Dossier zur Nutzenbewertung gemäß § 35a SGB V

Lebrikizumab (Ebglyss®)

Almirall Hermal GmbH

Modul 4A Anhang 4-G

Behandlung von mittelschwerer bis schwerer atopischer Dermatitis bei Erwachsenen und Jugendlichen ab 12 Jahren mit einem Körpergewicht von mindestens 40 kg, die für eine systemische Therapie in Betracht kommen.

Ergänzende Informationen zu den Studien ADvocate 1, Advocate 2 und ADhere

Stand: 01.12.2023

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Abkürzungsverzeichnis

Abkürzung	**Bedeutung**
AD	Atopische Dermatitis
BSA	*Body Surface Area*
CDLQI	*Children Dermatology Life Quality Index*
DLQI	*Dermatology Life Quality Index*
EASI	*Eczema Area and Severity Index*
IGA	*Investigators Global Assessment*
MedDRA	*Medical Dictionary for Regulatory Activities*
MTC	*Mixed Treatment Comparison*
NRS	*Numerical Rating Scale*
OR	*Odds Ratio*
POEM	*Patient Oriented Eczema Measure*
PROMIS	*Patient-Reported Outcomes Measurement Information System*
PT	Bevorzugter Begriff *(Preferred Term)*
RCT	Randomisierte kontrollierte Studie *(Randomized Controlled Trial)*
RD	*Risk Difference*
RR	*Risk Ratio*
SCORAD	*SCORing Atopic Dermatitis*
SCS	Systemische Kortikosteroide
SMQs	*Standardised MedDRA Query*
SOC	System-Organ-Klasse *(System Organ Class)*
SUE	Schwerwiegendes UE
TCI	Topische Calcineurin-Inhibitoren
TCS	Topische Kortikosteroide
UE	Unerwünschtes Ereignis

4 Ergänzende Informationen zu den Studien ADvocate 1, ADvocate 2 und ADhere

4.1 Hintergrund

Auf den nachfolgenden Seiten finden sich die Plots für die kontinuierlichen Endpunkte der Studien ADvocate 1, ADvocate 2 und ADhere, sowie alle Subgruppenanalysen für die Hauptanalysen der patientenrelevanten Endpunkte (inklusive Forest-Plots) für die Meta-Analyse. Zudem werden jegliche UE anhand von SOC und PT auf Studienebene und Subgruppenebene für die Meta-Analyse dargestellt.

Alle Analysen werden als Ausgabe der Statistik-Software dargestellt.

4.2 Plots der kontinuierlichen Endpunkte

4.2.1 ADvocate 1

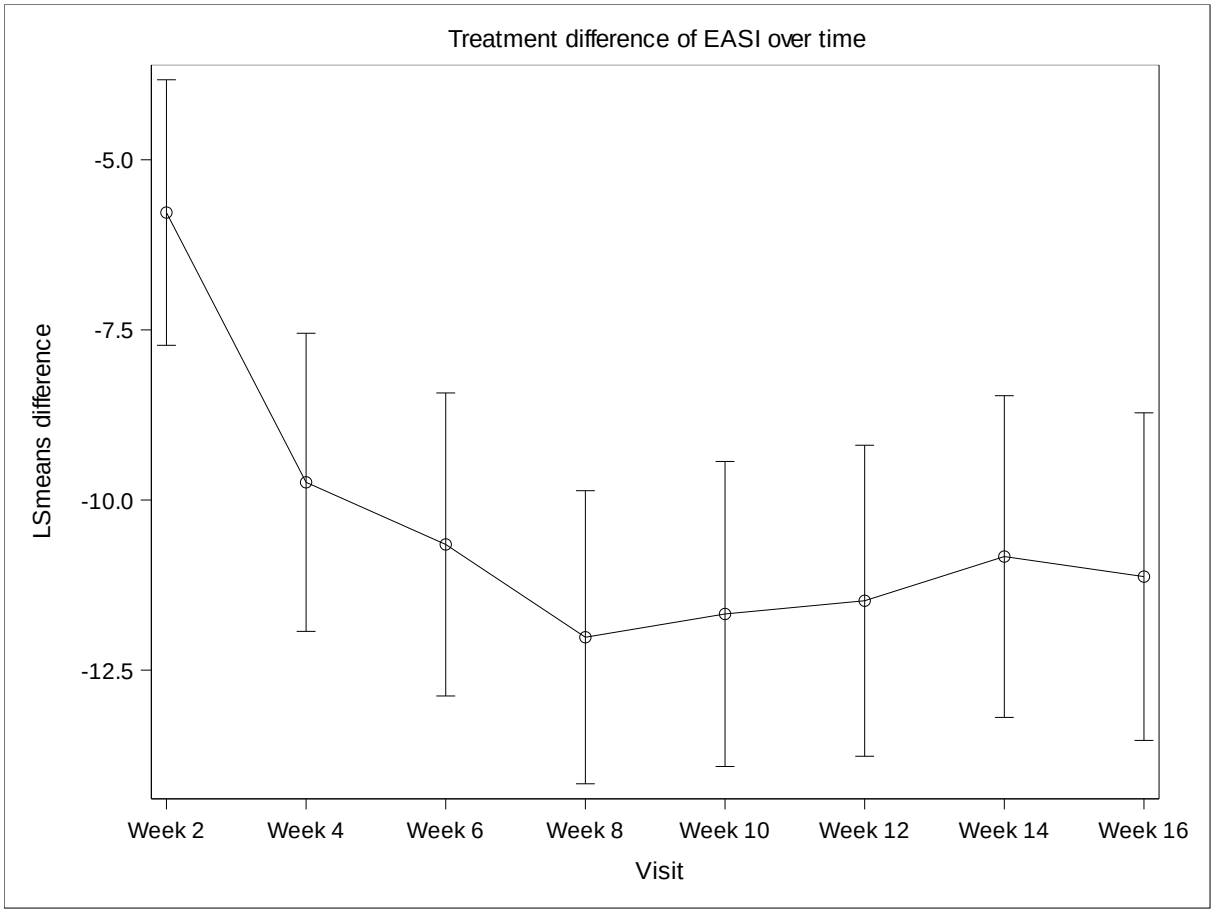

Abbildung 4-1: Veränderung des EASI bis Woche 16 in der Studie ADvocate 1

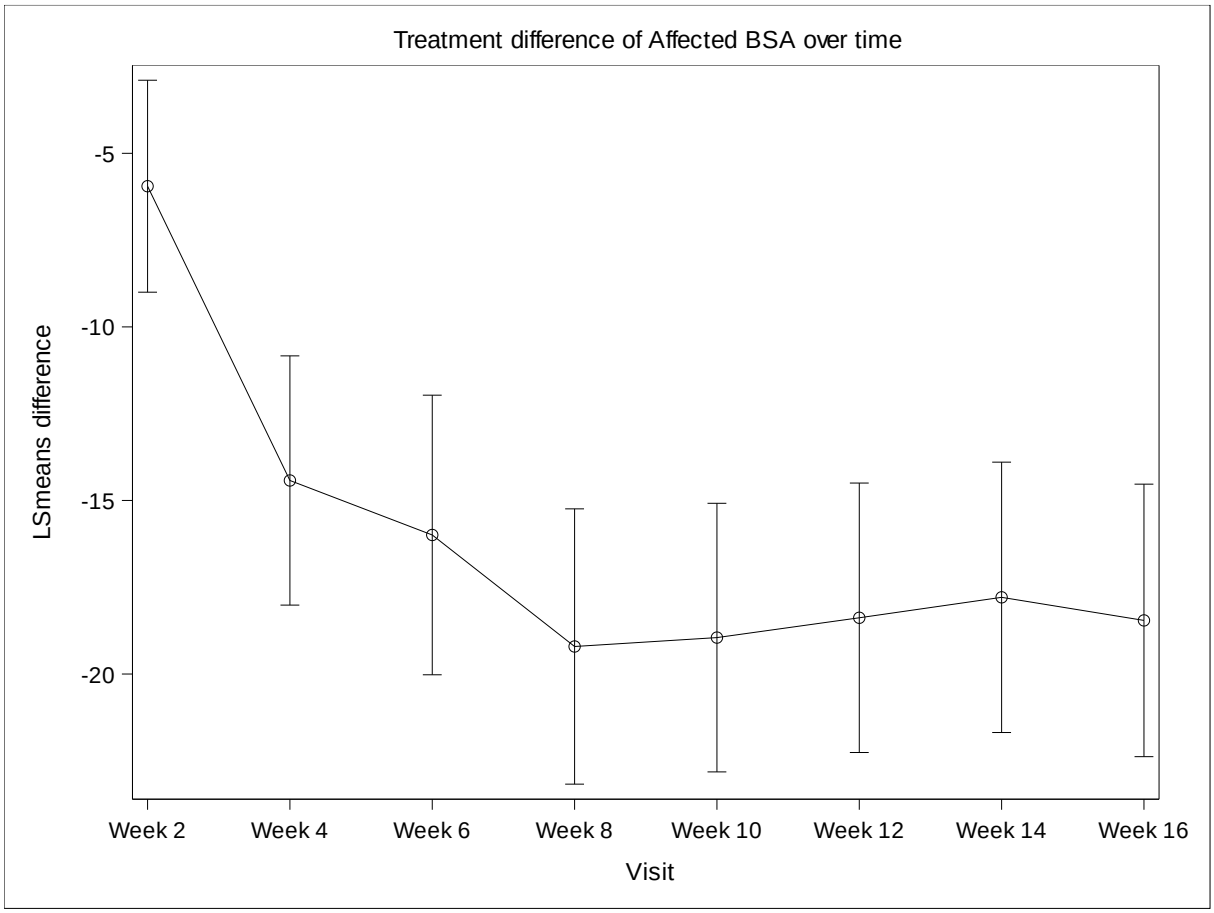

Abbildung 4-2: Veränderung des EASI-BSA bis Woche 16 in der Studie ADvocate 1

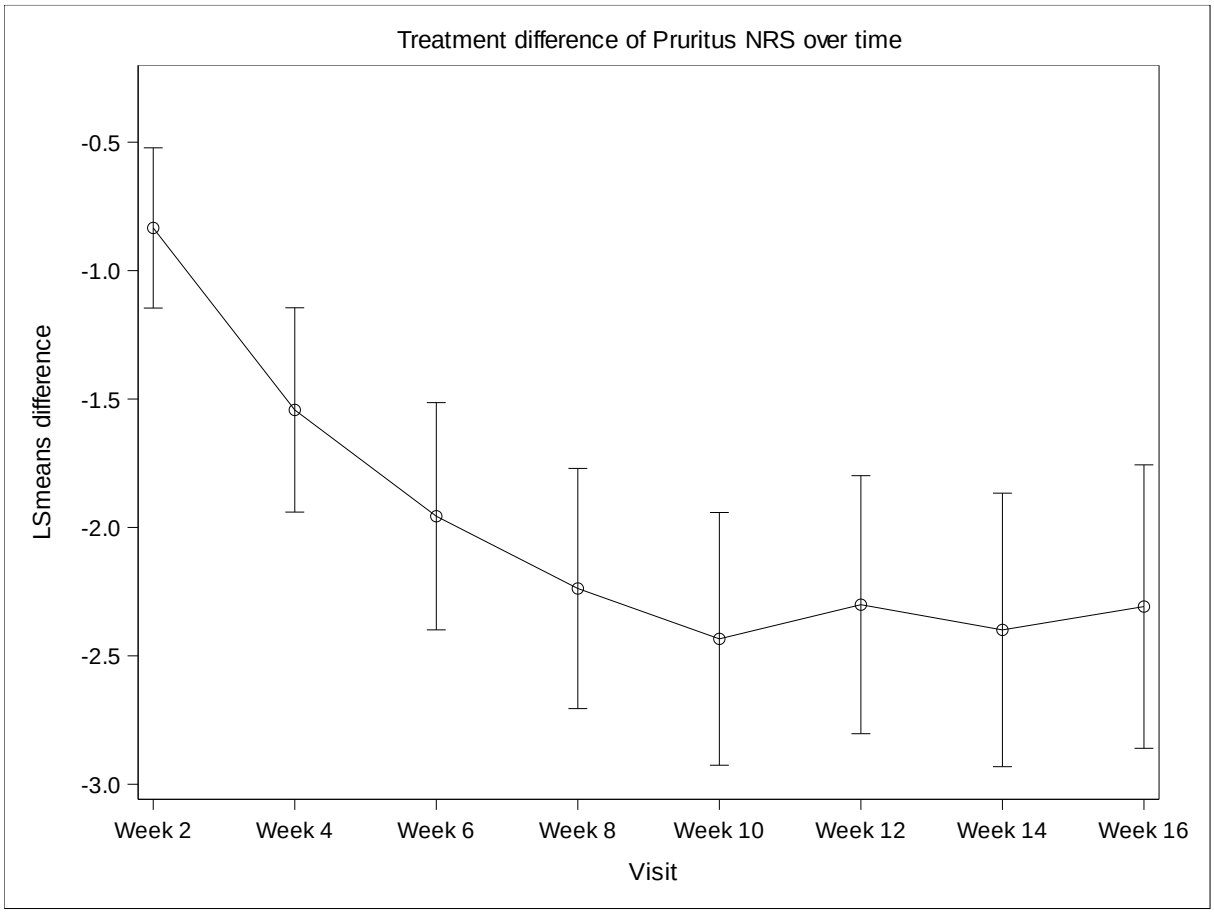

Abbildung 4-3: Veränderung des Pruritus-NRS bis Woche 16 in der Studie ADvocate 1

