Dossier zur Nutzenbewertung gemäß § 35a SGB V

Tezepelumab (Tezspire®)

AstraZeneca GmbH

Modul 4 A – Anhang 4-G-11

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

Ergänzende Ergebnisse
Studien NAVIGATOR, PATHWAY, DRI12544, QUEST
Indirekte Vergleiche auf Basis randomisierter kontrollierter Studien

Stand: 11.11.2022

Table MT1IE_ILIDI: AAER during 24 weeks treatment period - indirect comparison with pooled QR
DITTL

Variable	Study	Indirect comparison (Bucher) Risk Ratio	95% CI	p-value	
AAER during 24 weeks treatment period	Pooled NP	0.432	(0.346, 0.539)	<0.001	*
	Pooled QR	0.470	(0.330, 0.650)	<0.01	*
	Pooled NP/Pooled QR	0.919	(0.620, 1.361)	0.672	

Note: DITTL = Dossier Label Intent-to-Treat Set.
CI = confidence interval. Pooled NP = Pooled NAVIGATOR (adult)/PATHWAY. Pooled QR = pooled QUEST/DRI12522.
AAER = annual asthma exacerbation rates.
Source tables: MT1IE_ILIN2, IT1E_ILMN0.

Table MT1IE_ILIN2: AAER during 24 weeks treatment period -complete follow-up period as offset DITTL

AAER during 24 weeks treatment period					Adjusted rates		Rate ratio		
Treatment	N	nev	Time at risk (years)	Crude rate	Estimate	95% CI	Estimate	95% CI	p-value
Tezepelumab	446	182	218.9	0.83	0.83	(0.70, 0.99)	0.432	(0.346, 0.539)	<0.001 *
Placebo	436	410	214.1	1.91	1.92	(1.68, 2.21)			

Note: DITTL = Dossier Label Intent-to-Treat Set.
N = total number of patients in analysis set. nev = number of events within considered period. NE = not evaluable.
95% CI = 95% confidence interval coming from a negative binomial model.
A negative binomial model was applied with factors treatment. The logarithm of follow-up time (including duration of exacerbations) was used as offset. No additional factors were considered to achieve robust results across all analyses.
Source Data: aaer, created on: 27APR2022

Table NT1IE_ILIN2: AAER during 24 weeks treatment period -complete follow-up period as offset
DITTL

AAER during 24 weeks treatment period					Adjusted rates		Rate ratio			
Treatment	N	nev	Time at risk (years)	Crude rate	Estimate	95% CI	Estimate	95% CI	p-value	
Tezepelumab	395	182	194.6	0.94	0.93	(0.78, 1.11)	0.463	(0.370, 0.580)	<0.001	*
Placebo	391	386	192.2	2.01	2.02	(1.75, 2.32)				

Note: DITTL = Dossier Label Intent-to-Treat Set.
N = total number of patients in analysis set. nev = number of events within considered period. NE = not evaluable.
95% CI = 95% confidence interval coming from a negative binomial model.
A negative binomial model was applied with factors treatment. The logarithm of follow-up time (including duration of exacerbations) was used as offset. No additional factors were considered to achieve robust results across all analyses.
Source Data: aaer, created on: 27APR2022

Table PT3IE_ILIN2: AAER during 24 weeks treatment period -complete follow-up period as offset
DITTL

AAER during 24 weeks treatment period					Adjusted rates		Rate ratio			
Treatment	N	nev	Time at risk (years)	Crude rate	Estimate	95% CI	Estimate	95% CI	p-value	
Tezepelumab	66	7	31.3	0.22	0.22	(0.10, 0.49)	0.204	(0.084, 0.497)	<0.001	*
Placebo	65	35	31.9	1.10	1.09	(0.72, 1.67)				

Note: DITTL = Dossier Label Intent-to-Treat Set.
N = total number of patients in analysis set. nev = number of events within considered period. NE = not evaluable.
95% CI = 95% confidence interval coming from a negative binomial model.
A negative binomial model was applied with factors treatment. The logarithm of follow-up time (including duration of exacerbations) was used as offset. No additional factors were considered to achieve robust results across all analyses.
Source Data: aaer, created on: 27APR2022

Table MT1IE_ILIND: AAER during 24 weeks treatment period by subgroups relevant for ITC - complete follow-up period as offset DITTL

