 4	0.664
period		[5.2, 27.4]	10	[0.1, 26.0]	[0.334, 20.075]		[-9.7, 26.4]	

Note: DSAFNB - LTE - adult = Dossier Biomarker Safety Set - predecessor NAVIGATOR - Long term extension - adults. N = total number of patients in analysis set. n = number of patients with events. 95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). p-value = exact test of Fisher. * = significant treatment effect. + = adding of + 0.5 to each cell. TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. Source Data: aae, created on: 15JUL2022