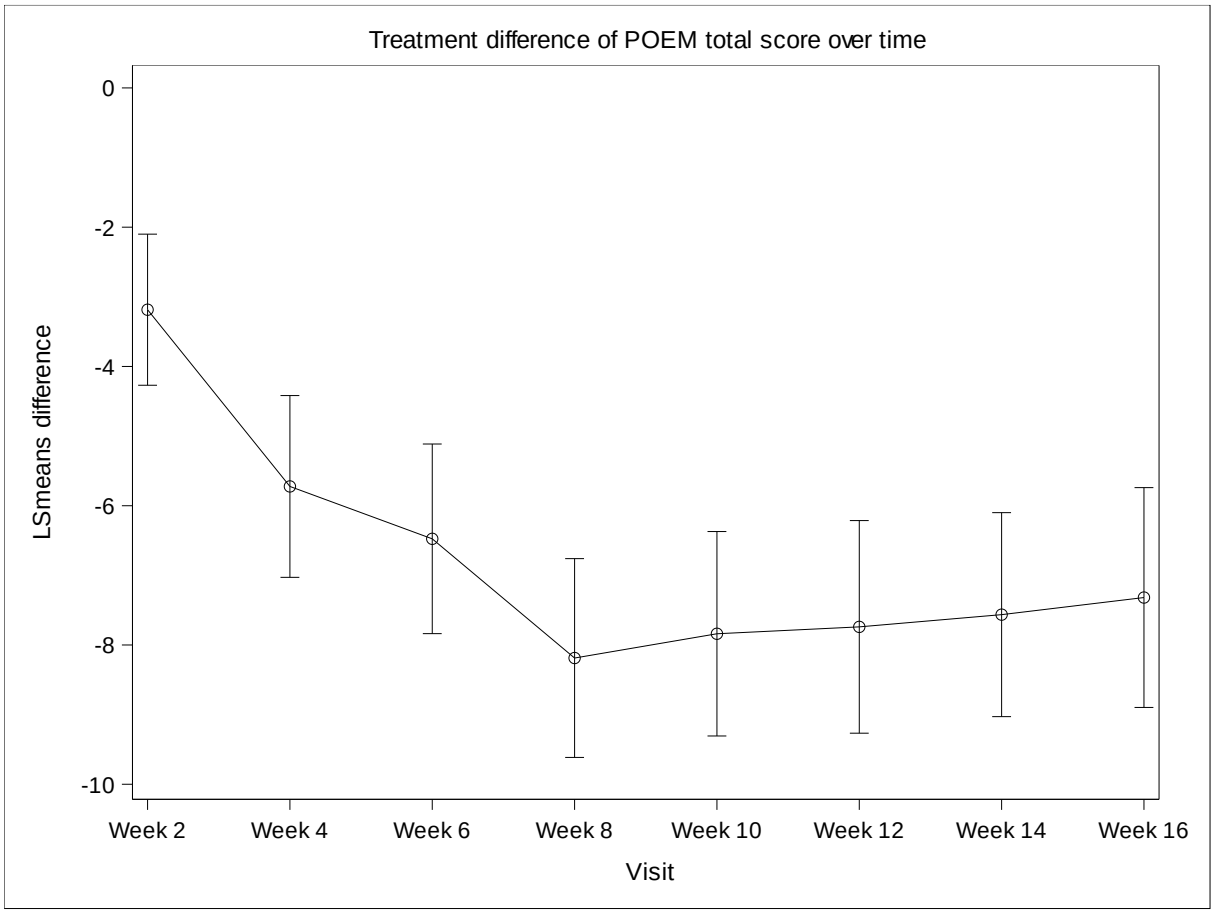

Abbildung 4-4: Veränderung des POEM bis Woche 16 in der Studie ADvocate 1

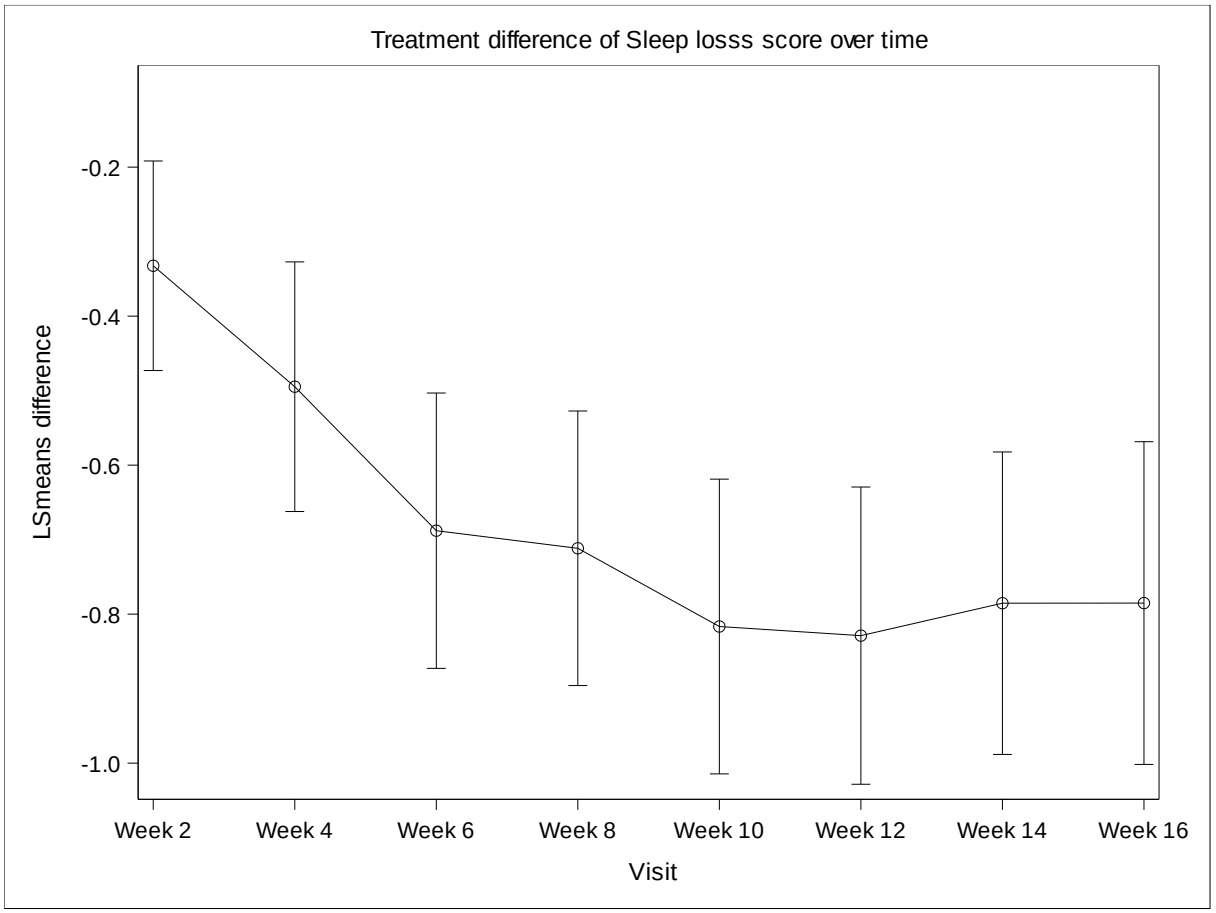

Abbildung 4-5: Veränderung des Sleep-Loss bis Woche 16 in der Studie ADvocate 1

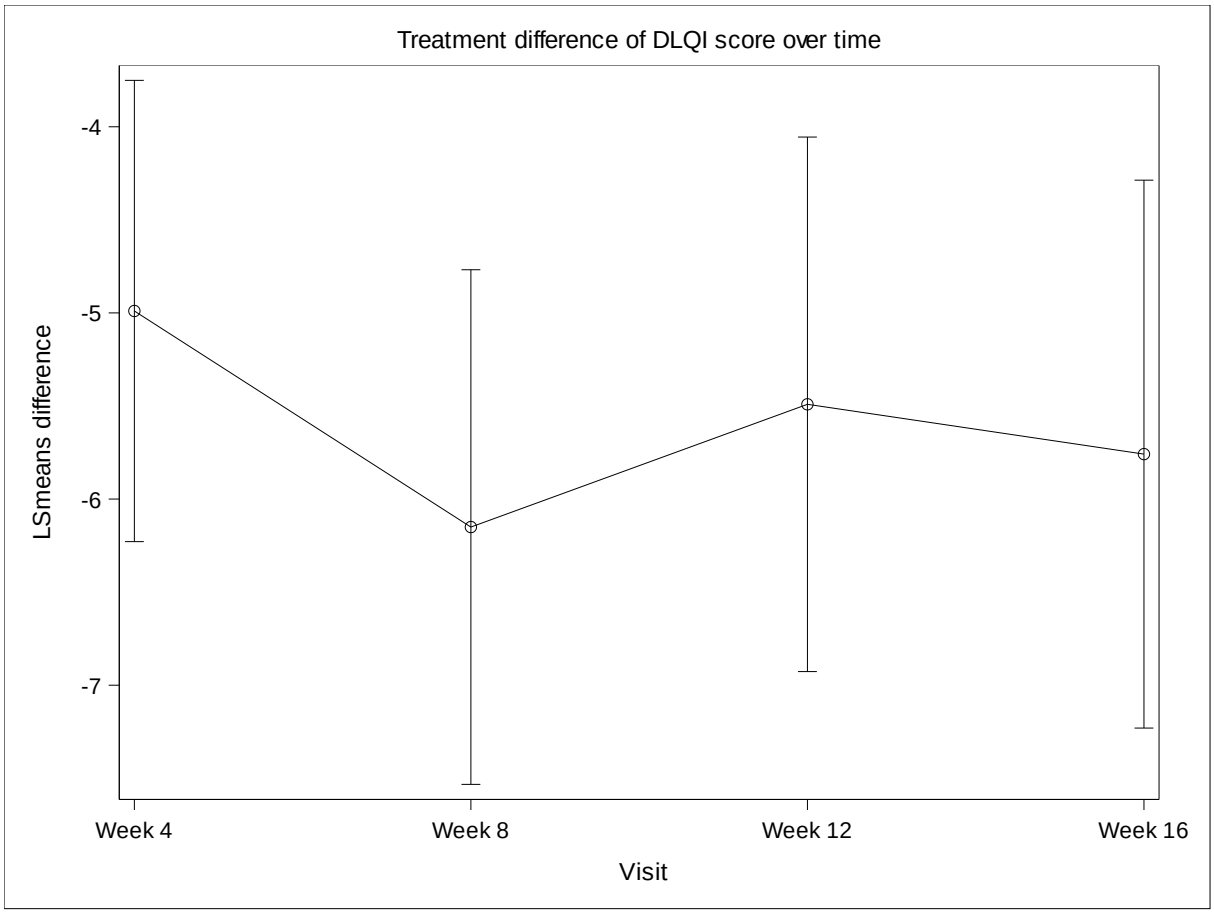

Abbildung 4-6: Veränderung des DLQI bis Woche 16 in der Studie ADvocate 1

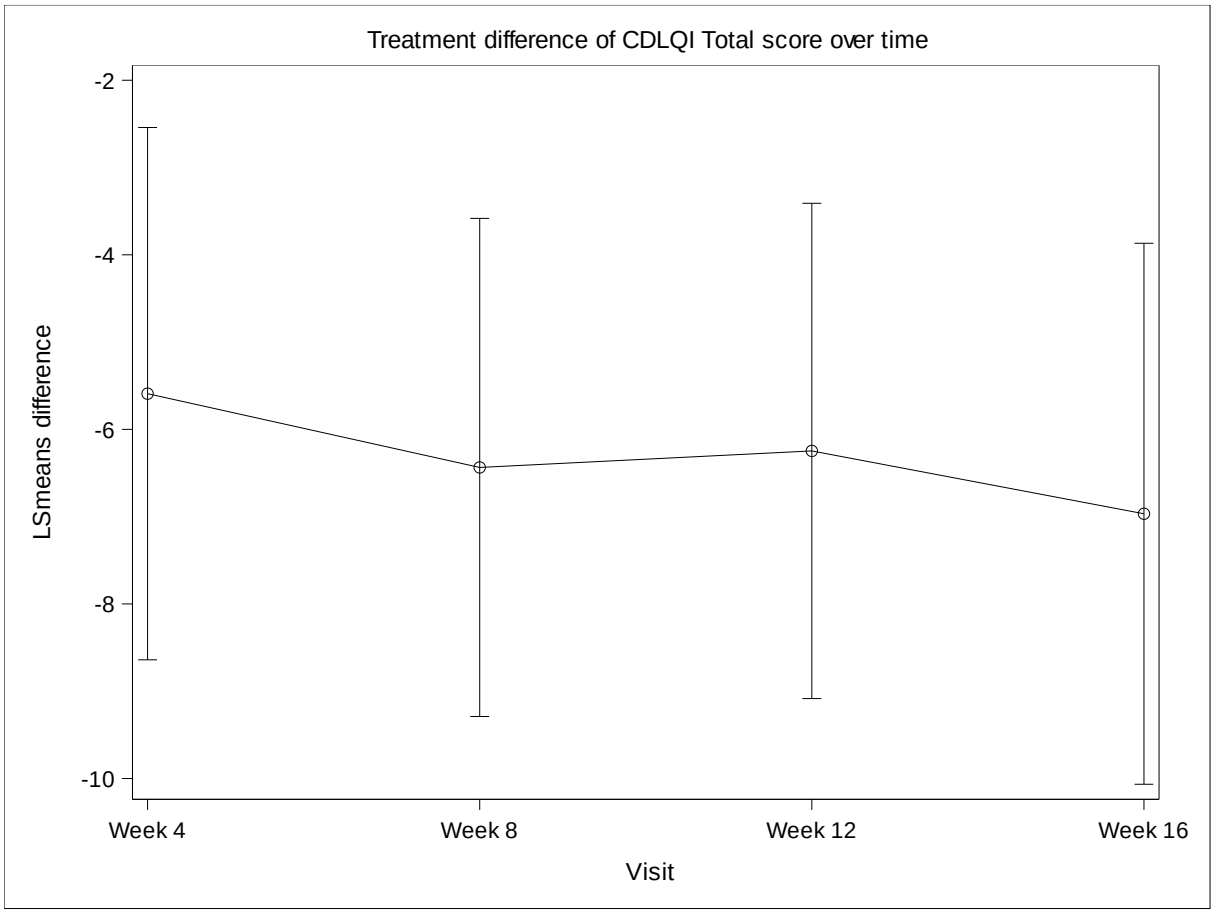

Abbildung 4-7: Veränderung des CDLQI bis Woche 16 in der Studie ADvocate 1

4.2.2 ADvocate 2

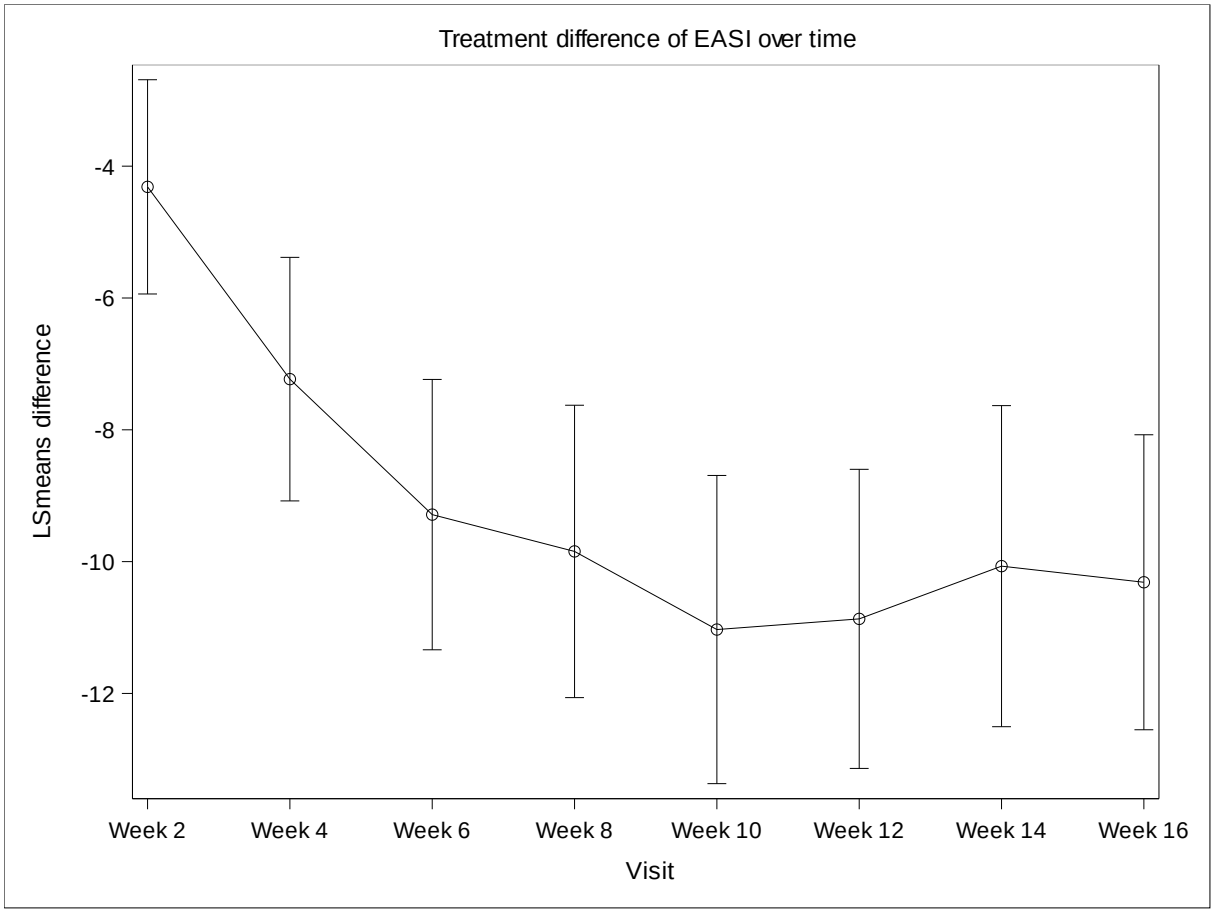

Abbildung 4-8: Veränderung des EASI bis Woche 16 in der Studie ADvocate 2

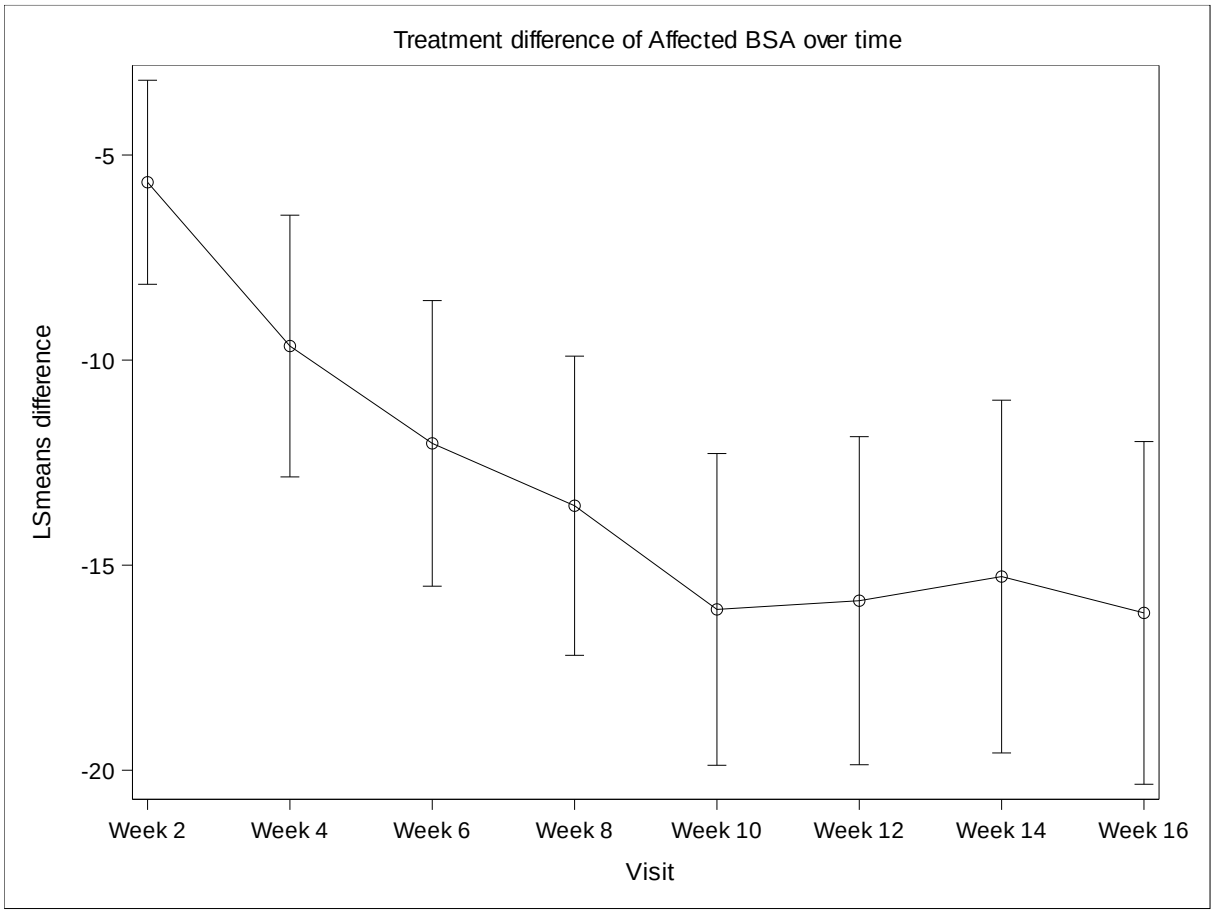

Abbildung 4-9: Veränderung des EASI-BSA bis Woche 16 in der Studie ADvocate 2

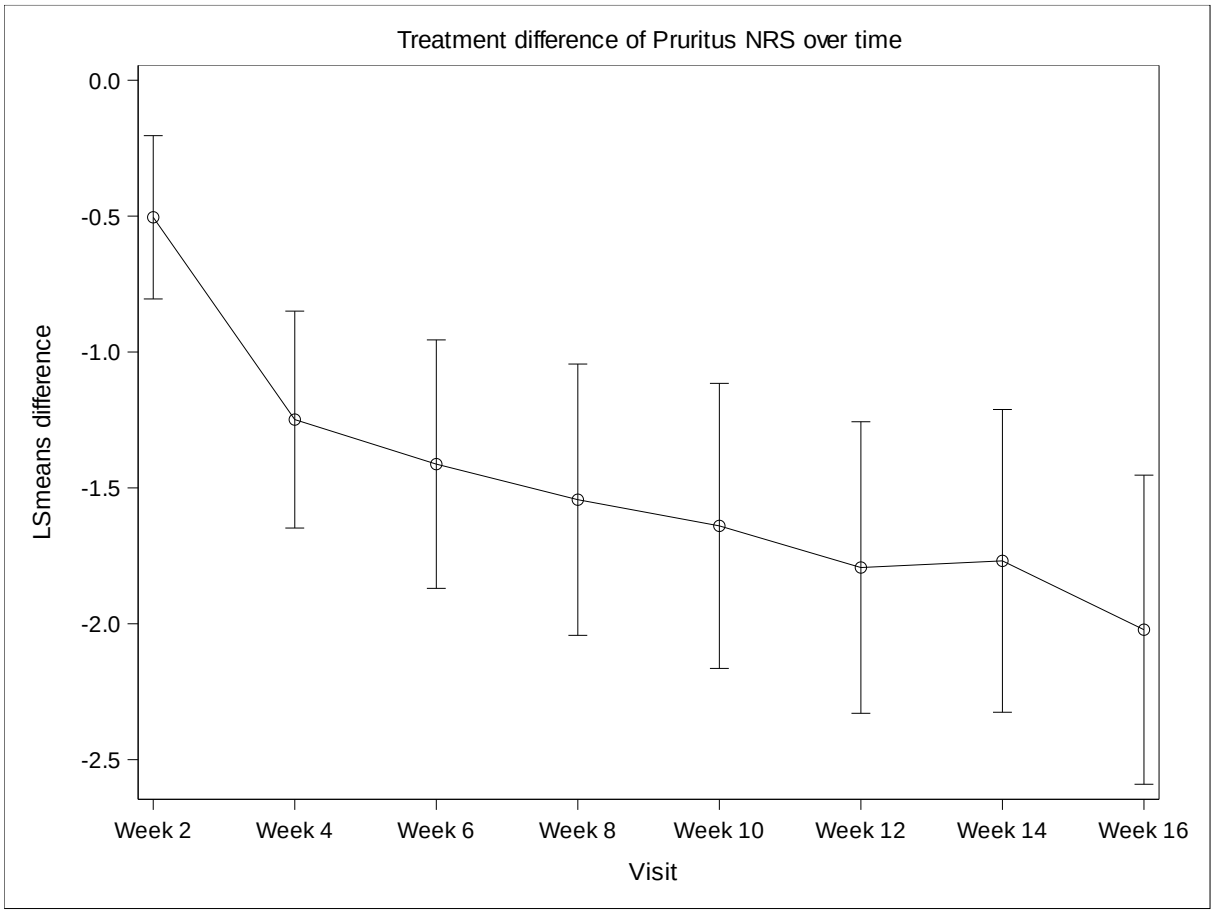

Abbildung 4-10: Veränderung des Pruritus-NRS bis Woche 16 in der Studie ADvocate 2

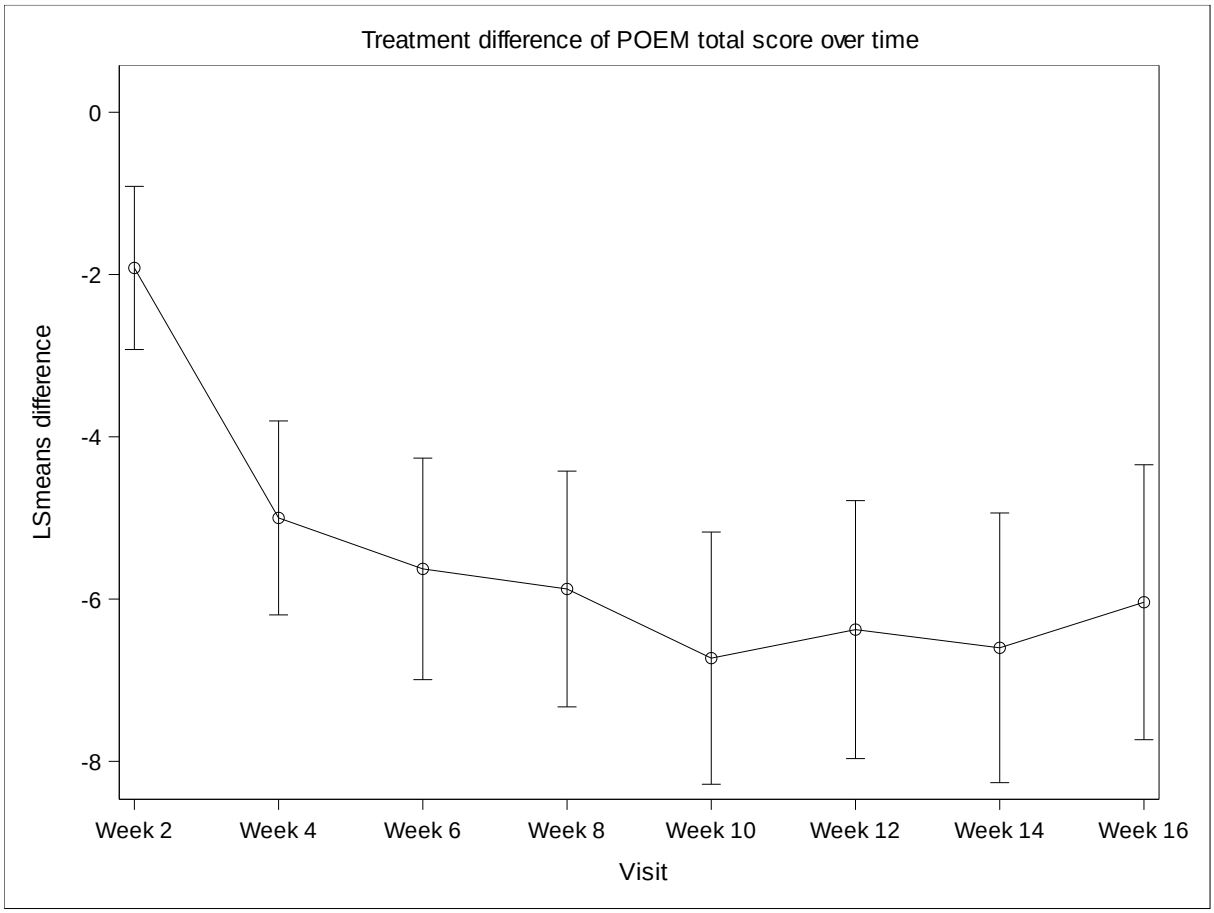

Abbildung 4-11: Veränderung des POEM bis Woche 16 in der Studie ADvocate 2

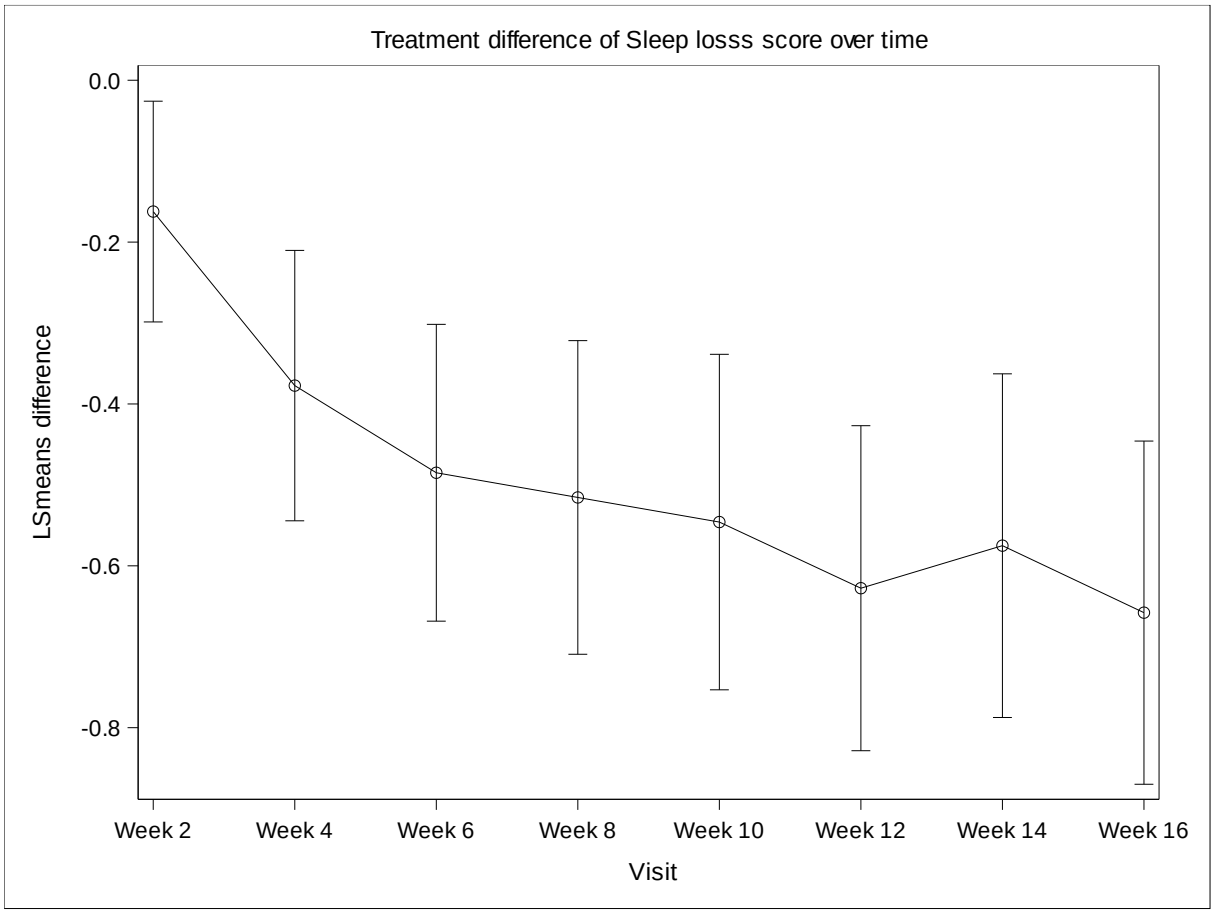

Abbildung 4-12: Veränderung des Sleep-Loss-Scores bis Woche 16 in der Studie ADvocate 2