AAER during 24 weeks treatment period						Adjusted rates		Rate ratio			
Subgroup	Treatment	N	nev	Time at risk (years)	Crude rate	Estimate	95% CI	Estimate	95% CI	p-value	
OCS at baseline	Tezepelumab									0.205	
Yes	Tezepelumab	55	37	27.0	1.37	1.37	(0.90, 2.08)	0.600	(0.344, 1.045)	0.071	
Yes	Placebo	55	61	26.6	2.29	2.28	(1.58, 3.29)				
No	Tezepelumab	391	145	191.8	0.76	0.75	(0.62, 0.91)	0.403	(0.316, 0.514)	<0.001	*
No	Placebo	381	349	187.5	1.86	1.87	(1.61, 2.17)				

Note: DITTL = Dossier Label Intent-to-Treat Set.
N = total number of patients in analysis set. nev = number of events within considered period. NE = not evaluable.
95% CI = 95% confidence interval coming from a negative binomial model.
A negative binomial model was applied with factors treatment. The logarithm of follow-up time (including duration of exacerbations) was used as offset. No additional factors were considered to achieve robust results across all analyses.
Source Data: aaer, created on: 27APR2022

Table MT1IES_ILIDI: Severe AAER during 24 weeks treatment period - indirect comparison with pooled QR
DITTL

Variable	Study	Indirect comparison (Bucher) Risk Ratio	95% CI	p-value	
Severe AAER during 24 weeks treatment period	Pooled NP	0.228	(0.118, 0.440)	<0.001	*
	Pooled QR	0.560	(0.230, 1.370)	0.210	
	Pooled NP/Pooled QR	0.408	(0.134, 1.237)	0.113	

Note: DITTL = Dossier Label Intent-to-Treat Set.
CI = confidence interval. Pooled NP = Pooled NAVIGATOR (adult)/PATHWAY. Pooled QR = pooled QUEST/DRI12522.
AAER = annual asthma exacerbation rates.
Source tables: MT1IES_ILIN2, IT1ES_ILMN0.

Table MT1IES_ILIN2: Severe AAER during 24 weeks treatment period -complete follow-up period as offset DITTL

Severe AAER during 24 weeks treatment period					Adjusted rates		Rate ratio			
Treatment	N	nev	Time at risk (years)	Crude rate	Estimate	95% CI	Estimate	95% CI	p-value	
Tezepelumab	446	15	218.9	0.07	0.07	(0.04, 0.12)	0.228	(0.118, 0.440)	<0.001	*
Placebo	436	64	214.1	0.30	0.30	(0.21, 0.42)				

Note: DITTL = Dossier Label Intent-to-Treat Set.
N = total number of patients in analysis set. nev = number of events within considered period. NE = not evaluable.
95% CI = 95% confidence interval coming from a negative binomial model.
A negative binomial model was applied with factors treatment. The logarithm of follow-up time (including duration of exacerbations) was used as offset. No additional factors were considered to achieve robust results across all analyses.
Source Data: aaer, created on: 27APR2022

Table NT1IES_ILIN2: Severe AAER during 24 weeks treatment period -complete follow-up period as offset DITTL

Severe AAER during 24 weeks treatment period					Adjusted rates		Rate ratio			
Treatment	N	nev	Time at risk (years)	Crude rate	Estimate	95% CI	Estimate	95% CI	p-value	
Tezepelumab	395	12	194.6	0.06	0.06	(0.03, 0.11)	0.197	(0.096, 0.404)	<0.001	*
Placebo	391	60	192.2	0.31	0.31	(0.22, 0.45)				

Note: DITTL = Dossier Label Intent-to-Treat Set.
N = total number of patients in analysis set. nev = number of events within considered period. NE = not evaluable.
95% CI = 95% confidence interval coming from a negative binomial model.
A negative binomial model was applied with factors treatment. The logarithm of follow-up time (including duration of exacerbations) was used as offset. No additional factors were considered to achieve robust results across all analyses.
Source Data: aaer, created on: 27APR2022

Table PT3IES_ILIN2: Severe AAER during 24 weeks treatment period -complete follow-up period as offset DITTL

Severe AAER during 24 weeks treatment period					Adjusted rates		Rate ratio		
Treatment	N	nev	Time at risk (years)	Crude rate	Estimate	95% CI	Estimate	95% CI	p-value
Tezepelumab	66	3	31.3	0.10	0.10	(0.03, 0.31)	0.507	(0.115, 2.230)	0.369
Placebo	65	6	31.9	0.19	0.19	(0.08, 0.45)			