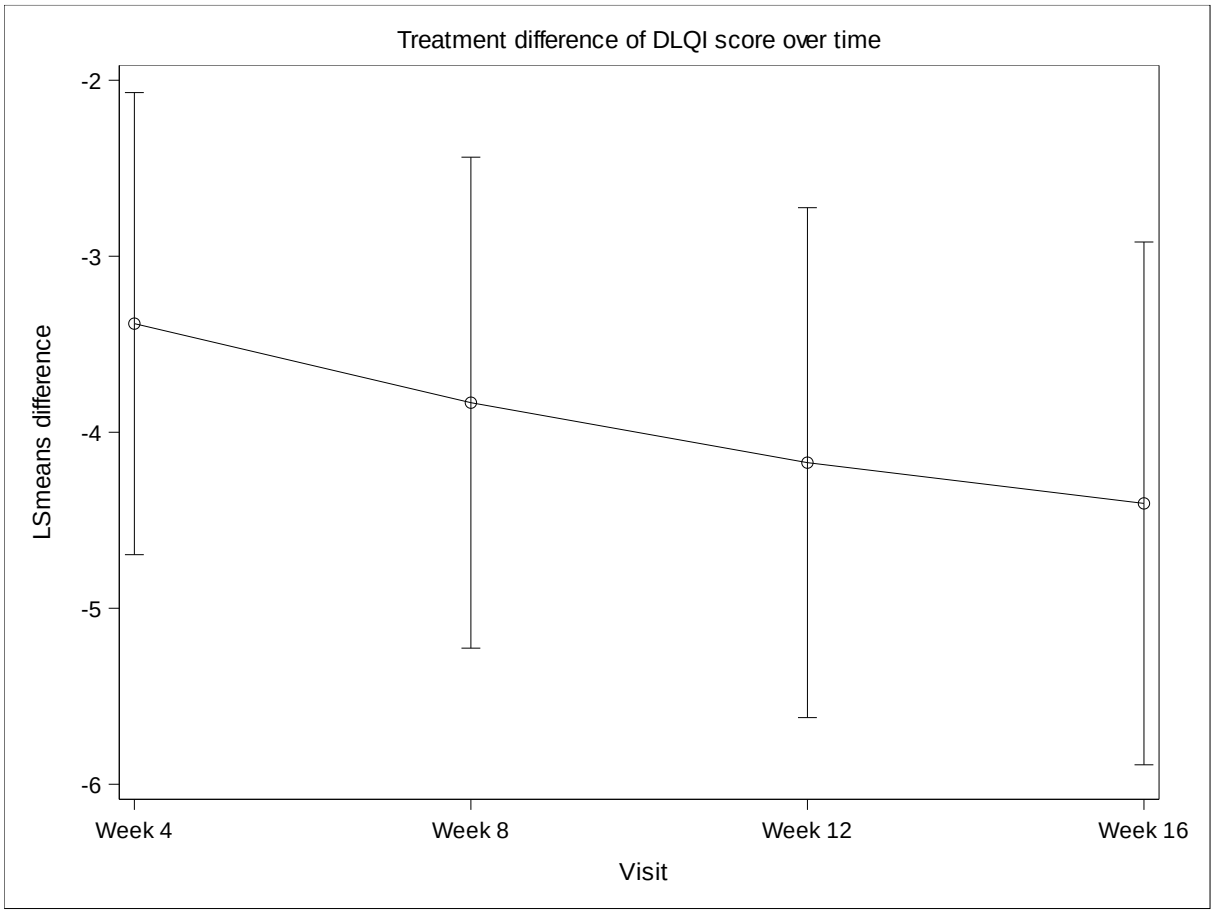

Abbildung 4-13: Veränderung des DLQI bis Woche 16 in der Studie ADvocate 2

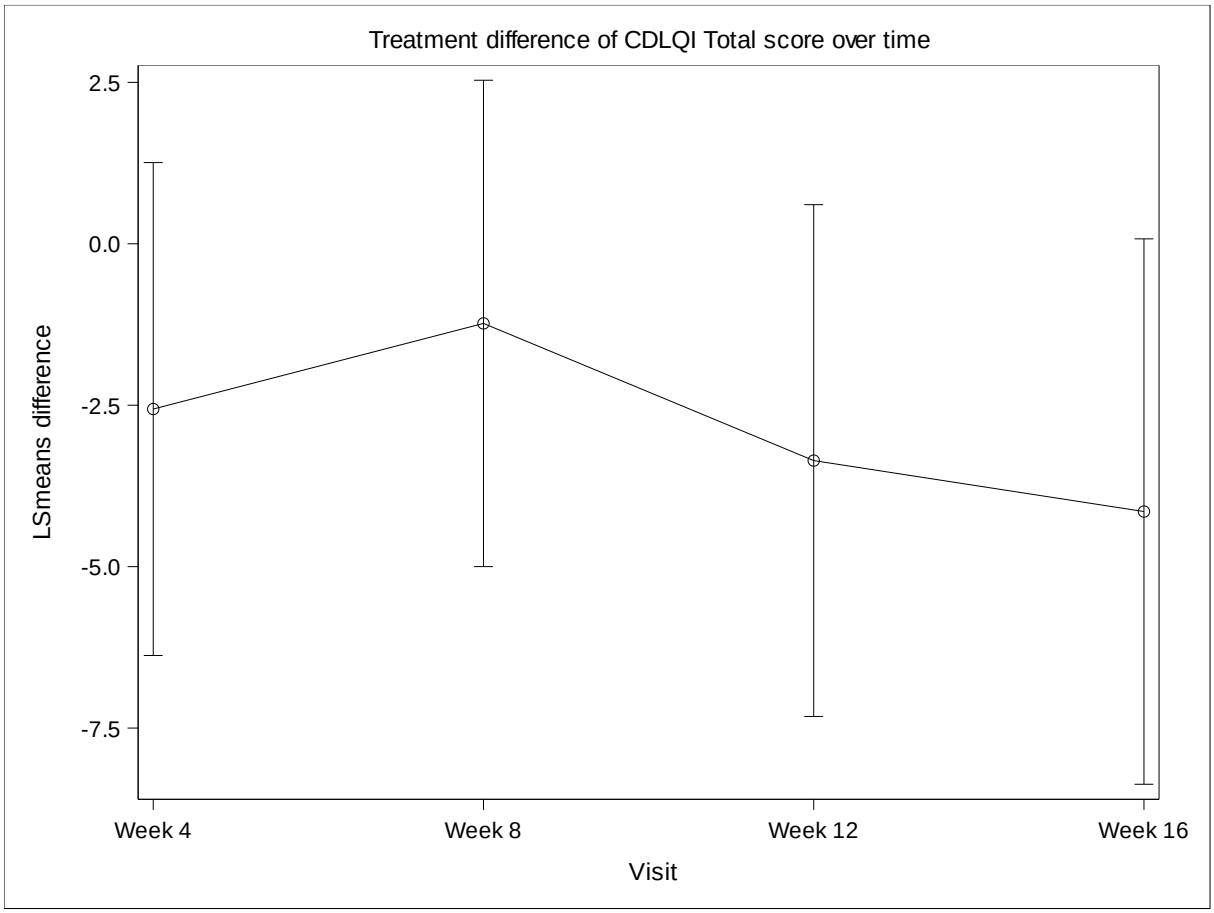

Abbildung 4-14: Veränderung des CDLQI bis Woche 16 in der Studie ADvocate 2

4.2.3 ADhere

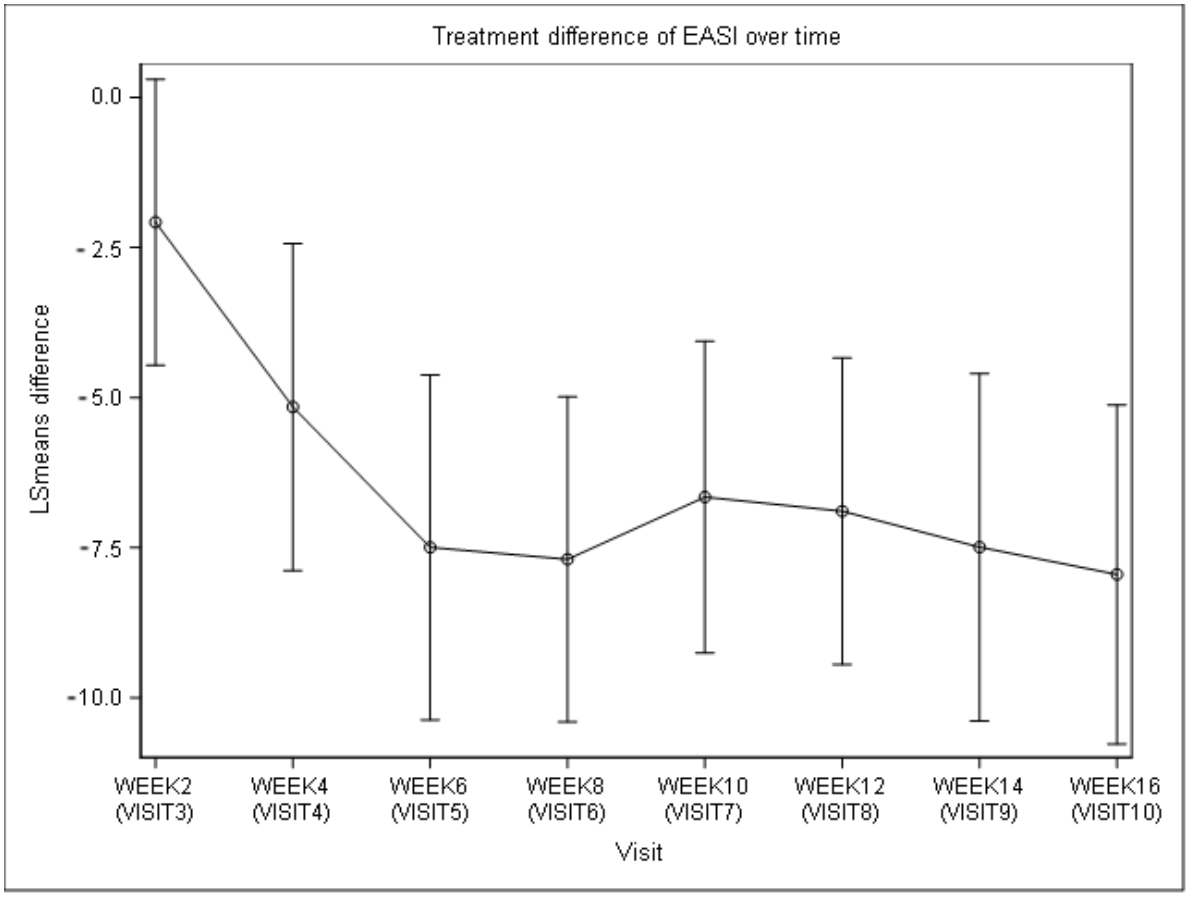

Abbildung 4-15: Veränderung des EASI bis Woche 16 in der Studie ADhere

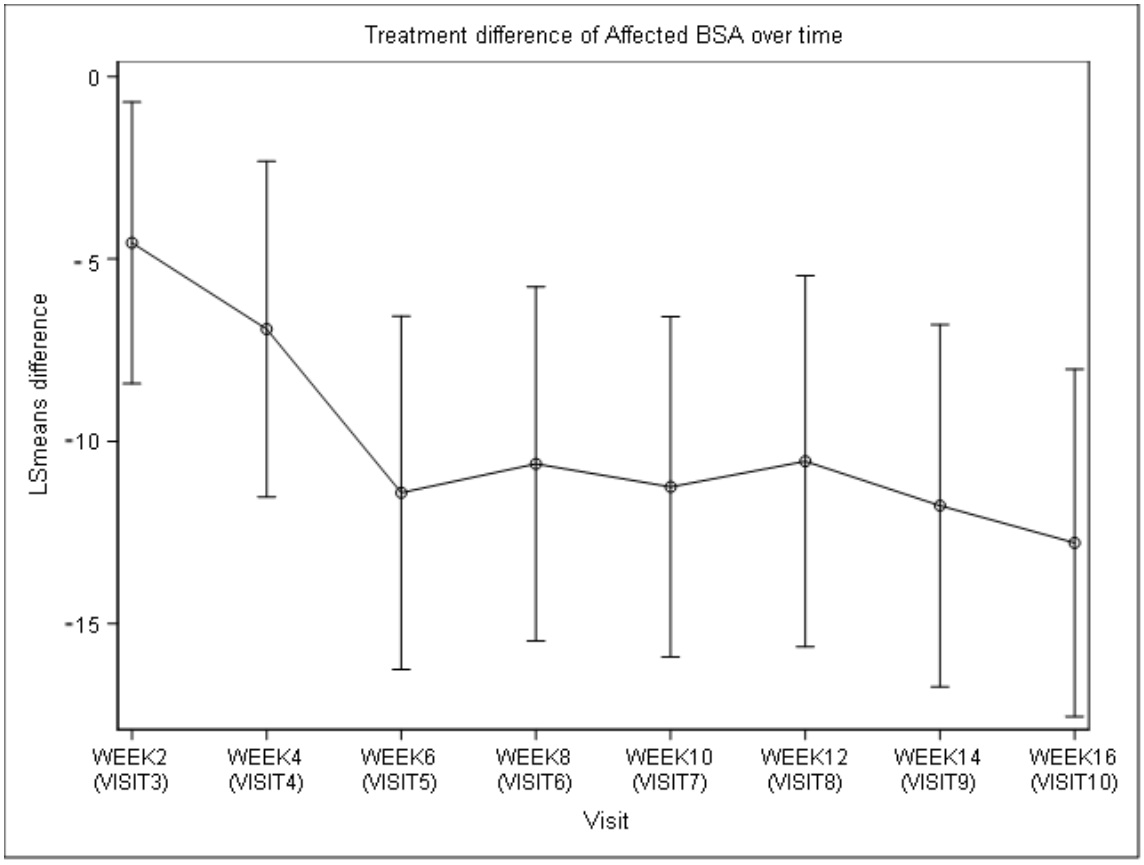

Abbildung 4-16: Veränderung des EASI-BSA bis Woche 16 in der Studie ADhere

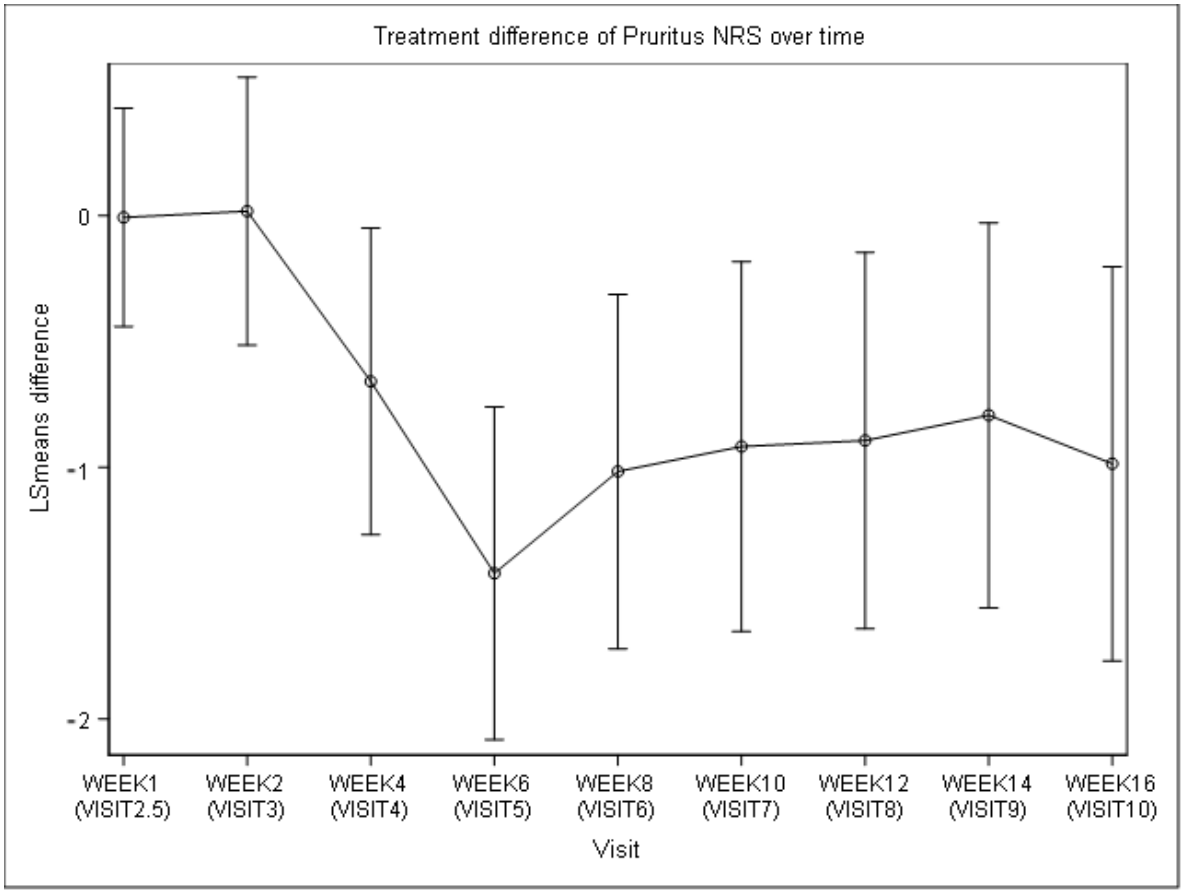

Abbildung 4-17: Veränderung des Pruritus-NRS bis Woche 16 in der Studie ADhere

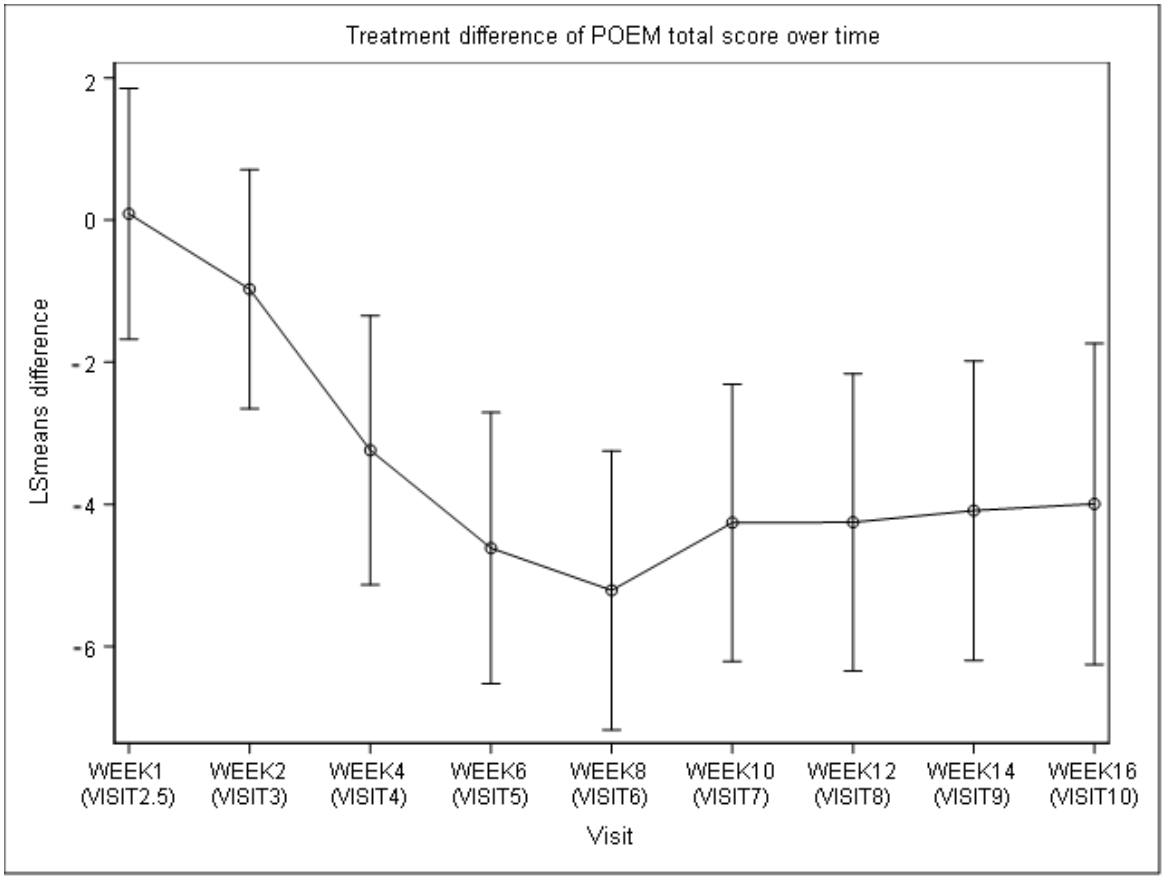

Abbildung 4-18: Veränderung des POEM bis Woche 16 in der Studie ADhere

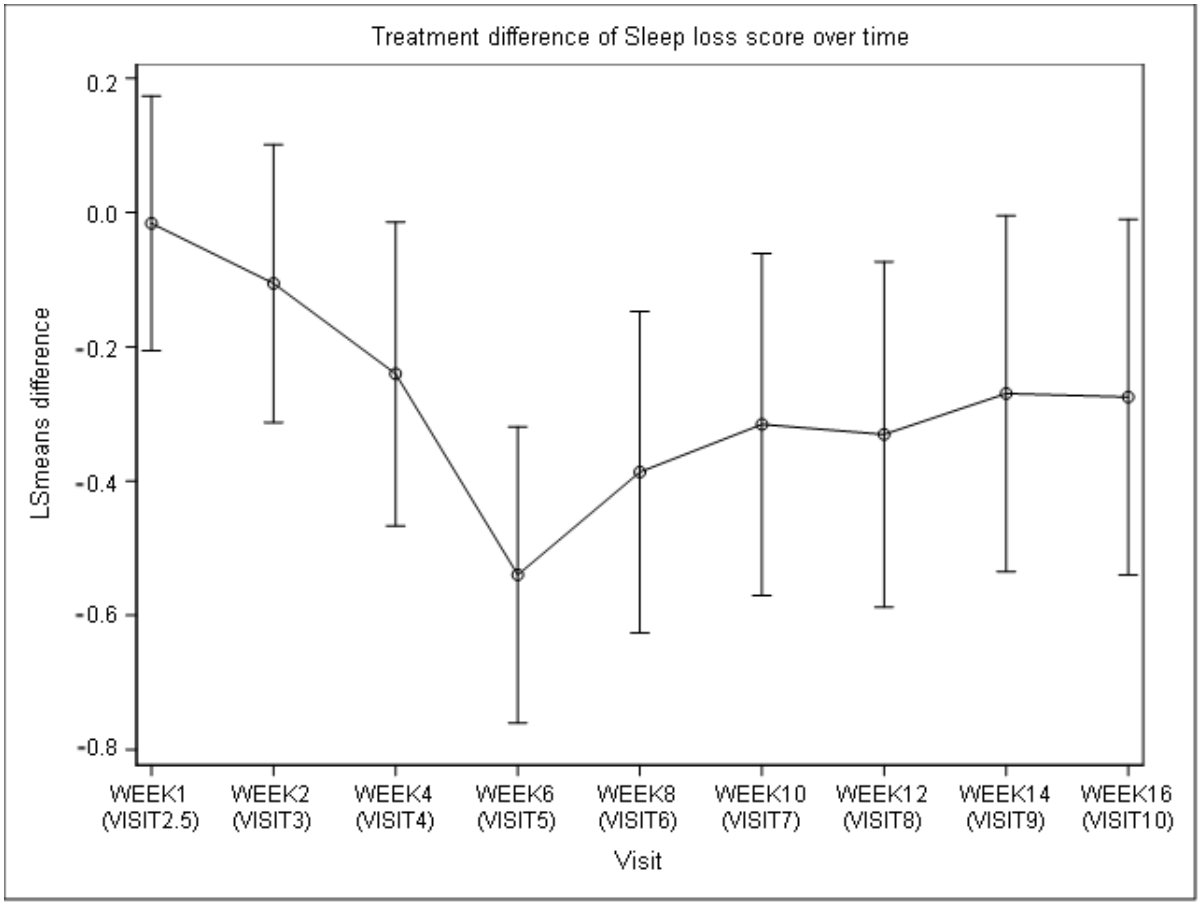

Abbildung 4-19: Veränderung des Sleep-Loss-Scores bis Woche 16 in der Studie ADhere

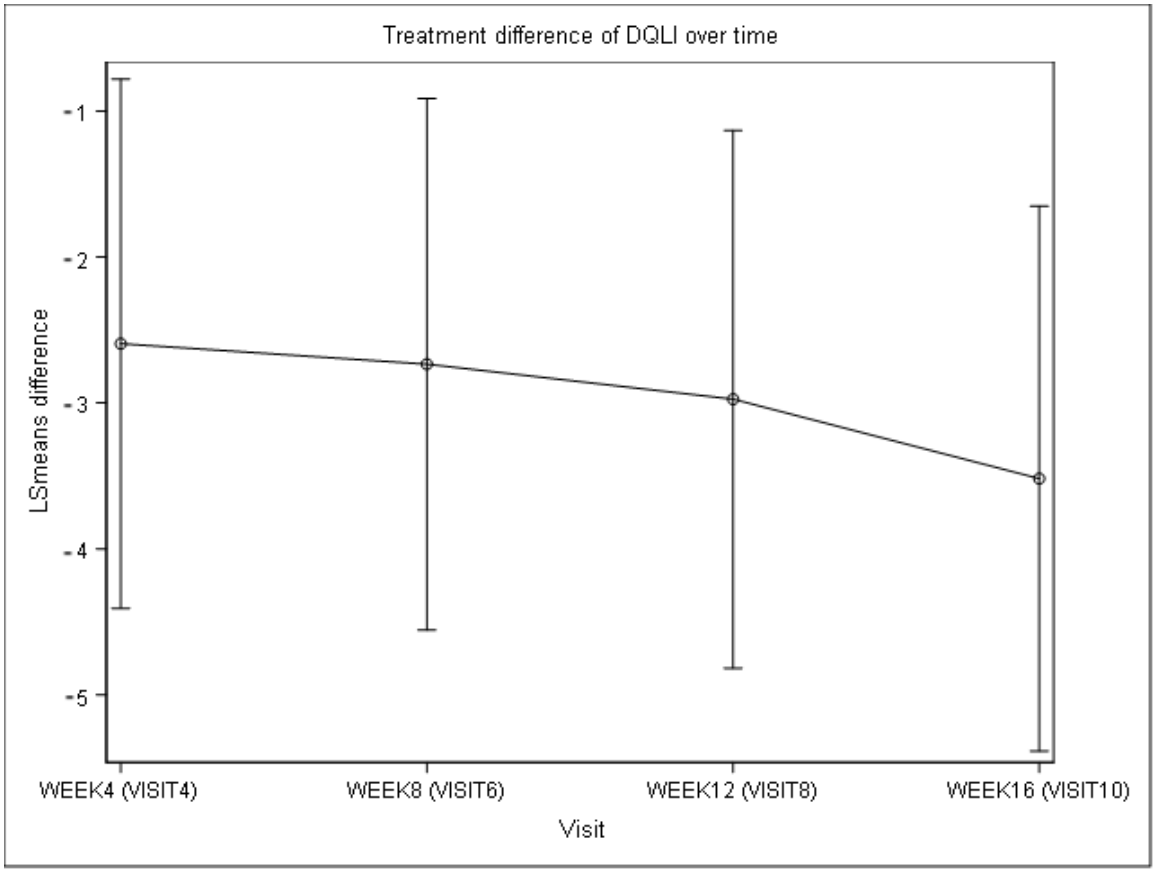

Abbildung 4-20: Veränderung des DLQI bis Woche 16 in der Studie ADhere

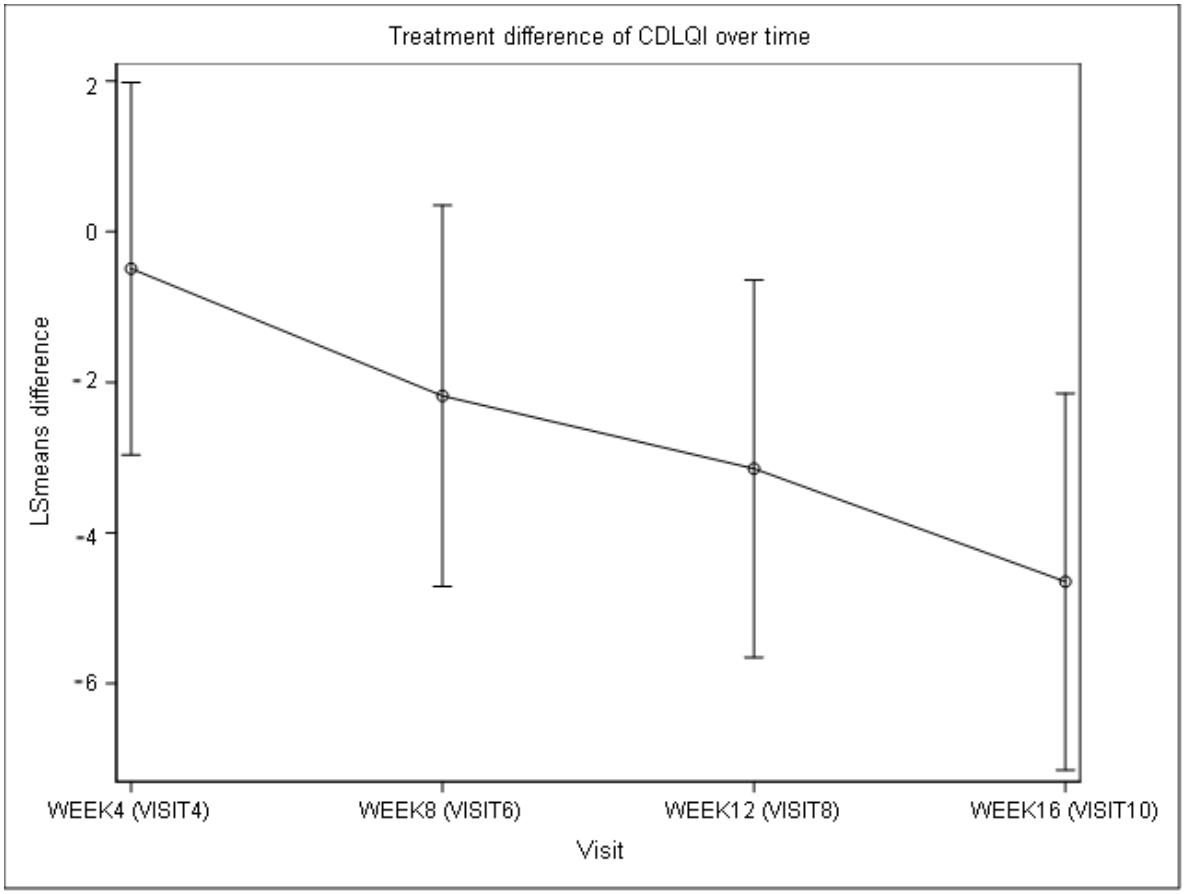

Abbildung 4-21: Veränderung des CDLQI bis Woche 16 in der Studie ADhere

4.3 UESI

4.3.1 ADvocate 1

ADvocate 1. Safety analysis, patients with at least one Severe AE without PT of Pruritus and Dermatitis Atopic, up to Week 16 (mSAFETY)

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		4 (2.84%)	5 (1.77%)
Number of patients with no event, n(%)		137 (97.16%)	277 (98.23%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.618 (0.131 , 3.171)
	Relative Risk (95% CI) [3]		0.830 (0.461 , 1.495)
	Relative Risk (95% CI) [4]		0.830 (0.152 , 1.284)
	Common Risk Difference (95% CI) [3]		-1.064 (-4.207 , 2.080)
	Fisher's Exact test p-value		0.488987

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.

ADvocate 1. Safety analysis, patients with at least one Serious Adverse Event (SAE), up to Week 16 (mSAFETY)

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		1 (0.71%)	6 (2.13%)
Number of patients with no event, n(%)		140 (99.29%)	276 (97.87%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		3.043 (0.363 , 140.98)
	Relative Risk (95% CI) [3]		1.292 (0.947 , 1.762)
	Relative Risk (95% CI) [4]		1.292 (0.294 , 1.543)
	Common Risk Difference (95% CI) [3]		1.418 (-0.762 , 3.599)
	Fisher's Exact test p-value		0.432639

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster, up to Week 16 (mSAFETY)

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		6 (4.26%)	9 (3.19%)
Number of patients with no event, n(%)		135 (95.74%)	273 (96.81%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.742 (0.230 , 2.589)
	Relative Risk (95% CI) [3]		0.897 (0.590 , 1.363)
	Relative Risk (95% CI) [4]		0.897 (0.281 , 1.251)
	Common Risk Difference (95% CI) [3]		-1.064 (-4.976 , 2.849)
	Fisher's Exact test p-value		0.584874

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis, up to Week 16 (mSAFETY)

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		5 (3.55%)	28 (9.93%)
Number of patients with no event, n(%)		136 (96.45%)	254 (90.07%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		2.998 (1.106 , 10.151)
	Relative Risk (95% CI) [3]		1.303 (1.109 , 1.531)
	Relative Risk (95% CI) [4]		1.303 (0.805 , 1.492)
	Common Risk Difference (95% CI) [3]		6.383 (1.746 , 11.020)
	Fisher's Exact test p-value		0.020950

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - parasitic infection or an infection related to an intracellular pathogen, up to Week 16 (mSAFETY)

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		1 (0.71%)	1 (0.35%)
Number of patients with no event, n(%)		140 (99.29%)	281 (99.65%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.498 (0.006 , 39.385)
	Relative Risk (95% CI) [3]		0.749 (0.187 , 3.000)
	Relative Risk (95% CI) [4]		0.749 (0.021 , 1.468)
	Common Risk Difference (95% CI) [3]		-0.355 (-1.904 , 1.195)
	Fisher's Exact test p-value		1.000000

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.

4.3.2 ADvocate 2

ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics, up to Week 16 (mSAFETY)

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		82 (56.55%)	139 (49.47%)
Number of patients with no event, n(%)		63 (43.45%)	142 (50.53%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.752 (0.492 , 1.148)
	Relative Risk (95% CI) [3]		0.908 (0.792 , 1.041)
	Relative Risk (95% CI) [4]		0.908 (0.790 , 1.042)
	Common Risk Difference (95% CI) [3]		-7.086 (-17.05 , 2.878)
	Fisher's Exact test p-value		0.183824

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.

ADvocate 2. Safety analysis, patients with at least one Severe AE, up to Week 16 (mSAFETY)

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		7 (4.83%)	7 (2.49%)
Number of patients with no event, n(%)		138 (95.17%)	274 (97.51%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.504 (0.148 , 1.722)
	Relative Risk (95% CI) [3]		0.752 (0.443 , 1.275)
	Relative Risk (95% CI) [4]		0.752 (0.185 , 1.167)
	Common Risk Difference (95% CI) [3]		-2.336 (-6.273 , 1.600)
	Fisher's Exact test p-value		0.251659

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.

ADvocate 2. Safety analysis, patients with at least one Severe AE without PT of Pruritus and Dermatitis Atopic, up to Week 16 (mSAFETY)

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		5 (3.45%)	6 (2.14%)
Number of patients with no event, n(%)		140 (96.55%)	275 (97.86%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.611 (0.153 , 2.580)
	Relative Risk (95% CI) [3]		0.823 (0.478 , 1.418)
	Relative Risk (95% CI) [4]		0.823 (0.168 , 1.255)
	Common Risk Difference (95% CI) [3]		-1.313 (-4.730 , 2.104)
	Fisher's Exact test p-value		0.520872

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.

ADvocate 2. Safety analysis, patients with at least one Serious Adverse Event (SAE), up to Week 16 (mSAFETY)

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		4 (2.76%)	2 (0.71%)
Number of patients with no event, n(%)		141 (97.24%)	279 (99.29%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.253 (0.023 , 1.793)
	Relative Risk (95% CI) [3]		0.502 (0.162 , 1.559)
	Relative Risk (95% CI) [4]		0.502 (0.031 , 1.192)
	Common Risk Difference (95% CI) [3]		-2.047 (-4.888 , 0.794)
	Fisher's Exact test p-value		0.186534

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster, up to Week 16 (mSAFETY)

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		7 (4.83%)	9 (3.20%)
Number of patients with no event, n(%)		138 (95.17%)	272 (96.80%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.652 (0.211 , 2.110)
	Relative Risk (95% CI) [3]		0.848 (0.547 , 1.313)
	Relative Risk (95% CI) [4]		0.848 (0.260 , 1.216)
	Common Risk Difference (95% CI) [3]		-1.625 (-5.676 , 2.426)
	Fisher's Exact test p-value		0.426707

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis, up to Week 16 (mSAFETY)

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		5 (3.45%)	31 (11.03%)
Number of patients with no event, n(%)		140 (96.55%)	250 (88.97%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		3.472 (1.295 , 11.670)
	Relative Risk (95% CI) [3]		1.343 (1.155 , 1.562)
	Relative Risk (95% CI) [4]		1.343 (0.878 , 1.528)
	Common Risk Difference (95% CI) [3]		7.584 (2.868 , 12.299)
	Fisher's Exact test p-value		0.009089

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - parasitic infection or an infection related to an intracellular pathogen, up to Week 16 (mSAFETY)

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		1 (0.69%)	4 (1.42%)
Number of patients with no event, n(%)		144 (99.31%)	277 (98.58%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		2.079 (0.203 , 103.11)
	Relative Risk (95% CI) [3]		1.216 (0.780 , 1.895)
	Relative Risk (95% CI) [4]		1.216 (0.171 , 1.539)
	Common Risk Difference (95% CI) [3]		0.734 (-1.198 , 2.666)
	Fisher's Exact test p-value		0.665511

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.

4.3.3 ADhere

ADhere. Safety analysis, patients with at least one Severe AE without PT of Pruritus and Dermatitis Atopic, up to Week 16 (mSAFETY)

		PBO N=75	LEB250Q2W N=153
Number of patients with >=1 event [1], n(%)		1 (1.33%)	3 (1.96%)
Number of patients with no event, n(%)		74 (98.67%)	150 (98.04%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.480 (0.151 , 14.473)
	Relative Risk (95% CI) [3]		1.471 (0.156 , 13.900)
	Relative Risk (95% CI) [4]		1.471 (0.216 , 10.201)
	Common Risk Difference (95% CI) [3]		-0.006 (-0.028 , 0.040)
	Fisher's Exact test p-value		1.000000

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.

ADhere. Safety analysis, patients with at least one Serious Adverse Event (SAE), up to Week 16 (mSAFETY)

		PBO N=75	LEB250Q2W N=153
Number of patients with >=1 event [1], n(%)		1 (1.33%)	2 (1.31%)
Number of patients with no event, n(%)		74 (98.67%)	151 (98.69%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.980 (0.087 , 10.984)
	Relative Risk (95% CI) [3]		0.980 (0.090 , 10.641)
	Relative Risk (95% CI) [4]		0.980 (0.131 , 7.437)
	Common Risk Difference (95% CI) [3]		0.000 (-0.032 , 0.031)
	Fisher's Exact test p-value		1.000000

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.

ADhere. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster, up to Week 16 (mSAFETY)

		PBO N=75	LEB250Q2W N=153
Number of patients with >=1 event [1], n(%)		1 (1.33%)	5 (3.27%)
Number of patients with no event, n(%)		74 (98.67%)	148 (96.73%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		2.500 (0.287 , 21.788)
	Relative Risk (95% CI) [3]		2.451 (0.292 , 20.608)
	Relative Risk (95% CI) [4]		2.451 (0.391 , 15.724)
	Common Risk Difference (95% CI) [3]		0.019 (-0.019 , 0.058)
	Fisher's Exact test p-value		0.666433

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.

ADhere. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis, up to Week 16 (mSAFETY)

		PBO N=75	LEB250Q2W N=153
Number of patients with >=1 event [1], n(%)		0 (0.00%)	12 (7.84%)
Number of patients with no event, n(%)		75 (100.00%)	141 (92.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		13.339 (0.779 , 228.418)
	Relative Risk (95% CI) [3]		12.296 (0.738 , 204.906)
	Relative Risk (95% CI) [4]		12.296 (1.294 , 121.213)
	Common Risk Difference (95% CI) [3]		0.078 (0.036 , 0.121)
	Fisher's Exact test p-value		0.0099247

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.

ADhere. Safety analysis, Adverse Events of Special Interest (AESIs) - parasitic infection or an infection related to an intracellular pathogen, up to Week 16 (mSAFETY)

		PBO N=75	LEB250Q2W N=153
Number of patients with >=1 event [1], n(%)		0 (0.00%)	3 (1.96%)
Number of patients with no event, n(%)		75 (100.00%)	150 (98.04%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		3.512 (0.179 , 68.864)
	Relative Risk (95% CI) [3]		3.443 (0.180 , 65.805)
	Relative Risk (95% CI) [4]		2.941 (0.330 , 36.679)
	Common Risk Difference (95% CI) [3]		0.020 (-0.002 , 0.042)
	Fisher's Exact test p-value		0.5526490

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.