Note: DITTL = Dossier Label Intent-to-Treat Set.
N = total number of patients in analysis set. nev = number of events within considered period. NE = not evaluable.
95% CI = 95% confidence interval coming from a negative binomial model.
A negative binomial model was applied with factors treatment. The logarithm of follow-up time (including duration of exacerbations) was used as offset. No additional factors were considered to achieve robust results across all analyses.
Source Data: aaer, created on: 27APR2022

Table MT1IES_ILIND: Severe AAER during 24 weeks treatment period by subgroups relevant for ITC - complete follow-up period as offset
DITTL

Severe AAER during 24 weeks treatment period						Adjusted rates		Rate ratio			
Subgroup	Treatment	N	nev	Time at risk (years)	Crude rate	Estimate	95% CI	Estimate	95% CI	p-value	
OCS at baseline	Tezepelumab									0.300	
Yes	Tezepelumab	55	1	27.0	0.04	0.04	(0.01, 0.27)	0.083	(0.010, 0.679)	0.020	*
Yes	Placebo	55	12	26.6	0.45	0.45	(0.23, 0.88)				
No	Tezepelumab	391	14	191.8	0.07	0.07	(0.04, 0.13)	0.261	(0.128, 0.532)	<0.001	*
No	Placebo	381	52	187.5	0.28	0.28	(0.19, 0.41)				

Note: DITTL = Dossier Label Intent-to-Treat Set.
N = total number of patients in analysis set. nev = number of events within considered period. NE = not evaluable.
95% CI = 95% confidence interval coming from a negative binomial model.
A negative binomial model was applied with factors treatment. The logarithm of follow-up time (including duration of exacerbations) was used as offset. No additional factors were considered to achieve robust results across all analyses.
Source Data: aaer, created on: 27APR2022

Table MT1IE_ICIDI: AAER during 24 weeks treatment period - indirect comparison with pooled QR
DITTL - patients without OCS medications

		Indirect comparison (Bucher)			
Variable	Study	Risk Ratio	95% CI	p-value	
AAER during 24 weeks treatment period	Pooled NP	0.403	(0.316, 0.514)	<0.001	*
	Pooled QR	0.470	(0.330, 0.650)	<0.01	*
	Pooled NP/Pooled QR	0.858	(0.572, 1.286)	0.459	

Note: DITTL - patients without OCS medications = Dossier Label Intent-to-Treat Set - patients without OCS medications.
CI = confidence interval. Pooled NP = Pooled NAVIGATOR (adult)/PATHWAY. Pooled QR = pooled QUEST/DRI12522.
AAER = annual asthma exacerbation rates.
Source tables: MT1IE_ILIND, IT1IE_ILMN0.

Table MT1IES_ICIDI: Severe AAER during 24 weeks treatment period - indirect comparison with pooled QR
DITTL - patients without OCS medications

		Indirect comparison (Bucher)			
Variable	Study	Risk Ratio	95% CI	p-value	
Severe AAER during 24 weeks treatment period	Pooled NP	0.261	(0.128, 0.532)	<0.001	*
	Pooled QR	0.560	(0.230, 1.370)	0.210	
	Pooled NP/Pooled QR	0.467	(0.149, 1.463)	0.191	

Note: DITTL - patients without OCS medications = Dossier Label Intent-to-Treat Set - patients without OCS medications.
CI = confidence interval. Pooled NP = Pooled NAVIGATOR (adult)/PATHWAY. Pooled QR = pooled QUEST/DRI12522.
AAER = annual asthma exacerbation rates.
Source tables: MT1IES_ILIND, IT1IES_ILMN0.

Table MT1IA_SLII0: Incidence of TEAEs during 24 weeks treatment period
DSAFL

	Tezepelumab		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
TEAEs during 24 weeks treatment period	446	290 (65.0) [60.4, 69.4]	436	303 (69.5) [64.9, 73.8]	0.936 [0.853, 1.026]	0.816 [0.616, 1.082]	-4.5 [-10.9, 1.9]	0.173

Note: DSAFL = Dossier Label 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: 26APR2022

Table NT1IA_SLII0: Incidence of TEAEs during 24 weeks treatment period
DSAFL

	Tezepelumab		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
TEAEs during 24 weeks treatment period	395	260 (65.8) [60.9, 70.5]	391	279 (71.4) [66.6, 75.8]	0.922 [0.839, 1.014]	0.773 [0.572, 1.046]	-5.5 [-12.3, 1.2]	0.107