4.4 Jegliche UE nach SOC und PT

4.4.1 ADvocate 1

Lebrikizumab

Any AE by SOC and PT (mSAFETY)

System Organ Class Preferred Term	Lebrikizumab N=282			Placebo N=141		
	n	(%)	event	n	(%)	event
OVERALL	130	(46.1)	237	74	(52.5)	158
Blood and lymphatic system disorders	6	(2.1)	7	2	(1.4)	2
Anaemia	1	(0.4)	1	0	(0.0)	0
Eosinophilia	1	(0.4)	1	2	(1.4)	2
Erythropenia	1	(0.4)	1	0	(0.0)	0
Iron deficiency anaemia	1	(0.4)	1	0	(0.0)	0
Lymphopenia	1	(0.4)	1	0	(0.0)	0
Thrombocytopenia	2	(0.7)	2	0	(0.0)	0
Cardiac disorders	2	(0.7)	2	1	(0.7)	1
Angina pectoris	1	(0.4)	1	0	(0.0)	0
Myocardial infarction	1	(0.4)	1	0	(0.0)	0
Palpitations	0	(0.0)	0	1	(0.7)	1
Endocrine disorders	0	(0.0)	0	1	(0.7)	1
Hyperparathyroidism secondary	0	(0.0)	0	1	(0.7)	1

System Organ Class Preferred Term	Lebrikizumab N=282			Placebo N=141		
	n	(%)	event	n	(%)	event
Eye disorders	19	(6.7)	22	6	(4.3)	6
Anisocoria	1	(0.4)	1	0	(0.0)	0
Blepharitis	3	(1.1)	3	0	(0.0)	0
Chalazion	2	(0.7)	2	0	(0.0)	0
Conjunctival hyperaemia	1	(0.4)	1	0	(0.0)	0
Conjunctivitis allergic	7	(2.5)	7	1	(0.7)	1
Dry eye	1	(0.4)	1	2	(1.4)	2
Eye irritation	2	(0.7)	2	0	(0.0)	0
Eye pruritus	1	(0.4)	1	0	(0.0)	0
Eyelids pruritus	1	(0.4)	1	0	(0.0)	0
Keratitis	0	(0.0)	0	1	(0.7)	1
Keratoconus	0	(0.0)	0	1	(0.7)	1
Vernal keratoconjunctivitis	1	(0.4)	1	0	(0.0)	0
Vision blurred	1	(0.4)	1	0	(0.0)	0
Visual impairment	1	(0.4)	1	0	(0.0)	0
Vitreous floaters	0	(0.0)	0	1	(0.7)	1
Gastrointestinal disorders	3	(1.1)	3	8	(5.7)	8
Abdominal pain	1	(0.4)	1	0	(0.0)	0
Anal haemorrhage	0	(0.0)	0	1	(0.7)	1
Gastric polyps	0	(0.0)	0	1	(0.7)	1
Gastrointestinal inflammation	0	(0.0)	0	1	(0.7)	1
Nausea	0	(0.0)	0	2	(1.4)	2
Odynophagia	0	(0.0)	0	1	(0.7)	1
Toothache	1	(0.4)	1	1	(0.7)	1
Vomiting	1	(0.4)	1	1	(0.7)	1

System Organ Class Preferred Term	Lebrikizumab N=282			Placebo N=141		
	n	(%)	event	n	(%)	event
General disorders and administration site conditions	10	(3.5)	18	5	(3.5)	12
Administration site reaction	1	(0.4)	1	0	(0.0)	0
Asthenia	1	(0.4)	2	0	(0.0)	0
Chest discomfort	0	(0.0)	0	1	(0.7)	1
Chills	0	(0.0)	0	1	(0.7)	2
Fatigue	2	(0.7)	2	1	(0.7)	1
Hyperthermia	1	(0.4)	1	0	(0.0)	0
Injection site bruising	0	(0.0)	0	1	(0.7)	2
Injection site erythema	2	(0.7)	2	0	(0.0)	0
Injection site pain	1	(0.4)	2	2	(1.4)	6
Injection site pruritus	1	(0.4)	1	0	(0.0)	0
Injection site reaction	1	(0.4)	1	0	(0.0)	0
Oedema peripheral	3	(1.1)	5	0	(0.0)	0
Pyrexia	1	(0.4)	1	0	(0.0)	0
Hepatobiliary disorders	1	(0.4)	1	0	(0.0)	0
Non-alcoholic steatohepatitis	1	(0.4)	1	0	(0.0)	0
Immune system disorders	1	(0.4)	1	1	(0.7)	1
Food allergy	0	(0.0)	0	1	(0.7)	1
Hypersensitivity	1	(0.4)	1	0	(0.0)	0
Infections and infestations	62	(22.0)	78	28	(19.9)	46
Abscess neck	0	(0.0)	0	1	(0.7)	1
Bacterial vaginosis	1	(0.4)	1	0	(0.0)	0
Bronchitis	2	(0.7)	2	0	(0.0)	0
COVID-19	5	(1.8)	5	3	(2.1)	3

System Organ Class Preferred Term	Lebrikizumab N=282			Placebo N=141		
	n	(%)	event	n	(%)	event
Cellulitis	0	(0.0)	0	1	(0.7)	2
Conjunctivitis	22	(7.8)	24	4	(2.8)	4
Ear infection	0	(0.0)	0	1	(0.7)	1
Ecthyma	0	(0.0)	0	1	(0.7)	1
Eczema herpeticum	0	(0.0)	0	1	(0.7)	1
Folliculitis	3	(1.1)	3	1	(0.7)	1
Furuncle	0	(0.0)	0	2	(1.4)	3
Gastroenteritis	2	(0.7)	3	0	(0.0)	0
Gastroenteritis viral	2	(0.7)	2	0	(0.0)	0
Helicobacter infection	1	(0.4)	1	0	(0.0)	0
Herpes zoster	1	(0.4)	1	0	(0.0)	0
Impetigo	4	(1.4)	4	2	(1.4)	2
Influenza	1	(0.4)	1	0	(0.0)	0
Lower respiratory tract infection	1	(0.4)	1	0	(0.0)	0
Nasopharyngitis	11	(3.9)	11	4	(2.8)	4
Oral herpes	9	(3.2)	9	5	(3.5)	10
Paronychia	1	(0.4)	1	0	(0.0)	0
Pharyngitis	0	(0.0)	0	1	(0.7)	1
Pneumonia aspiration	1	(0.4)	1	0	(0.0)	0
Sepsis	0	(0.0)	0	1	(0.7)	1
Skin infection	1	(0.4)	1	2	(1.4)	2
Tinea capitis	1	(0.4)	1	0	(0.0)	0
Tonsillitis	1	(0.4)	1	2	(1.4)	2
Tooth abscess	0	(0.0)	0	1	(0.7)	1
Upper respiratory tract infection	1	(0.4)	1	2	(1.4)	3
Urinary tract infection	2	(0.7)	2	1	(0.7)	1
Vaginal infection	0	(0.0)	0	1	(0.7)	1

System Organ Class Preferred Term	Lebrikizumab N=282 n	(%)	event	Placebo N=141 n	(%)	event
Viral upper respiratory tract infection	0	(0.0)	0	1	(0.7)	1
Vulvovaginal candidiasis	2	(0.7)	2	0	(0.0)	0
Injury, poisoning and procedural complications	7	(2.5)	8	3	(2.1)	3
Accidental overdose	1	(0.4)	1	0	(0.0)	0
Back injury	1	(0.4)	1	0	(0.0)	0
Contusion	0	(0.0)	0	1	(0.7)	1
Head injury	1	(0.4)	1	0	(0.0)	0
Ligament sprain	1	(0.4)	1	0	(0.0)	0
Meniscus injury	1	(0.4)	1	0	(0.0)	0
Muscle strain	1	(0.4)	1	0	(0.0)	0
Overdose	1	(0.4)	1	0	(0.0)	0
Post procedural inflammation	0	(0.0)	0	1	(0.7)	1
Sunburn	0	(0.0)	0	1	(0.7)	1
Tooth injury	1	(0.4)	1	0	(0.0)	0
Investigations	2	(0.7)	2	2	(1.4)	5
Blood lactate dehydrogenase increased	0	(0.0)	0	1	(0.7)	1
Blood pressure increased	0	(0.0)	0	1	(0.7)	1
Eosinophil count increased	0	(0.0)	0	1	(0.7)	1
Hepatic enzyme increased	1	(0.4)	1	0	(0.0)	0
Neutrophil count decreased	1	(0.4)	1	0	(0.0)	0
Neutrophil count increased	0	(0.0)	0	1	(0.7)	1
Platelet count increased	0	(0.0)	0	1	(0.7)	1
Metabolism and nutrition disorders	3	(1.1)	3	2	(1.4)	2
Decreased appetite	0	(0.0)	0	1	(0.7)	1

System Organ Class Preferred Term	Lebrikizumab N=282 n	(%)	event	Placebo N=141 n	(%)	event
Dehydration	1	(0.4)	1	0	(0.0)	0
Hyperlipidaemia	1	(0.4)	1	0	(0.0)	0
Hypokalaemia	1	(0.4)	1	0	(0.0)	0
Vitamin D deficiency	0	(0.0)	0	1	(0.7)	1
Musculoskeletal and connective tissue disorders	**12**	**(4.3)**	**12**	**3**	**(2.1)**	**4**
Arthralgia	3	(1.1)	3	0	(0.0)	0
Back pain	2	(0.7)	2	1	(0.7)	1
Bursitis	1	(0.4)	1	1	(0.7)	1
Growing pains	1	(0.4)	1	0	(0.0)	0
Muscle twitching	1	(0.4)	1	0	(0.0)	0
Musculoskeletal chest pain	1	(0.4)	1	0	(0.0)	0
Musculoskeletal stiffness	1	(0.4)	1	0	(0.0)	0
Myalgia	0	(0.0)	0	1	(0.7)	2
Pain in extremity	1	(0.4)	1	0	(0.0)	0
Synovitis	1	(0.4)	1	0	(0.0)	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1**	**(0.4)**	**1**	**1**	**(0.7)**	**2**
Acrochordon	0	(0.0)	0	1	(0.7)	2
Haemangioma	1	(0.4)	1	0	(0.0)	0
Nervous system disorders	**14**	**(5.0)**	**20**	**5**	**(3.5)**	**6**
Carpal tunnel syndrome	1	(0.4)	1	0	(0.0)	0
Dizziness	2	(0.7)	5	1	(0.7)	1
Dysgeusia	0	(0.0)	0	1	(0.7)	1
Epilepsy	1	(0.4)	1	0	(0.0)	0
Headache	9	(3.2)	10	2	(1.4)	2

System Organ Class Preferred Term	Lebrikizumab N=282			Placebo N=141		
	n	(%)	event	n	(%)	event
Hypersomnia	1	(0.4)	1	0	(0.0)	0
Post herpetic neuralgia	1	(0.4)	1	0	(0.0)	0
Radiculopathy	1	(0.4)	1	0	(0.0)	0
Seizure	0	(0.0)	0	1	(0.7)	1
Syncope	0	(0.0)	0	1	(0.7)	1
Psychiatric disorders	7	(2.5)	9	5	(3.5)	5
Anxiety	4	(1.4)	6	0	(0.0)	0
Attention deficit hyperactivity disorder	0	(0.0)	0	1	(0.7)	1
Depression	2	(0.7)	2	1	(0.7)	1
Insomnia	1	(0.4)	1	1	(0.7)	1
Persistent depressive disorder	0	(0.0)	0	1	(0.7)	1
Stress	0	(0.0)	0	1	(0.7)	1
Renal and urinary disorders	1	(0.4)	1	1	(0.7)	1
Cystitis noninfective	1	(0.4)	1	0	(0.0)	0
Nephrolithiasis	0	(0.0)	0	1	(0.7)	1
Reproductive system and breast disorders	4	(1.4)	6	0	(0.0)	0
Dysmenorrhoea	3	(1.1)	5	0	(0.0)	0
Heavy menstrual bleeding	1	(0.4)	1	0	(0.0)	0
Respiratory, thoracic and mediastinal disorders	8	(2.8)	9	6	(4.3)	6
Asthma	3	(1.1)	3	1	(0.7)	1
Chronic obstructive pulmonary disease	1	(0.4)	1	0	(0.0)	0
Cough	1	(0.4)	1	1	(0.7)	1
Dyspnoea	0	(0.0)	0	1	(0.7)	1

System Organ Class Preferred Term	Lebrikizumab N=282			Placebo N=141		
	n	(%)	event	n	(%)	event
Nasal congestion	1	(0.4)	1	0	(0.0)	0
Oropharyngeal pain	1	(0.4)	1	0	(0.0)	0
Rhinitis allergic	2	(0.7)	2	1	(0.7)	1
Rhinorrhoea	0	(0.0)	0	1	(0.7)	1
Sleep apnoea syndrome	0	(0.0)	0	1	(0.7)	1
Skin and subcutaneous tissue disorders	**25**	**(8.9)**	**30**	**34**	**(24.1)**	**46**
Dermal cyst	1	(0.4)	1	0	(0.0)	0
Dermatitis atopic	16	(5.7)	17	30	(21.3)	33
Dermatitis contact	0	(0.0)	0	1	(0.7)	1
Drug eruption	1	(0.4)	1	0	(0.0)	0
Dyshidrotic eczema	0	(0.0)	0	1	(0.7)	1
Eczema	1	(0.4)	1	0	(0.0)	0
Ingrowing nail	1	(0.4)	1	0	(0.0)	0
Milia	0	(0.0)	0	1	(0.7)	1
Photosensitivity reaction	1	(0.4)	1	0	(0.0)	0
Pruritus	3	(1.1)	3	6	(4.3)	7
Rash	1	(0.4)	1	0	(0.0)	0
Seborrhoea	1	(0.4)	1	0	(0.0)	0
Seborrhoeic dermatitis	2	(0.7)	2	1	(0.7)	1
Skin burning sensation	1	(0.4)	1	0	(0.0)	0
Solar dermatitis	0	(0.0)	0	1	(0.7)	1
Urticaria	0	(0.0)	0	1	(0.7)	1
Vascular disorders	**4**	**(1.4)**	**4**	**1**	**(0.7)**	**1**
Hypertension	3	(1.1)	3	1	(0.7)	1
Peripheral venous disease	1	(0.4)	1	0	(0.0)	0

System Organ Class Preferred Term	Lebrikizumab N=282 n	(%)	event	Placebo N=141 n	(%)	event

If more than one AE is coded to the same preferred term for a subject, the subject will be counted only once for that preferred term.

If more than one preferred term is coded to the same SOC for a subject, the subject will be counted only once for that SOC.

Severe AE by SOC and PT (mSAFETY)

System Organ Class Preferred Term	Lebrikizumab N=282			Placebo N=141		
	n	(%)	event	n	(%)	event
OVERALL	6	(2.1)	10	7	(5.0)	9
Eye disorders	1	(0.4)	1	1	(0.7)	1
Blepharitis	1	(0.4)	1	0	(0.0)	0
Keratoconus	0	(0.0)	0	1	(0.7)	1
Gastrointestinal disorders	1	(0.4)	1	0	(0.0)	0
Abdominal pain	1	(0.4)	1	0	(0.0)	0
General disorders and administration site conditions	2	(0.7)	3	0	(0.0)	0
Asthenia	1	(0.4)	2	0	(0.0)	0
Oedema peripheral	1	(0.4)	1	0	(0.0)	0
Infections and infestations	1	(0.4)	1	2	(1.4)	4
Cellulitis	0	(0.0)	0	1	(0.7)	1
Eczema herpeticum	0	(0.0)	0	1	(0.7)	1
Sepsis	0	(0.0)	0	1	(0.7)	1
Skin infection	1	(0.4)	1	0	(0.0)	0
Tooth abscess	0	(0.0)	0	1	(0.7)	1
Injury, poisoning and procedural complications	1	(0.4)	1	0	(0.0)	0
Accidental overdose	1	(0.4)	1	0	(0.0)	0

System Organ Class Preferred Term	Lebrikizumab N=282 n	(%)	event	Placebo N=141 n	(%)	event
Musculoskeletal and connective tissue disorders	1	(0.4)	1	0	(0.0)	0
Arthralgia	1	(0.4)	1	0	(0.0)	0
Nervous system disorders	1	(0.4)	1	1	(0.7)	1
Headache	1	(0.4)	1	0	(0.0)	0
Seizure	0	(0.0)	0	1	(0.7)	1
Skin and subcutaneous tissue disorders	1	(0.4)	1	3	(2.1)	3
Dermatitis atopic	1	(0.4)	1	3	(2.1)	3

If more than one AE is coded to the same preferred term for a subject, the subject will be counted only once for that preferred term.

If more than one preferred term is coded to the same SOC for a subject, the subject will be counted only once for that SOC.

SAE by SOC and PT (mSAFETY)

System Organ Class Preferred Term	Lebrikizumab N=282			Placebo N=141		
	n	(%)	event	n	(%)	event
OVERALL	6	(2.1)	6	1	(0.7)	2
Cardiac disorders	1	(0.4)	1	0	(0.0)	0
Myocardial infarction	1	(0.4)	1	0	(0.0)	0
General disorders and administration site conditions	1	(0.4)	1	0	(0.0)	0
Oedema peripheral	1	(0.4)	1	0	(0.0)	0
Infections and infestations	0	(0.0)	0	1	(0.7)	2
Cellulitis	0	(0.0)	0	1	(0.7)	1
Sepsis	0	(0.0)	0	1	(0.7)	1
Injury, poisoning and procedural complications	1	(0.4)	1	0	(0.0)	0
Accidental overdose	1	(0.4)	1	0	(0.0)	0
Musculoskeletal and connective tissue disorders	2	(0.7)	2	0	(0.0)	0
Arthralgia	1	(0.4)	1	0	(0.0)	0
Synovitis	1	(0.4)	1	0	(0.0)	0
Nervous system disorders	1	(0.4)	1	0	(0.0)	0
Carpal tunnel syndrome	1	(0.4)	1	0	(0.0)	0

If more than one AE is coded to the same preferred term for a subject, the subject will be counted only once for that preferred term.

If more than one preferred term is coded to the same SOC for a subject, the subject will be counted only once for that SOC.

4.4.2 ADvocate 2

Lebrikizumab
Any AE by SOC and PT (mSAFETY)

System Organ Class Preferred Term	Lebrikizumab N=281			Placebo N=145		
	n	(%)	event	n	(%)	event
OVERALL	151	(53.7)	313	96	(66.2)	199
Blood and lymphatic system disorders	4	(1.4)	4	2	(1.4)	2
Eosinophilia	1	(0.4)	1	0	(0.0)	0
Iron deficiency anaemia	1	(0.4)	1	0	(0.0)	0
Lymphadenitis	1	(0.4)	1	0	(0.0)	0
Lymphadenopathy	1	(0.4)	1	0	(0.0)	0
Lymphocytosis	0	(0.0)	0	1	(0.7)	1
Lymphopenia	0	(0.0)	0	1	(0.7)	1
Cardiac disorders	2	(0.7)	2	2	(1.4)	2
Cardiac failure	1	(0.4)	1	0	(0.0)	0
Myocardial infarction	0	(0.0)	0	1	(0.7)	1
Tachycardia	1	(0.4)	1	1	(0.7)	1
Ear and labyrinth disorders	4	(1.4)	4	0	(0.0)	0
Ear discomfort	1	(0.4)	1	0	(0.0)	0
Paraesthesia ear	1	(0.4)	1	0	(0.0)	0
Tinnitus	1	(0.4)	1	0	(0.0)	0
Vertigo	1	(0.4)	1	0	(0.0)	0
Eye disorders	24	(8.5)	31	10	(6.9)	10
Atopic keratoconjunctivitis	2	(0.7)	3	0	(0.0)	0
Blepharitis	2	(0.7)	3	1	(0.7)	1

System Organ Class Preferred Term	Lebrikizumab N=281			Placebo N=145		
	n	(%)	event	n	(%)	event
Cataract	1	(0.4)	1	2	(1.4)	2
Conjunctivitis allergic	7	(2.5)	7	2	(1.4)	2
Dark circles under eyes	0	(0.0)	0	1	(0.7)	1
Dry eye	7	(2.5)	8	0	(0.0)	0
Episcleritis	1	(0.4)	1	0	(0.0)	0
Eye discharge	2	(0.7)	2	0	(0.0)	0
Eye pruritus	1	(0.4)	1	0	(0.0)	0
Eyelid cyst	1	(0.4)	1	0	(0.0)	0
Eyelid erosion	0	(0.0)	0	2	(1.4)	2
Keratitis	1	(0.4)	2	0	(0.0)	0
Lacrimation increased	0	(0.0)	0	1	(0.7)	1
Ocular hyperaemia	1	(0.4)	1	0	(0.0)	0
Vision blurred	1	(0.4)	1	0	(0.0)	0
Vitreous floaters	0	(0.0)	0	1	(0.7)	1
Gastrointestinal disorders	13	(4.6)	17	6	(4.1)	7
Abdominal pain	1	(0.4)	1	0	(0.0)	0
Breath odour	1	(0.4)	1	0	(0.0)	0
Constipation	1	(0.4)	1	1	(0.7)	1
Diarrhoea	2	(0.7)	2	1	(0.7)	1
Dyspepsia	1	(0.4)	1	1	(0.7)	1
Flatulence	1	(0.4)	1	0	(0.0)	0
Gastrointestinal inflammation	0	(0.0)	0	1	(0.7)	1
Haematemesis	1	(0.4)	1	0	(0.0)	0
Haemorrhoids	1	(0.4)	1	1	(0.7)	1
Hiatus hernia	1	(0.4)	1	0	(0.0)	0
Inguinal hernia	1	(0.4)	1	1	(0.7)	1

System Organ Class Preferred Term	Lebrikizumab N=281			Placebo N=145		
	n	(%)	event	n	(%)	event
Nausea	3	(1.1)	3	0	(0.0)	0
Tooth impacted	1	(0.4)	1	0	(0.0)	0
Toothache	0	(0.0)	0	1	(0.7)	1
Vomiting	1	(0.4)	2	0	(0.0)	0
General disorders and administration site conditions	12	(4.3)	17	6	(4.1)	8
Chills	1	(0.4)	1	0	(0.0)	0
Cyst	1	(0.4)	1	0	(0.0)	0
Cyst rupture	1	(0.4)	1	0	(0.0)	0
Fatigue	3	(1.1)	3	2	(1.4)	2
Injection site discomfort	1	(0.4)	1	0	(0.0)	0
Injection site erythema	1	(0.4)	2	0	(0.0)	0
Injection site pain	2	(0.7)	3	1	(0.7)	1
Injection site reaction	2	(0.7)	4	0	(0.0)	0
Injection site swelling	0	(0.0)	0	1	(0.7)	1
Oedema	0	(0.0)	0	1	(0.7)	1
Oedema peripheral	0	(0.0)	0	1	(0.7)	2
Swelling	0	(0.0)	0	1	(0.7)	1
Vaccination site pain	1	(0.4)	1	0	(0.0)	0
Hepatobiliary disorders	1	(0.4)	1	0	(0.0)	0
Hepatic steatosis	1	(0.4)	1	0	(0.0)	0
Immune system disorders	6	(2.1)	7	2	(1.4)	2
Allergy to animal	1	(0.4)	1	0	(0.0)	0
Drug hypersensitivity	1	(0.4)	1	0	(0.0)	0
Food allergy	0	(0.0)	0	1	(0.7)	1

System Organ Class Preferred Term	Lebrikizumab N=281 n	(%)	event	Placebo N=145 n	(%)	event
Seasonal allergy	4	(1.4)	5	1	(0.7)	1
Infections and infestations	**66**	**(23.5)**	**83**	**30**	**(20.7)**	**40**
Asymptomatic bacteriuria	0	(0.0)	0	1	(0.7)	1
COVID-19	2	(0.7)	2	2	(1.4)	2
Conjunctivitis	21	(7.5)	22	3	(2.1)	3
Conjunctivitis bacterial	3	(1.1)	3	0	(0.0)	0
Cystitis	2	(0.7)	2	1	(0.7)	1
Dermatitis infected	0	(0.0)	0	1	(0.7)	1
Eczema herpeticum	0	(0.0)	0	1	(0.7)	1
Eczema impetiginous	0	(0.0)	0	1	(0.7)	1
Eczema infected	1	(0.4)	2	0	(0.0)	0
Erysipelas	1	(0.4)	1	0	(0.0)	0
Folliculitis	1	(0.4)	1	3	(2.1)	3
Gastroenteritis	3	(1.1)	4	1	(0.7)	1
Genital herpes simplex	0	(0.0)	0	1	(0.7)	1
Herpes dermatitis	1	(0.4)	1	2	(1.4)	2
Herpes simplex	3	(1.1)	4	0	(0.0)	0
Herpes zoster	1	(0.4)	1	0	(0.0)	0
Hordeolum	1	(0.4)	1	1	(0.7)	1
Impetigo	0	(0.0)	0	3	(2.1)	3
Large intestine infection	1	(0.4)	2	0	(0.0)	0
Molluscum contagiosum	1	(0.4)	1	0	(0.0)	0
Nasopharyngitis	14	(5.0)	16	3	(2.1)	3
Oral herpes	5	(1.8)	5	3	(2.1)	3
Oral infection	1	(0.4)	1	0	(0.0)	0
Otitis externa	1	(0.4)	1	1	(0.7)	1

System Organ Class Preferred Term	Lebrikizumab N=281 n	(%)	event	Placebo N=145 n	(%)	event
Paronychia	2	(0.7)	2	0	(0.0)	0
Pharyngitis	0	(0.0)	0	1	(0.7)	1
Pharyngitis streptococcal	0	(0.0)	0	1	(0.7)	1
Pharyngotonsillitis	1	(0.4)	1	0	(0.0)	0
Post procedural infection	0	(0.0)	0	1	(0.7)	1
Rhinitis	1	(0.4)	1	0	(0.0)	0
Skin infection	1	(0.4)	2	1	(0.7)	1
Superinfection	0	(0.0)	0	1	(0.7)	1
Tinea cruris	1	(0.4)	1	0	(0.0)	0
Tinea infection	0	(0.0)	0	1	(0.7)	1
Tinea pedis	1	(0.4)	1	0	(0.0)	0
Tooth abscess	1	(0.4)	1	1	(0.7)	1
Tooth infection	1	(0.4)	1	1	(0.7)	1
Upper respiratory tract infection	0	(0.0)	0	2	(1.4)	2
Urinary tract infection	2	(0.7)	2	1	(0.7)	1
Viral infection	1	(0.4)	1	0	(0.0)	0
Vulvovaginal candidiasis	0	(0.0)	0	1	(0.7)	1
Injury, poisoning and procedural complications	19	(6.8)	22	13	(9.0)	17
Accident at work	1	(0.4)	1	0	(0.0)	0
Animal bite	1	(0.4)	1	0	(0.0)	0
Clavicle fracture	1	(0.4)	1	0	(0.0)	0
Concussion	1	(0.4)	1	1	(0.7)	1
Contusion	0	(0.0)	0	1	(0.7)	1
Epicondylitis	0	(0.0)	0	1	(0.7)	1
Fall	1	(0.4)	1	0	(0.0)	0
Fibula fracture	0	(0.0)	0	1	(0.7)	2

System Organ Class Preferred Term	Lebrikizumab N=281 n	(%)	event	Placebo N=145 n	(%)	event
Hand fracture	2	(0.7)	2	0	(0.0)	0
Injury corneal	1	(0.4)	1	0	(0.0)	0
Joint dislocation	0	(0.0)	0	1	(0.7)	1
Ligament sprain	0	(0.0)	0	1	(0.7)	1
Limb injury	0	(0.0)	0	1	(0.7)	1
Multiple injuries	1	(0.4)	1	0	(0.0)	0
Muscle strain	1	(0.4)	1	1	(0.7)	1
Overdose	3	(1.1)	4	1	(0.7)	1
Post procedural complication	0	(0.0)	0	1	(0.7)	1
Procedural headache	0	(0.0)	0	1	(0.7)	1
Procedural pain	0	(0.0)	0	2	(1.4)	2
Skin abrasion	1	(0.4)	1	0	(0.0)	0
Skin laceration	1	(0.4)	1	1	(0.7)	1
Thermal burn	1	(0.4)	1	0	(0.0)	0
Tibia fracture	0	(0.0)	0	1	(0.7)	2
Vaccination complication	2	(0.7)	3	0	(0.0)	0
Wound dehiscence	1	(0.4)	1	0	(0.0)	0
Wrist fracture	1	(0.4)	1	0	(0.0)	0
Investigations	3	(1.1)	5	4	(2.8)	5
Blood pressure increased	1	(0.4)	1	1	(0.7)	1
Eosinophil count increased	2	(0.7)	2	0	(0.0)	0
Neutrophil count decreased	0	(0.0)	0	1	(0.7)	1
Neutrophil count increased	0	(0.0)	0	1	(0.7)	1
Platelet count increased	1	(0.4)	1	2	(1.4)	2
White blood cell count increased	1	(0.4)	1	0	(0.0)	0

System Organ Class Preferred Term	Lebrikizumab N=281			Placebo N=145		
	n	(%)	event	n	(%)	event
Metabolism and nutrition disorders	2	(0.7)	2	2	(1.4)	2
Decreased appetite	1	(0.4)	1	0	(0.0)	0
Hypercholesterolaemia	0	(0.0)	0	1	(0.7)	1
Hypoglycaemia	0	(0.0)	0	1	(0.7)	1
Obesity	1	(0.4)	1	0	(0.0)	0
Musculoskeletal and connective tissue disorders	6	(2.1)	6	5	(3.4)	7
Arthralgia	3	(1.1)	3	1	(0.7)	1
Arthritis	0	(0.0)	0	1	(0.7)	1
Bursitis	0	(0.0)	0	1	(0.7)	1
Coccydynia	1	(0.4)	1	0	(0.0)	0
Joint swelling	0	(0.0)	0	1	(0.7)	1
Muscle spasms	1	(0.4)	1	0	(0.0)	0
Pain in extremity	1	(0.4)	1	1	(0.7)	2
Synovial cyst	0	(0.0)	0	1	(0.7)	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	4	(1.4)	4	4	(2.8)	4
Bowen's disease	0	(0.0)	0	1	(0.7)	1
Fibroadenoma of breast	0	(0.0)	0	1	(0.7)	1
Skin papilloma	3	(1.1)	3	0	(0.0)	0
Squamous cell carcinoma	1	(0.4)	1	1	(0.7)	1
Uterine leiomyoma	0	(0.0)	0	1	(0.7)	1
Nervous system disorders	20	(7.1)	27	10	(6.9)	10
Burning sensation	0	(0.0)	0	1	(0.7)	1
Cerebellar syndrome	1	(0.4)	3	0	(0.0)	0
Dizziness	3	(1.1)	3	0	(0.0)	0

System Organ Class Preferred Term	Lebrikizumab N=281			Placebo N=145		
	n	(%)	event	n	(%)	event
Headache	14	(5.0)	16	6	(4.1)	6
Hyperaesthesia	1	(0.4)	2	0	(0.0)	0
Hypoaesthesia	1	(0.4)	1	2	(1.4)	2
Neuralgia	1	(0.4)	1	0	(0.0)	0
Paraesthesia	1	(0.4)	1	1	(0.7)	1
Psychiatric disorders	3	(1.1)	3	6	(4.1)	7
Anxiety	0	(0.0)	0	3	(2.1)	3
Depression	0	(0.0)	0	1	(0.7)	1
Insomnia	1	(0.4)	1	1	(0.7)	2
Middle insomnia	1	(0.4)	1	0	(0.0)	0
Panic attack	1	(0.4)	1	0	(0.0)	0
Sleep disorder	0	(0.0)	0	1	(0.7)	1
Renal and urinary disorders	2	(0.7)	2	2	(1.4)	2
Bladder disorder	1	(0.4)	1	0	(0.0)	0
Bladder irritation	1	(0.4)	1	0	(0.0)	0
Nephrolithiasis	0	(0.0)	0	1	(0.7)	1
Renal pain	0	(0.0)	0	1	(0.7)	1
Reproductive system and breast disorders	1	(0.4)	1	2	(1.4)	2
Breast ulceration	0	(0.0)	0	1	(0.7)	1
Heavy menstrual bleeding	0	(0.0)	0	1	(0.7)	1
Vulvovaginal dryness	1	(0.4)	1	0	(0.0)	0
Respiratory, thoracic and mediastinal disorders	11	(3.9)	11	6	(4.1)	6
Asthma	1	(0.4)	1	1	(0.7)	1

System Organ Class Preferred Term	Lebrikizumab N=281 n	(%)	event	Placebo N=145 n	(%)	event
Cough	2	(0.7)	2	0	(0.0)	0
Dyspnoea	0	(0.0)	0	1	(0.7)	1
Epistaxis	0	(0.0)	0	1	(0.7)	1
Nasal congestion	1	(0.4)	1	1	(0.7)	1
Oropharyngeal pain	2	(0.7)	2	1	(0.7)	1
Rhinitis allergic	4	(1.4)	4	1	(0.7)	1
Sinus congestion	1	(0.4)	1	0	(0.0)	0
Skin and subcutaneous tissue disorders	52	(18.5)	61	49	(33.8)	62
Acne	1	(0.4)	1	3	(2.1)	3
Actinic keratosis	0	(0.0)	0	1	(0.7)	1
Alopecia	2	(0.7)	2	0	(0.0)	0
Alopecia areata	1	(0.4)	1	0	(0.0)	0
Angioedema	0	(0.0)	0	1	(0.7)	1
Dermatitis	2	(0.7)	2	1	(0.7)	1
Dermatitis atopic	29	(10.3)	33	38	(26.2)	42
Dermatitis contact	1	(0.4)	1	2	(1.4)	2
Dermatitis exfoliative generalised	1	(0.4)	1	1	(0.7)	1
Dermatitis psoriasiform	2	(0.7)	2	0	(0.0)	0
Diffuse alopecia	1	(0.4)	1	0	(0.0)	0
Dyshidrotic eczema	0	(0.0)	0	1	(0.7)	1
Eczema	1	(0.4)	1	1	(0.7)	1
Erythema	1	(0.4)	1	0	(0.0)	0
Hair disorder	1	(0.4)	1	0	(0.0)	0
Night sweats	2	(0.7)	2	0	(0.0)	0
Pityriasis rosea	1	(0.4)	1	0	(0.0)	0
Prurigo	0	(0.0)	0	1	(0.7)	1

System Organ Class Preferred Term	Lebrikizumab N=281 n	(%)	event	Placebo N=145 n	(%)	event
Pruritus	5	(1.8)	5	1	(0.7)	1
Rash	1	(0.4)	1	0	(0.0)	0
Rash erythematous	0	(0.0)	0	1	(0.7)	2
Rosacea	0	(0.0)	0	1	(0.7)	1
Seborrhoea	1	(0.4)	1	0	(0.0)	0
Skin disorder	0	(0.0)	0	1	(0.7)	1
Skin fissures	1	(0.4)	1	1	(0.7)	1
Skin lesion inflammation	0	(0.0)	0	1	(0.7)	1
Urticaria	2	(0.7)	3	1	(0.7)	1
Vascular disorders	3	(1.1)	3	4	(2.8)	4
Aortic arteriosclerosis	0	(0.0)	0	1	(0.7)	1
Haematoma	0	(0.0)	0	1	(0.7)	1
Hot flush	1	(0.4)	1	0	(0.0)	0
Hypertension	2	(0.7)	2	2	(1.4)	2

If more than one AE is coded to the same preferred term for a subject, the subject will be counted only once for that preferred term.

If more than one preferred term is coded to the same SOC for a subject, the subject will be counted only once for that SOC.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

Severe AE by SOC and PT (mSAFETY)

System Organ Class Preferred Term	Lebrikizumab N=281			Placebo N=145		
	n	(%)	event	n	(%)	event
OVERALL	7	(2.5)	9	7	(4.8)	8
Cardiac disorders	0	(0.0)	0	1	(0.7)	1
Myocardial infarction	0	(0.0)	0	1	(0.7)	1
Gastrointestinal disorders	1	(0.4)	1	0	(0.0)	0
Abdominal pain	1	(0.4)	1	0	(0.0)	0
Infections and infestations	1	(0.4)	1	0	(0.0)	0
Large intestine infection	1	(0.4)	1	0	(0.0)	0
Injury, poisoning and procedural complications	0	(0.0)	0	1	(0.7)	2
Fibula fracture	0	(0.0)	0	1	(0.7)	1
Tibia fracture	0	(0.0)	0	1	(0.7)	1
Musculoskeletal and connective tissue disorders	1	(0.4)	1	0	(0.0)	0
Arthralgia	1	(0.4)	1	0	(0.0)	0
Nervous system disorders	1	(0.4)	2	0	(0.0)	0
Cerebellar syndrome	1	(0.4)	2	0	(0.0)	0
Reproductive system and breast disorders	0	(0.0)	0	1	(0.7)	1
Heavy menstrual bleeding	0	(0.0)	0	1	(0.7)	1
Respiratory, thoracic and mediastinal disorders	1	(0.4)	1	0	(0.0)	0

System Organ Class Preferred Term	Lebrikizumab N=281 n	(%)	event	Placebo N=145 n	(%)	event
Cough	1	(0.4)	1	0	(0.0)	0
Skin and subcutaneous tissue disorders	3	(1.1)	3	4	(2.8)	4
Dermatitis atopic	1	(0.4)	1	2	(1.4)	2
Dermatitis contact	1	(0.4)	1	0	(0.0)	0
Dermatitis exfoliative generalised	1	(0.4)	1	1	(0.7)	1
Eczema	0	(0.0)	0	1	(0.7)	1

If more than one AE is coded to the same preferred term for a subject, the subject will be counted only once for that preferred term.

If more than one preferred term is coded to the same SOC for a subject, the subject will be counted only once for that SOC.

Lebrikizumab

SAE by SOC and PT (mSAFETY)

System Organ Class Preferred Term	Lebrikizumab N=281			Placebo N=145		
	n	(%)	event	n	(%)	event
OVERALL	2	(0.7)	5	4	(2.8)	5
Cardiac disorders	1	(0.4)	1	1	(0.7)	1
Cardiac failure	1	(0.4)	1	0	(0.0)	0
Myocardial infarction	0	(0.0)	0	1	(0.7)	1
Infections and infestations	1	(0.4)	1	0	(0.0)	0
Large intestine infection	1	(0.4)	1	0	(0.0)	0
Injury, poisoning and procedural complications	1	(0.4)	1	1	(0.7)	2
Fibula fracture	0	(0.0)	0	1	(0.7)	1
Multiple injuries	1	(0.4)	1	0	(0.0)	0
Tibia fracture	0	(0.0)	0	1	(0.7)	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0	(0.0)	0	1	(0.7)	1
Uterine leiomyoma	0	(0.0)	0	1	(0.7)	1
Nervous system disorders	1	(0.4)	1	0	(0.0)	0
Cerebellar syndrome	1	(0.4)	1	0	(0.0)	0
Skin and subcutaneous tissue disorders	1	(0.4)	1	1	(0.7)	1
Dermatitis atopic	1	(0.4)	1	1	(0.7)	1

If more than one AE is coded to the same preferred term for a subject, the subject will be counted only once for that preferred term.

If more than one preferred term is coded to the same SOC for a subject, the subject will be counted only once for that SOC.

4.4.3 ADhere

Lebrikizumab
Any AE by SOC and PT (mSAFETY)

System Organ Class Preferred Term	Lebrikizumab N=153 n	(%)	event	Placebo N=75 n	(%)	event
OVERALL	67	(43.8)	130	27	(36.0)	39
Blood and lymphatic system disorders	5	(3.3)	7	1	(1.3)	1
Eosinophilia	1	(0.7)	1	0	(0.0)	0
Iron deficiency anaemia	1	(0.7)	1	0	(0.0)	0
Lymphadenopathy	1	(0.7)	1	1	(1.3)	1
Lymphocytosis	1	(0.7)	1	0	(0.0)	0
Neutropenia	1	(0.7)	1	0	(0.0)	0
Thrombocytopenia	2	(1.3)	2	0	(0.0)	0
Cardiac disorders	1	(0.7)	1	0	(0.0)	0
Sinus node dysfunction	1	(0.7)	1	0	(0.0)	0
Eye disorders	8	(5.2)	9	1	(1.3)	1
Blepharitis	1	(0.7)	1	0	(0.0)	0
Conjunctival haemorrhage	0	(0.0)	0	1	(1.3)	1
Dry eye	3	(2.0)	3	0	(0.0)	0
Eye irritation	1	(0.7)	2	0	(0.0)	0
Lacrimation increased	1	(0.7)	1	0	(0.0)	0
Vernal keratoconjunctivitis	1	(0.7)	1	0	(0.0)	0
Xerophthalmia	1	(0.7)	1	0	(0.0)	0
Gastrointestinal disorders	5	(3.3)	7	1	(1.3)	1
Diarrhoea	1	(0.7)	1	1	(1.3)	1

System Organ Class Preferred Term	Lebrikizumab N=153 n	(%)	event	Placebo N=75 n	(%)	event
Flatulence	1	(0.7)	1	0	(0.0)	0
Gastrointestinal inflammation	1	(0.7)	1	0	(0.0)	0
Nausea	2	(1.3)	2	0	(0.0)	0
Vomiting	2	(1.3)	2	0	(0.0)	0
General disorders and administration site conditions	4	(2.6)	8	2	(2.7)	2
Injection site erythema	1	(0.7)	1	0	(0.0)	0
Injection site pruritus	1	(0.7)	2	0	(0.0)	0
Injection site rash	2	(1.3)	2	0	(0.0)	0
Injection site reaction	2	(1.3)	2	1	(1.3)	1
Injection site swelling	1	(0.7)	1	0	(0.0)	0
Vaccination site pain	0	(0.0)	0	1	(1.3)	1
Hepatobiliary disorders	1	(0.7)	3	0	(0.0)	0
Cholelithiasis	1	(0.7)	1	0	(0.0)	0
Hepatic steatosis	1	(0.7)	1	0	(0.0)	0
Hepatomegaly	1	(0.7)	1	0	(0.0)	0
Immune system disorders	2	(1.3)	2	1	(1.3)	1
Drug hypersensitivity	1	(0.7)	1	0	(0.0)	0
Hypersensitivity	0	(0.0)	0	1	(1.3)	1
Seasonal allergy	1	(0.7)	1	0	(0.0)	0
Infections and infestations	26	(17.0)	34	10	(13.3)	12
Bacteraemia	1	(0.7)	1	0	(0.0)	0
Bacterial colitis	1	(0.7)	1	0	(0.0)	0
Bronchitis	1	(0.7)	1	0	(0.0)	0

System Organ Class Preferred Term	Lebrikizumab N=153			Placebo N=75		
	n	(%)	event	n	(%)	event
COVID-19	2	(1.3)	2	0	(0.0)	0
Cellulitis	1	(0.7)	1	1	(1.3)	1
Conjunctivitis	7	(4.6)	8	0	(0.0)	0
Furuncle	0	(0.0)	0	1	(1.3)	1
Herpes zoster	2	(1.3)	2	0	(0.0)	0
Impetigo	2	(1.3)	2	1	(1.3)	1
Nasopharyngitis	3	(2.0)	5	5	(6.7)	6
Ophthalmic herpes simplex	1	(0.7)	1	0	(0.0)	0
Oral herpes	3	(2.0)	3	1	(1.3)	1
Tonsillitis	1	(0.7)	1	0	(0.0)	0
Tooth abscess	1	(0.7)	1	0	(0.0)	0
Tooth infection	1	(0.7)	1	0	(0.0)	0
Upper respiratory tract infection	1	(0.7)	1	2	(2.7)	2
Urinary tract infection	3	(2.0)	3	0	(0.0)	0
Injury, poisoning and procedural complications	10	(6.5)	10	0	(0.0)	0
Concussion	1	(0.7)	1	0	(0.0)	0
Corneal abrasion	1	(0.7)	1	0	(0.0)	0
Fall	2	(1.3)	2	0	(0.0)	0
Fibula fracture	1	(0.7)	1	0	(0.0)	0
Ligament sprain	1	(0.7)	1	0	(0.0)	0
Limb injury	1	(0.7)	1	0	(0.0)	0
Muscle strain	1	(0.7)	1	0	(0.0)	0
Suture related complication	1	(0.7)	1	0	(0.0)	0
Vaccination complication	1	(0.7)	1	0	(0.0)	0
Investigations	3	(2.0)	7	2	(2.7)	2

System Organ Class Preferred Term	Lebrikizumab N=153			Placebo N=75		
	n	(%)	event	n	(%)	event
Alanine aminotransferase increased	1	(0.7)	1	1	(1.3)	1
Aspartate aminotransferase increased	1	(0.7)	1	0	(0.0)	0
Blood alkaline phosphatase increased	1	(0.7)	1	0	(0.0)	0
Blood pressure increased	1	(0.7)	2	1	(1.3)	1
Gamma-glutamyltransferase increased	1	(0.7)	1	0	(0.0)	0
Weight increased	1	(0.7)	1	0	(0.0)	0
Metabolism and nutrition disorders	7	(4.6)	8	3	(4.0)	3
Alcohol intolerance	1	(0.7)	2	0	(0.0)	0
Dehydration	0	(0.0)	0	1	(1.3)	1
Hypercholesterolaemia	0	(0.0)	0	1	(1.3)	1
Hyperglycaemia	0	(0.0)	0	1	(1.3)	1
Hyperkalaemia	1	(0.7)	1	0	(0.0)	0
Hypokalaemia	1	(0.7)	1	0	(0.0)	0
Malnutrition	1	(0.7)	1	0	(0.0)	0
Type 2 diabetes mellitus	2	(1.3)	2	0	(0.0)	0
Vitamin D deficiency	1	(0.7)	1	0	(0.0)	0
Musculoskeletal and connective tissue disorders	1	(0.7)	1	3	(4.0)	3
Back pain	0	(0.0)	0	1	(1.3)	1
Bursitis	0	(0.0)	0	1	(1.3)	1
Myalgia	1	(0.7)	1	0	(0.0)	0
Spinal pain	0	(0.0)	0	1	(1.3)	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1	(0.7)	1	0	(0.0)	0
Keratoacanthoma	1	(0.7)	1	0	(0.0)	0