Note: DSAFL = Dossier Label 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: 26APR2022

Table PT3IA_SLII0: Incidence of TEAEs during 24 weeks treatment period
DSAFL

	Tezepelumab		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
TEAEs during 24 weeks treatment period	66	37 (56.1) [43.3, 68.3]	65	37 (56.9) [44.0, 69.2]	0.985 [0.729, 1.330]	0.966 [0.484, 1.927]	-0.9 [-19.4, 17.6]	1.000

Note: DSAFL = Dossier Label 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: 26APR2022

Table MT1IA_SLIDI: Incidence of TEAEs during 24 weeks treatment period - indirect comparison with pooled QC
DSAFL

		Indirect comparison (Bucher)			
Variable	Study	Relative Risk Ratio	95% CI	p-value	
TEAEs during 24 weeks treatment period	Pooled NP	0.936	(0.853, 1.026)	0.173	
	Pooled QR	1.100	(0.990, 1.220)	0.060	
	Pooled NP/Pooled QR	0.851	(0.740, 0.977)	0.022	*

Note: DSAFL = Dossier Label Safety Set.
CI = confidence interval. Pooled NP = Pooled NAVIGATOR (adult)/PATHWAY. Pooled QR = pooled QUEST/DRI12522.
TEAE = treatment emergent adverse event.
Source tables: MT1IA_SLII0, IT1IA_SLMI0

Table MT1IA_SLIID: Incidence of TEAEs during 24 weeks treatment period by subgroups relevant for ITC
DSAFL

TEAEs during 24 weeks treatment period	Tezepelumab N	Tezepelumab n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
OCS at baseline								0.309
Yes	55	46 (83.6) [71.2, 92.2]	55	45 (81.8) [69.1, 90.9]	1.022 [0.862, 1.213]	1.136 [0.422, 3.056]	1.8 [-14.1, 17.8]	1.000
No	391	244 (62.4) [57.4, 67.2]	381	258 (67.7) [62.8, 72.4]	0.922 [0.831, 1.022]	0.791 [0.588, 1.065]	-5.3 [-12.3, 1.7]	0.131

Note: DSAFL = Dossier Label 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: 26APR2022

Table MT1IAN_SLII0: Incidence of non-severe TEAEs during 24 weeks treatment period
DSAFL

	Tezepelumab		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Non-severe TEAEs during 24 weeks treatment period	446	285 (63.9) [59.3, 68.4]	436	295 (67.7) [63.0, 72.0]	0.944 [0.859, 1.039]	0.846 [0.640, 1.118]	-3.8 [-10.2, 2.7]	0.256

Note: DSAFL = Dossier Label 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: 26APR2022

Table NT1IAN_SLII0: Incidence of non-severe TEAEs during 24 weeks treatment period
DSAFL

	Tezepelumab		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Non-severe TEAEs during 24 weeks treatment period	395	256 (64.8) [59.9, 69.5]	391	273 (69.8) [65.0, 74.3]	0.928 [0.842, 1.023]	0.796 [0.590, 1.073]	-5.0 [-11.8, 1.8]	0.149

Note: DSAFL = Dossier Label 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: 26APR2022

Table PT3IAN_SLII0: Incidence of non-severe TEAEs during 24 weeks treatment period
DSAFL

	Tezepelumab		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Non-severe TEAEs during 24 weeks treatment period	66	36 (54.5) [41.8, 66.9]	65	35 (53.8) [41.0, 66.3]	1.013 [0.739, 1.388]	1.029 [0.517, 2.045]	0.7 [-17.9, 19.3]	1.000

Note: DSAFL = Dossier Label 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: 26APR2022

Table MT1IAC_SLII0: Incidence of severe TEAEs during 24 weeks treatment period
DSAFL

	Tezepelumab		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Severe TEAEs during 24 weeks treatment period	446	30 (6.7) [4.6, 9.5]	436	47 (10.8) [8.0, 14.1]	0.624 [0.402, 0.967]	0.597 [0.370, 0.963]	-4.1 [-8.0, -0.1]	0.042 *

Note: DSAFL = Dossier Label 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: 26APR2022

Table NT1IAC_SLII0: Incidence of severe TEAEs during 24 weeks treatment period
DSAFL