System Organ Class Preferred Term	Lebrikizumab N=153			Placebo N=75		
	n	(%)	event	n	(%)	event
Nervous system disorders	10	(6.5)	11	1	(1.3)	1
Cervical radiculopathy	1	(0.7)	1	0	(0.0)	0
Dizziness	1	(0.7)	1	0	(0.0)	0
Headache	7	(4.6)	7	1	(1.3)	1
Ophthalmic migraine	1	(0.7)	1	0	(0.0)	0
Syncope	1	(0.7)	1	0	(0.0)	0
Psychiatric disorders	1	(0.7)	1	1	(1.3)	1
Attention deficit hyperactivity disorder	1	(0.7)	1	0	(0.0)	0
Insomnia	0	(0.0)	0	1	(1.3)	1
Renal and urinary disorders	0	(0.0)	0	1	(1.3)	1
Acute kidney injury	0	(0.0)	0	1	(1.3)	1
Respiratory, thoracic and mediastinal disorders	5	(3.3)	5	1	(1.3)	1
Asthma	1	(0.7)	1	0	(0.0)	0
Chronic obstructive pulmonary disease	1	(0.7)	1	0	(0.0)	0
Rhinitis allergic	1	(0.7)	1	0	(0.0)	0
Rhinorrhoea	1	(0.7)	1	1	(1.3)	1
Sinus congestion	1	(0.7)	1	0	(0.0)	0
Skin and subcutaneous tissue disorders	9	(5.9)	11	7	(9.3)	8
Acne	1	(0.7)	1	0	(0.0)	0
Alopecia areata	0	(0.0)	0	1	(1.3)	1
Dermatitis	1	(0.7)	1	0	(0.0)	0
Dermatitis acneiform	1	(0.7)	1	0	(0.0)	0
Dermatitis atopic	3	(2.0)	3	3	(4.0)	3

System Organ Class Preferred Term	Lebrikizumab N=153 n	(%)	event	Placebo N=75 n	(%)	event
Dermatitis contact	1	(0.7)	1	0	(0.0)	0
Eczema	1	(0.7)	1	1	(1.3)	1
Hyperhidrosis	0	(0.0)	0	1	(1.3)	1
Skin lesion inflammation	1	(0.7)	1	1	(1.3)	1
Urticaria	1	(0.7)	2	1	(1.3)	1
Vascular disorders	4	(2.6)	4	1	(1.3)	1
Hypertension	4	(2.6)	4	1	(1.3)	1

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If more than one preferred term is coded to the same SOC for a subject, the subject will be counted only once for that SOC.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

Severe AE by SOC and PT (mSAFETY)

System Organ Class Preferred Term	Lebrikizumab N=153			Placebo N=75		
	n	(%)	event	n	(%)	event
OVERALL	3	(2.0)	4	1	(1.3)	2
Cardiac disorders	1	(0.7)	1	0	(0.0)	0
Sinus node dysfunction	1	(0.7)	1	0	(0.0)	0
Immune system disorders	1	(0.7)	1	0	(0.0)	0
Drug hypersensitivity	1	(0.7)	1	0	(0.0)	0
Infections and infestations	1	(0.7)	1	0	(0.0)	0
Bacteraemia	1	(0.7)	1	0	(0.0)	0
Injury, poisoning and procedural complications	1	(0.7)	1	0	(0.0)	0
Fall	1	(0.7)	1	0	(0.0)	0
Metabolism and nutrition disorders	0	(0.0)	0	1	(1.3)	1
Dehydration	0	(0.0)	0	1	(1.3)	1
Renal and urinary disorders	0	(0.0)	0	1	(1.3)	1
Acute kidney injury	0	(0.0)	0	1	(1.3)	1

If more than one AE is coded to the same preferred term for a subject, the subject will be counted only once for that preferred term.

If more than one preferred term is coded to the same SOC for a subject, the subject will be counted only once for that SOC.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

SAE by SOC and PT (mSAFETY)

System Organ Class Preferred Term	Lebrikizumab N=153			Placebo N=75		
	n	(%)	event	n	(%)	event
OVERALL	2	(1.3)	2	1	(1.3)	2
Cardiac disorders	1	(0.7)	1	0	(0.0)	0
Sinus node dysfunction	1	(0.7)	1	0	(0.0)	0
Injury, poisoning and procedural complications	1	(0.7)	1	0	(0.0)	0
Fall	1	(0.7)	1	0	(0.0)	0
Metabolism and nutrition disorders	0	(0.0)	0	1	(1.3)	1
Dehydration	0	(0.0)	0	1	(1.3)	1
Renal and urinary disorders	0	(0.0)	0	1	(1.3)	1
Acute kidney injury	0	(0.0)	0	1	(1.3)	1

If more than one AE is coded to the same preferred term for a subject, the subject will be counted only once for that preferred term.

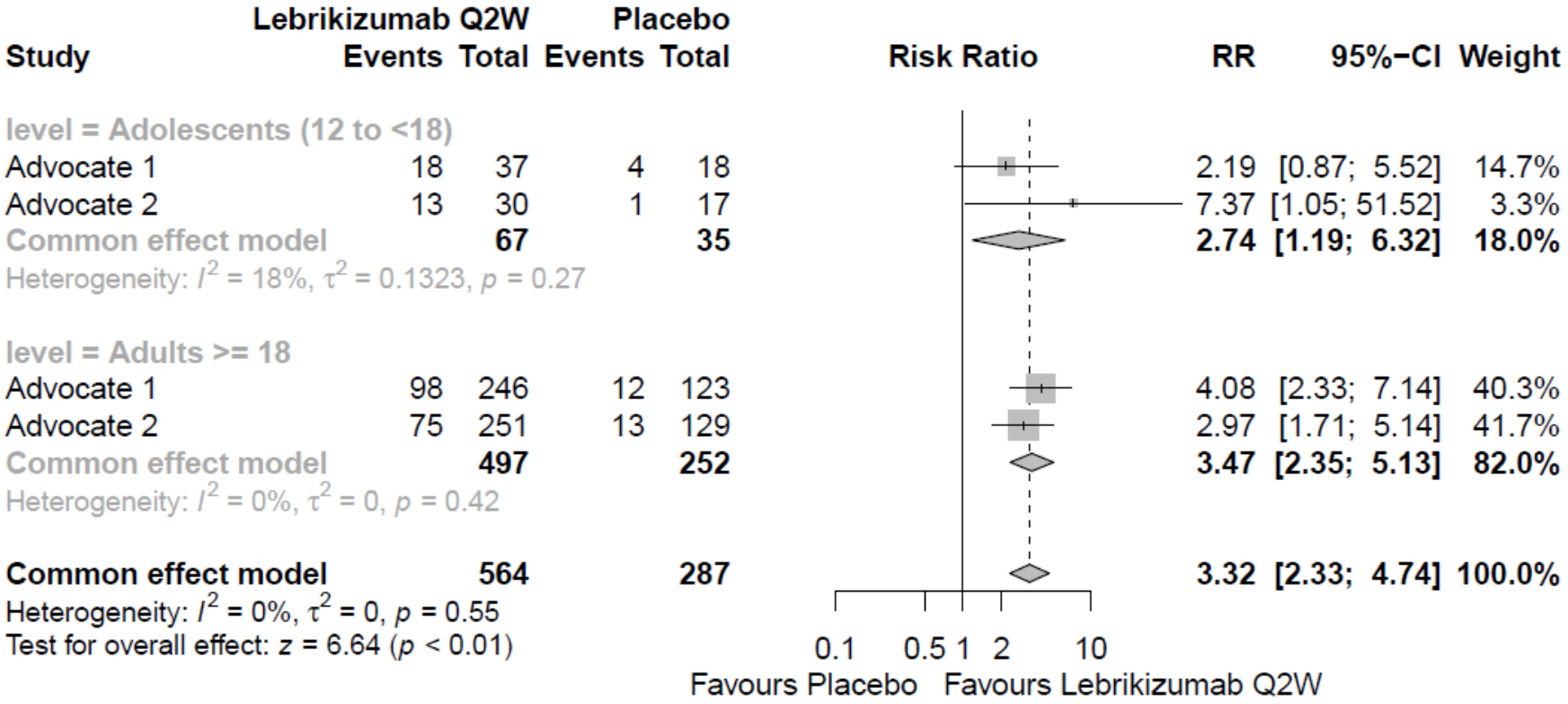
If more than one preferred term is coded to the same SOC for a subject, the subject will be counted only once for that SOC.

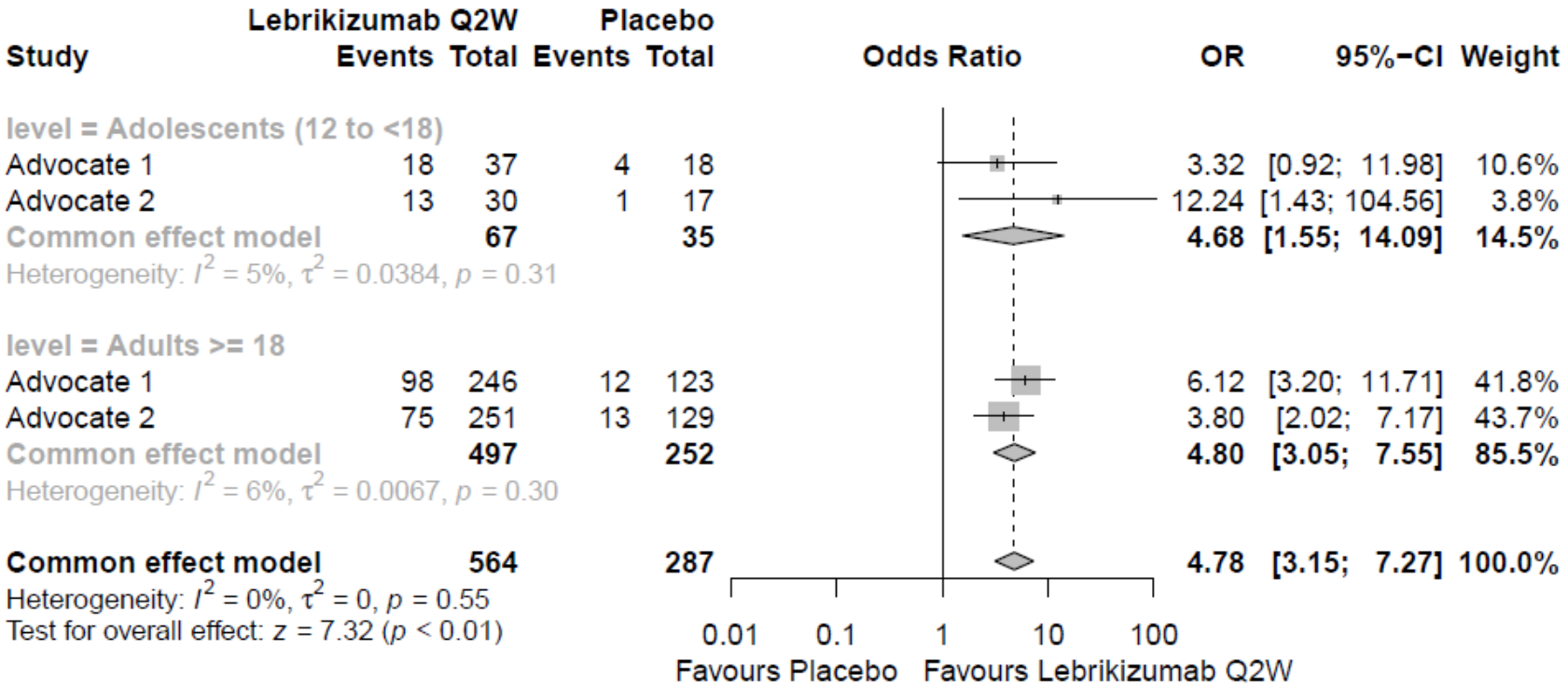
4.5 Subgruppenanalysen

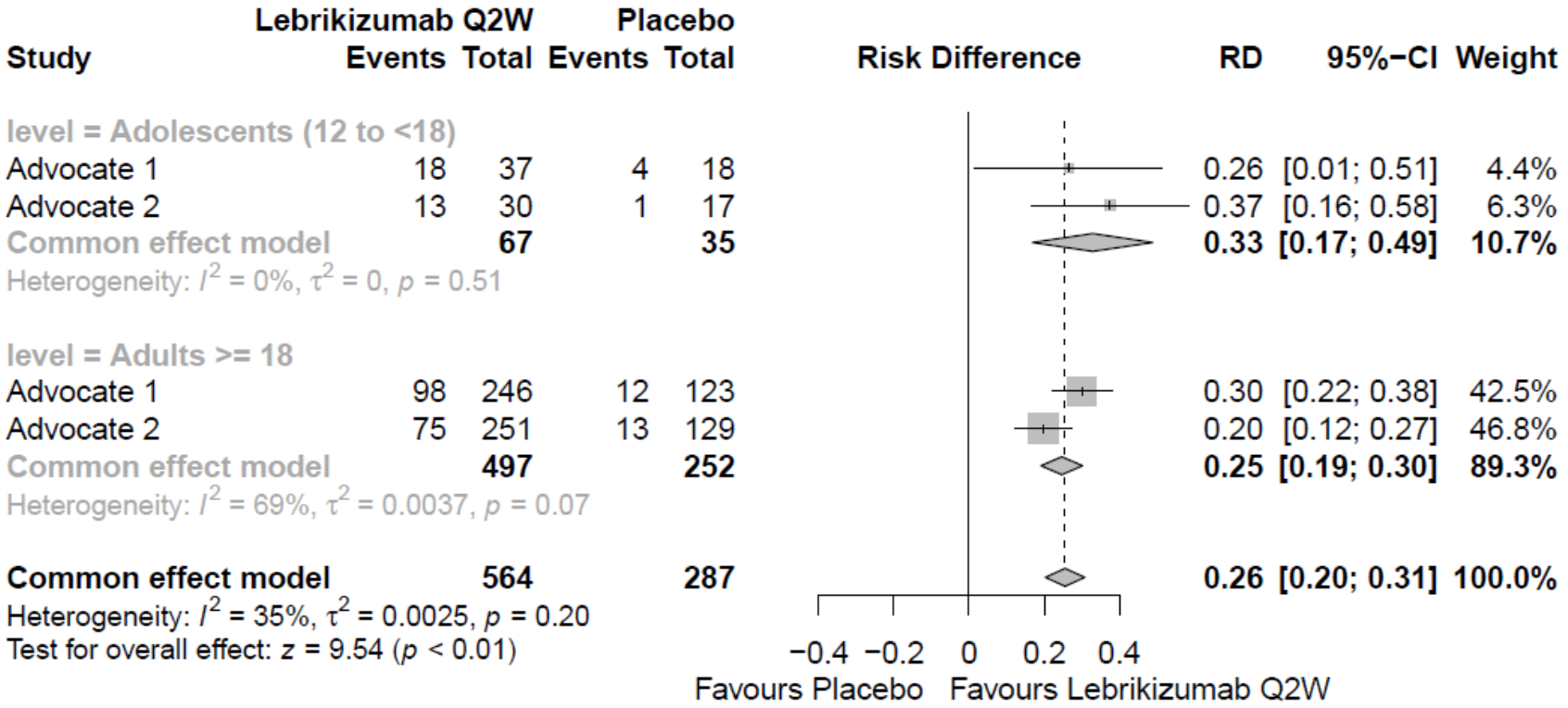
4.5.1 Subgruppenanalyse - Forest-Plots der Meta-Analyse