	Tezepelumab		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Severe TEAEs during 24 weeks treatment period	395	20 (5.1) [3.1, 7.7]	391	36 (9.2) [6.5, 12.5]	0.550 [0.324, 0.933]	0.526 [0.299, 0.926]	-4.1 [-8.0, -0.3]	0.026 *

Note: DSAFL = Dossier Label 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: 26APR2022

Table PT3IAC_SLII0: Incidence of severe TEAEs during 24 weeks treatment period
DSAFL

	Tezepelumab		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Severe TEAEs during 24 weeks treatment period	66	10 (15.2) [7.5, 26.1]	65	12 (18.5) [9.9, 30.0]	0.821 [0.381, 1.766]	0.789 [0.314, 1.978]	-3.3 [-17.6, 11.0]	0.647

Note: DSAFL = Dossier Label 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: 26APR2022

Table MT1IAS_SLII0: Incidence of serious TEAEs during 24 weeks treatment period
DSAFL

	Tezepelumab		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Serious TEAEs during 24 weeks treatment period	446	25 (5.6) [3.7, 8.2]	436	49 (11.2) [8.4, 14.6]	0.499 [0.314, 0.793]	0.469 [0.284, 0.774]	-5.6 [-9.5, -1.8]	0.003 *

Note: DSAFL = Dossier Label 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: 26APR2022

Table NT1IAS_SLII0: Incidence of serious TEAEs during 24 weeks treatment period
DSAFL

	Tezepelumab		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Serious TEAEs during 24 weeks treatment period	395	19 (4.8) [2.9, 7.4]	391	43 (11.0) [8.1, 14.5]	0.437 [0.260, 0.737]	0.409 [0.234, 0.715]	-6.2 [-10.2, -2.2]	0.001 *

Note: DSAFL = Dossier Label 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: 26APR2022

Table PT3IAS_SLII0: Incidence of serious TEAEs during 24 weeks treatment period
DSAFL

	Tezepelumab		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Serious TEAEs during 24 weeks treatment period	66	6 (9.1) [3.4, 18.7]	65	7 (10.8) [4.4, 20.9]	0.844 [0.300, 2.377]	0.829 [0.263, 2.613]	-1.7 [-13.4, 10.1]	0.778

Note: DSAFL = Dossier Label 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: 26APR2022

Table MT1IAS_SLIDI: Incidence of serious TEAEs during 24 weeks treatment period - indirect comparison with pooled QC
DSAFL

		Indirect comparison (Bucher)			
Variable	Study	Relative Risk Ratio	95% CI	p-value	
Serious TEAEs during 24 weeks treatment period	Pooled NP	0.499	(0.314, 0.793)	0.003	*
	Pooled QR	0.790	(0.400, 1.580)	0.510	
	Pooled NP/Pooled QR	0.631	(0.274, 1.453)	0.280	

Note: DSAFL = Dossier Label Safety Set.
CI = confidence interval. Pooled NP = Pooled NAVIGATOR (adult)/PATHWAY. Pooled QR = pooled QUEST/DRI12522.
TEAE = treatment emergent adverse event.
Source tables: MT1IAS_SLII0, IT1IAS_SLMI0

Table MT1IAS_SLIID: Incidence of serious TEAEs during 24 weeks treatment period by subgroups relevant for ITC DSAFL

	Tezepelumab		Placebo					
Serious TEAEs during 24 weeks treatment period	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
OCS at baseline								0.690
Yes	55	6 (10.9) [4.1, 22.2]	55	14 (25.5) [14.7, 39.0]	0.429 [0.178, 1.034]	0.359 [0.126, 1.017]	-14.5 [-30.5, 1.4]	0.082
No	391	19 (4.9) [3.0, 7.5]	381	35 (9.2) [6.5, 12.5]	0.529 [0.308, 0.908]	0.505 [0.283, 0.899]	-4.3 [-8.2, -0.5]	0.023 *

Note: DSAFL = Dossier Label 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: 26APR2022

Table MT1IAT_SLII0: Incidence of TEAEs leading to study drug discontinuation during 24 weeks treatment period
DSAFL

	Tezepelumab		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
TEAEs leading to study drug discontinuation during 24 weeks treatment period	446	8 (1.8) [0.8, 3.5]	436	15 (3.4) [1.9, 5.6]	0.521 [0.223, 1.217]	0.513 [0.215, 1.222]	-1.6 [-4.0, 0.7]	0.142

Note: DSAFL = Dossier Label 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: 26APR2022

Table NT1IAT_SLII0: Incidence of TEAEs leading to study drug discontinuation during 24 weeks treatment period
DSAFL

	Tezepelumab		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
TEAEs leading to study drug discontinuation during 24 weeks treatment period	395	7 (1.8) [0.7, 3.6]	391	15 (3.8) [2.2, 6.2]	0.462 [0.190, 1.121]	0.452 [0.182, 1.122]	-2.1 [-4.6, 0.5]	0.087

Note: DSAFL = Dossier Label 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: 26APR2022

Table PT3IAT_SLII0: Incidence of TEAEs leading to study drug discontinuation during 24 weeks treatment period
DSAFL

	Tezepelumab		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
TEAEs leading to study drug discontinuation during 24 weeks treatment period	66	1 (1.5) [0.0, 8.2]	65	0 (0.0) [0.0, 5.5]	2.955 + [0.123, 71.242]	3.000 + [0.120, 75.000]	1.5 [-3.0, 6.0]	1.000

Note: DSAFL = Dossier Label 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: 26APR2022

Table MT1IAD_SLII0: Incidence of fatal TEAEs during 24 weeks treatment period
DSAFL

	Tezepelumab		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Fatal TEAEs during 24 weeks treatment period	446	0 (0.0) [0.0, 0.8]	436	2 (0.5) [0.1, 1.6]	0.196 + [0.009, 4.061]	0.195 + [0.009, 4.066]	-0.5 [-1.3, 0.4]	0.244

Note: DSAFL = Dossier Label 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: 26APR2022

Table NT1IAD_SLII0: Incidence of fatal TEAEs during 24 weeks treatment period
DSAFL

	Tezepelumab		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Fatal TEAEs during 24 weeks treatment period	395	0 (0.0) [0.0, 0.9]	391	2 (0.5) [0.1, 1.8]	0.198 + [0.010, 4.111]	0.197 + [0.009, 4.116]	-0.5 [-1.5, 0.5]	0.247

Note: DSAFL = Dossier Label 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: 26APR2022

Table PT3IAD_SLII0: Incidence of fatal TEAEs during 24 weeks treatment period
DSAFL

	Tezepelumab		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Fatal TEAEs during 24 weeks treatment period	66	0 (0.0) [0.0, 5.4]	65	0 (0.0) [0.0, 5.5]				

Note: DSAFL = Dossier Label 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: 26APR2022

Table MT1IA_SCIDI: Incidence of TEAEs during 24 weeks treatment period - indirect comparison with pooled QR
DSAFL - patients without OCS medications

		Indirect comparison (Bucher)			
Variable	Study	Relative Risk Ratio	95% CI	p-value	
TEAEs during 24 weeks treatment period	Pooled NP	0.922	(0.831, 1.022)	0.131	
	Pooled QR	1.100	(0.990, 1.220)	0.060	
	Pooled NP/Pooled QR	0.838	(0.724, 0.970)	0.018	*

Note: DSAFL - patients without OCS medications = Dossier Label Safety Set - patients without OCS medications.
CI = confidence interval. Pooled NP = Pooled NAVIGATOR (adult)/PATHWAY. Pooled QR = pooled QUEST/DRI12522.
TEAE = treatment emergent adverse event.
Source tables: MT1IA_SLIID, IT1IA_SLMI0

Table MT1IAS_SCIDI: Incidence of serious TEAEs during 24 weeks treatment period - indirect comparison with pooled QR
DSAFL - patients without OCS medications

		Indirect comparison (Bucher)			
Variable	Study	Relative Risk Ratio	95% CI	p-value	
Serious TEAEs during 24 weeks treatment period	Pooled NP	0.529	(0.308, 0.908)	0.023	*
	Pooled QR	0.790	(0.400, 1.580)	0.510	
	Pooled NP/Pooled QR	0.670	(0.278, 1.613)	0.371	

Note: DSAFL - patients without OCS medications = Dossier Label Safety Set - patients without OCS medications.
CI = confidence interval. Pooled NP = Pooled NAVIGATOR (adult)/PATHWAY. Pooled QR = pooled QUEST/DRI12522.
TEAE = treatment emergent adverse event.
Source tables: MT1IAS_SLIID, IT1IAS_SLMI0