4.5.1.1 IGA 0 / 1

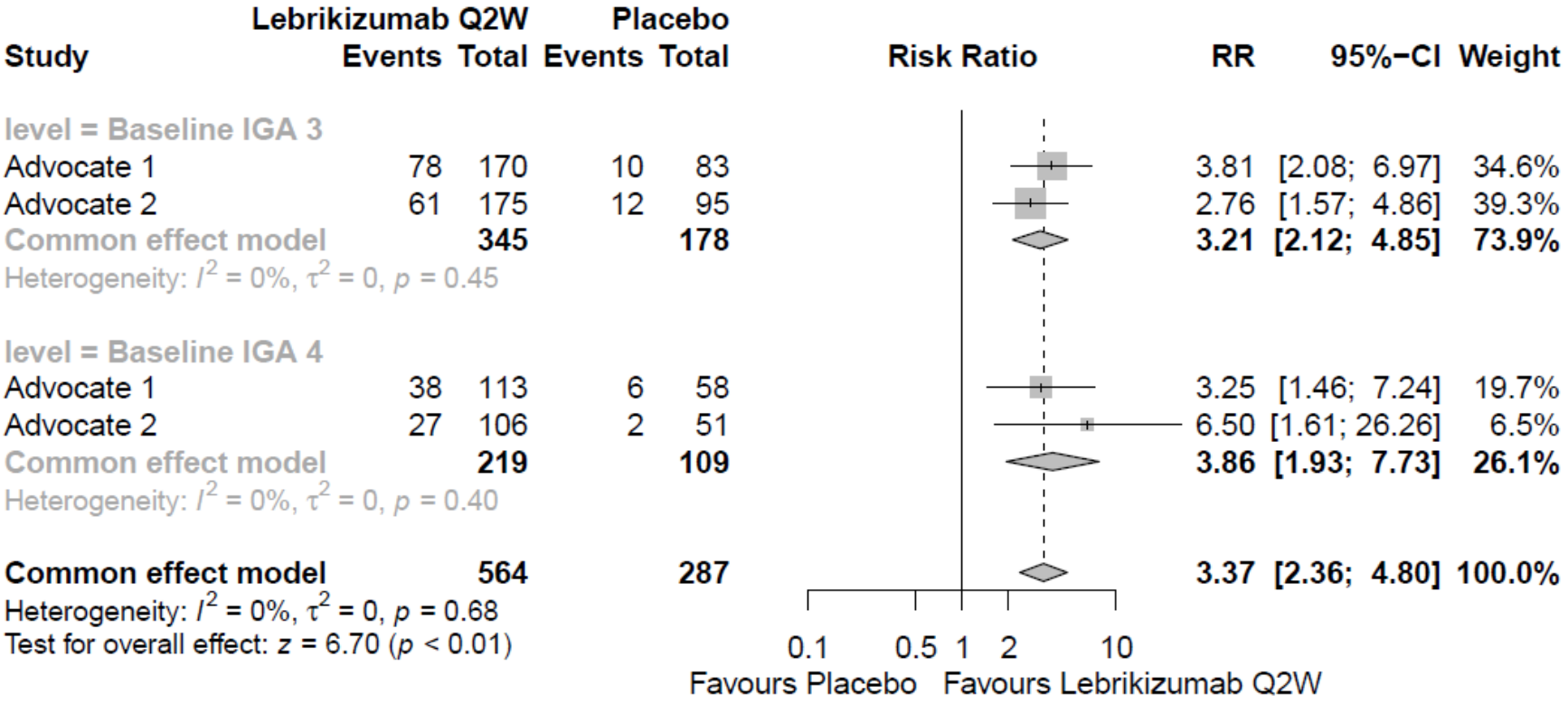
4.5.1.1.1 Altersgruppe

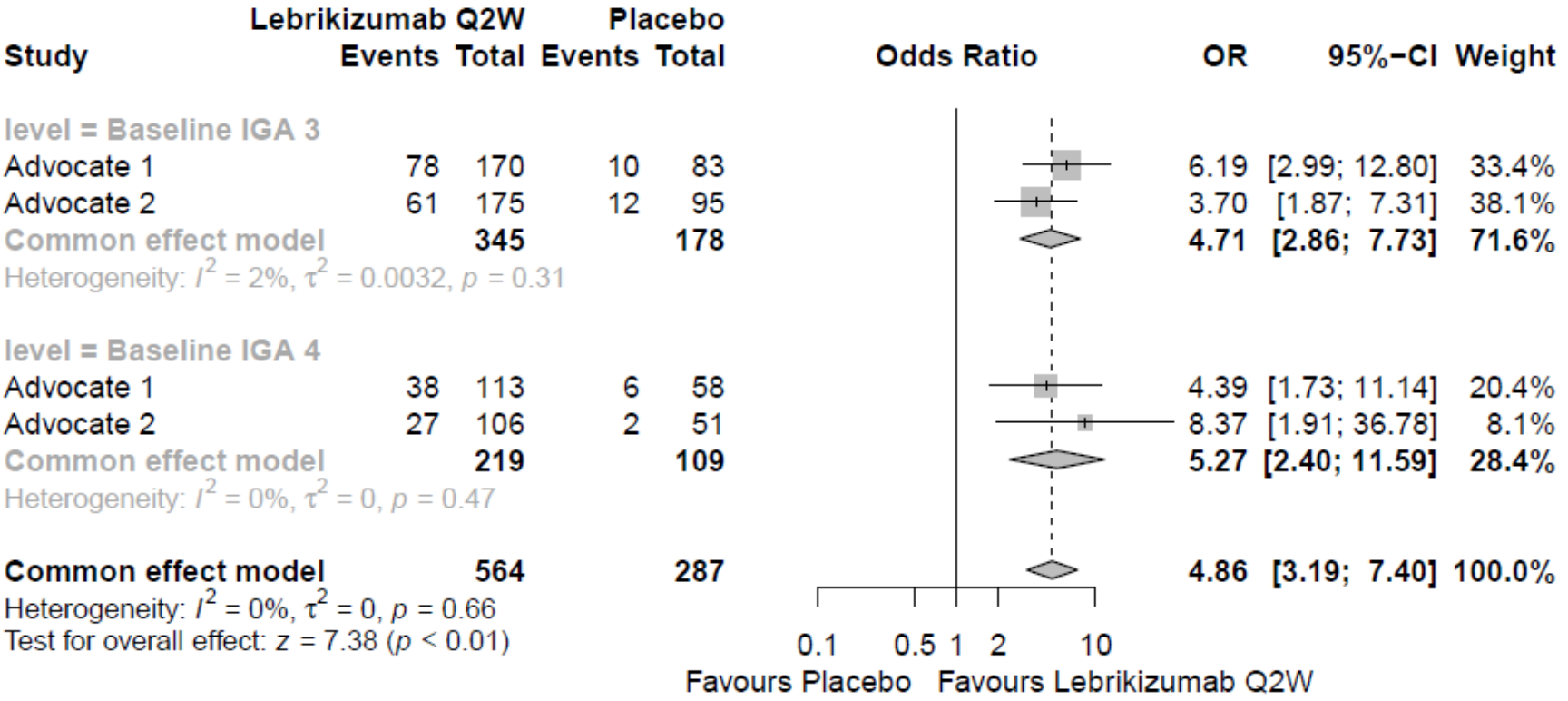


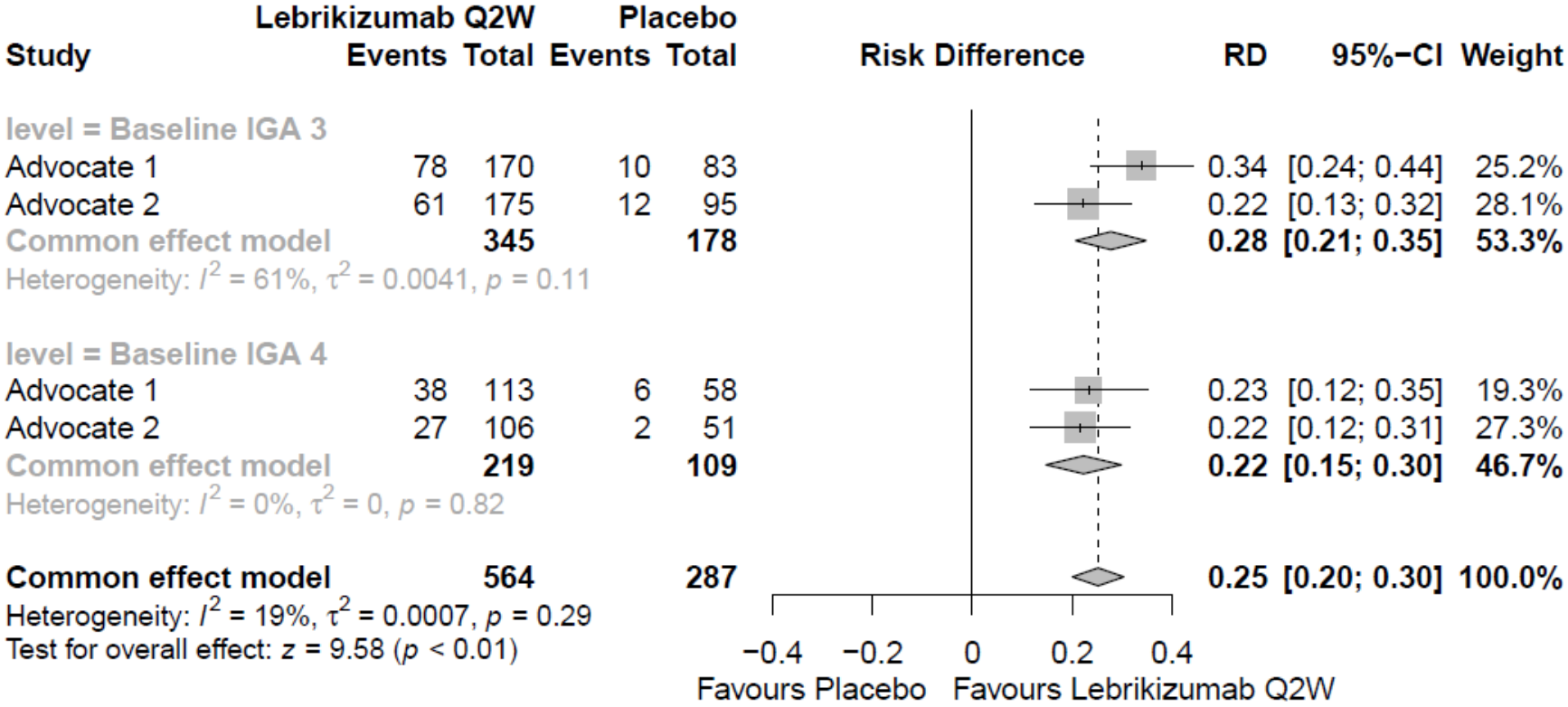

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 18 37 4 18 3.32 [0.92; 11.98] 10.6%
Advocate 2 13 30 1 17 12.24 [1.43; 104.56] 3.8%
Common effect model 67 35 4.68 [1.55; 14.09] 14.5%
Heterogeneity: I^2 = 5%, τ^2 = 0.0384, p = 0.31
level = Adults >= 18
Advocate 1 98 246 12 123 6.12 [3.20; 11.71] 41.8%
Advocate 2 75 251 13 129 3.80 [2.02; 7.17] 43.7%
Common effect model 497 252 4.80 [3.05; 7.55] 85.5%
Heterogeneity: I^2 = 6%, τ^2 = 0.0067, p = 0.30
Common effect model 564 287 4.78 [3.15; 7.27] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.55
Test for overall effect: z = 7.32 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 18 37 4 18 0.26 [0.01; 0.51] 4.4%
Advocate 2 13 30 1 17 0.37 [0.16; 0.58] 6.3%
Common effect model 67 35 0.33 [0.17; 0.49] 10.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.51
level = Adults >= 18
Advocate 1 98 246 12 123 0.30 [0.22; 0.38] 42.5%
Advocate 2 75 251 13 129 0.20 [0.12; 0.27] 46.8%
Common effect model 497 252 0.25 [0.19; 0.30] 89.3%
Heterogeneity: I^2 = 69%, τ^2 = 0.0037, p = 0.07
Common effect model 564 287 0.26 [0.20; 0.31] 100.0%
Heterogeneity: I^2 = 35%, τ^2 = 0.0025, p = 0.20
Test for overall effect: z = 9.54 (p < 0.01)
−0.4 −0.2 0 0.2 0.4
Favours Placebo
Favours Lebrikizumab Q2W

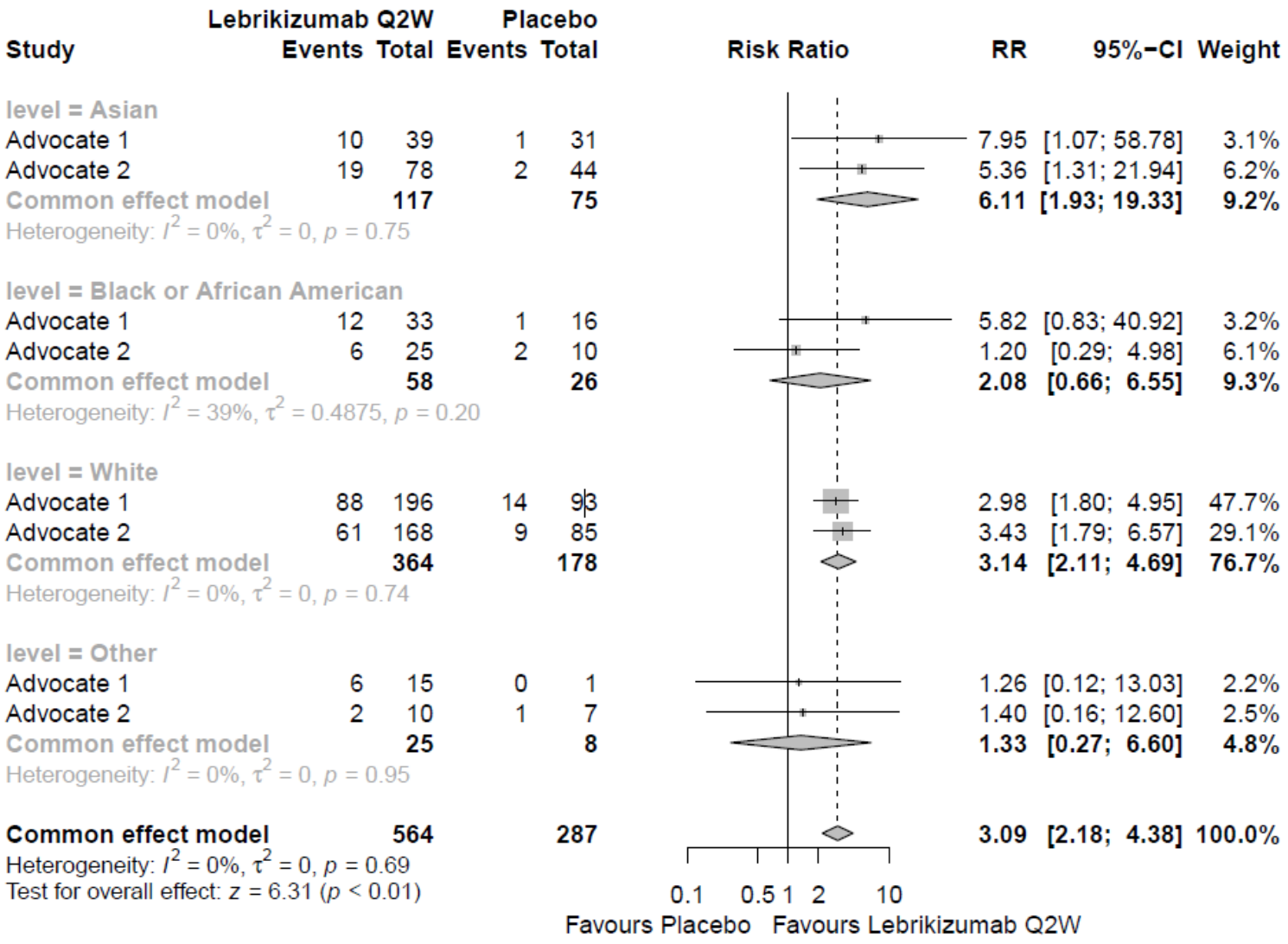
4.5.1.1.2 Krankheitsschwere

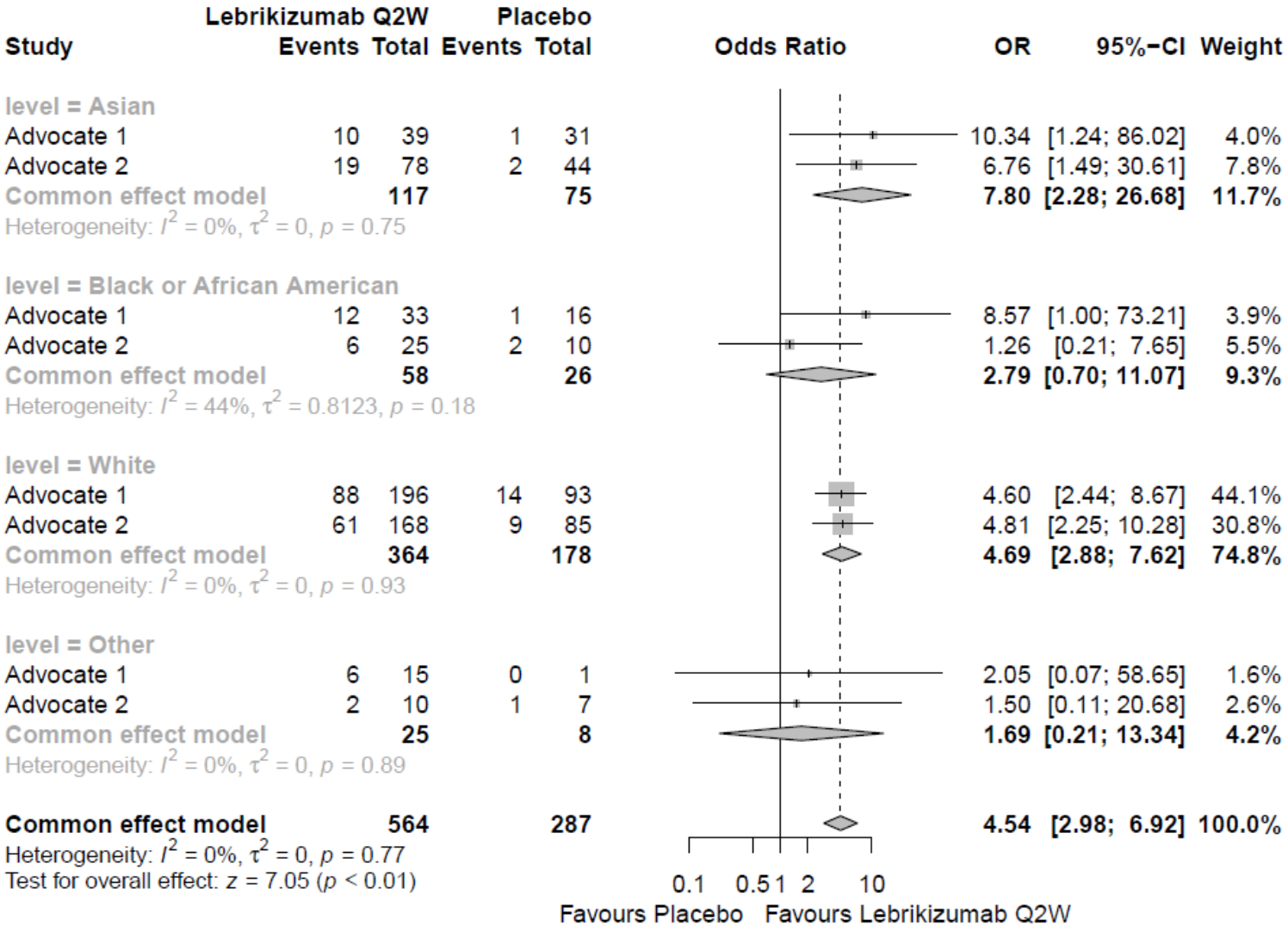


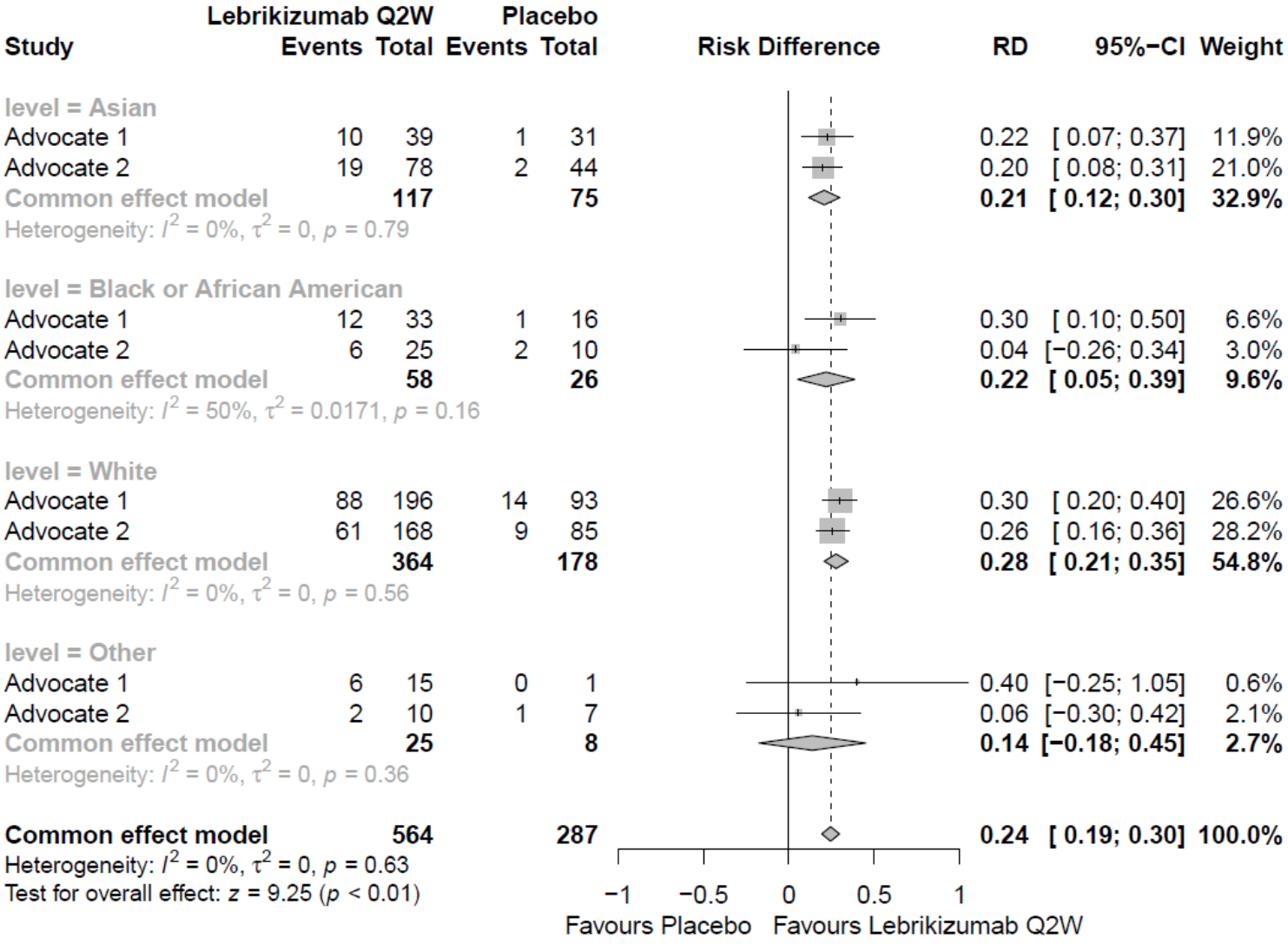

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Baseline IGA 3
Advocate 1 78 170 10 83 6.19 [2.99; 12.80] 33.4%
Advocate 2 61 175 12 95 3.70 [1.87; 7.31] 38.1%
Common effect model 345 178 4.71 [2.86; 7.73] 71.6%
Heterogeneity: I^2 = 2%, τ^2 = 0.0032, p = 0.31
level = Baseline IGA 4
Advocate 1 38 113 6 58 4.39 [1.73; 11.14] 20.4%
Advocate 2 27 106 2 51 8.37 [1.91; 36.78] 8.1%
Common effect model 219 109 5.27 [2.40; 11.59] 28.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.47
Common effect model 564 287 4.86 [3.19; 7.40] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.66
Test for overall effect: z = 7.38 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Baseline IGA 3
Advocate 1 78 170 10 83 0.34 [0.24; 0.44] 25.2%
Advocate 2 61 175 12 95 0.22 [0.13; 0.32] 28.1%
Common effect model 345 178 0.28 [0.21; 0.35] 53.3%
Heterogeneity: I^2 = 61%, τ^2 = 0.0041, p = 0.11
level = Baseline IGA 4
Advocate 1 38 113 6 58 0.23 [0.12; 0.35] 19.3%
Advocate 2 27 106 2 51 0.22 [0.12; 0.31] 27.3%
Common effect model 219 109 0.22 [0.15; 0.30] 46.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.82
Common effect model 564 287 0.25 [0.20; 0.30] 100.0%
Heterogeneity: I^2 = 19%, τ^2 = 0.0007, p = 0.29
Test for overall effect: z = 9.58 (p < 0.01)
−0.4
−0.2
0
0.2
0.4
Favours Placebo
Favours Lebrikizumab Q2W

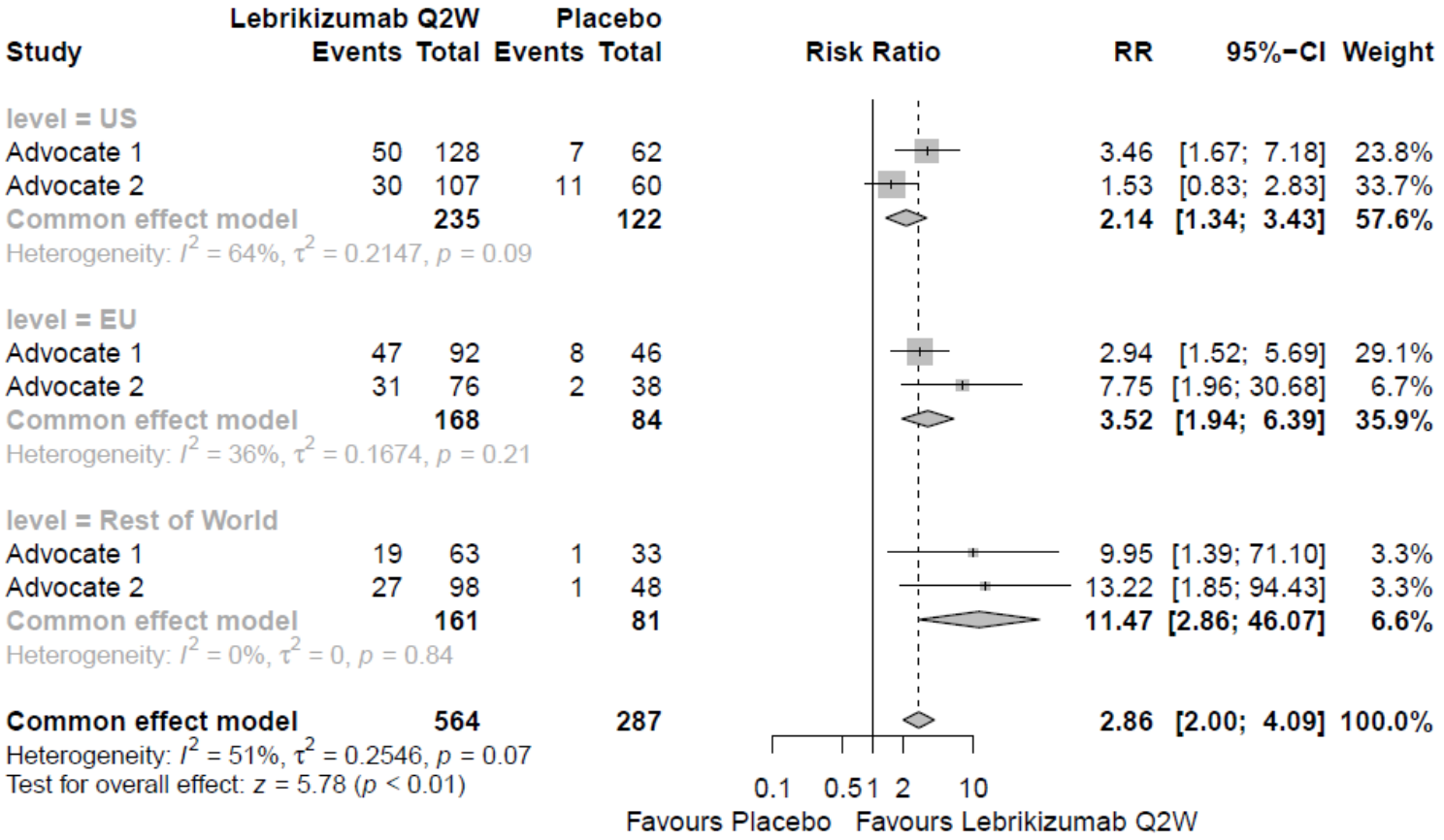
4.5.1.1.3 Ethnie

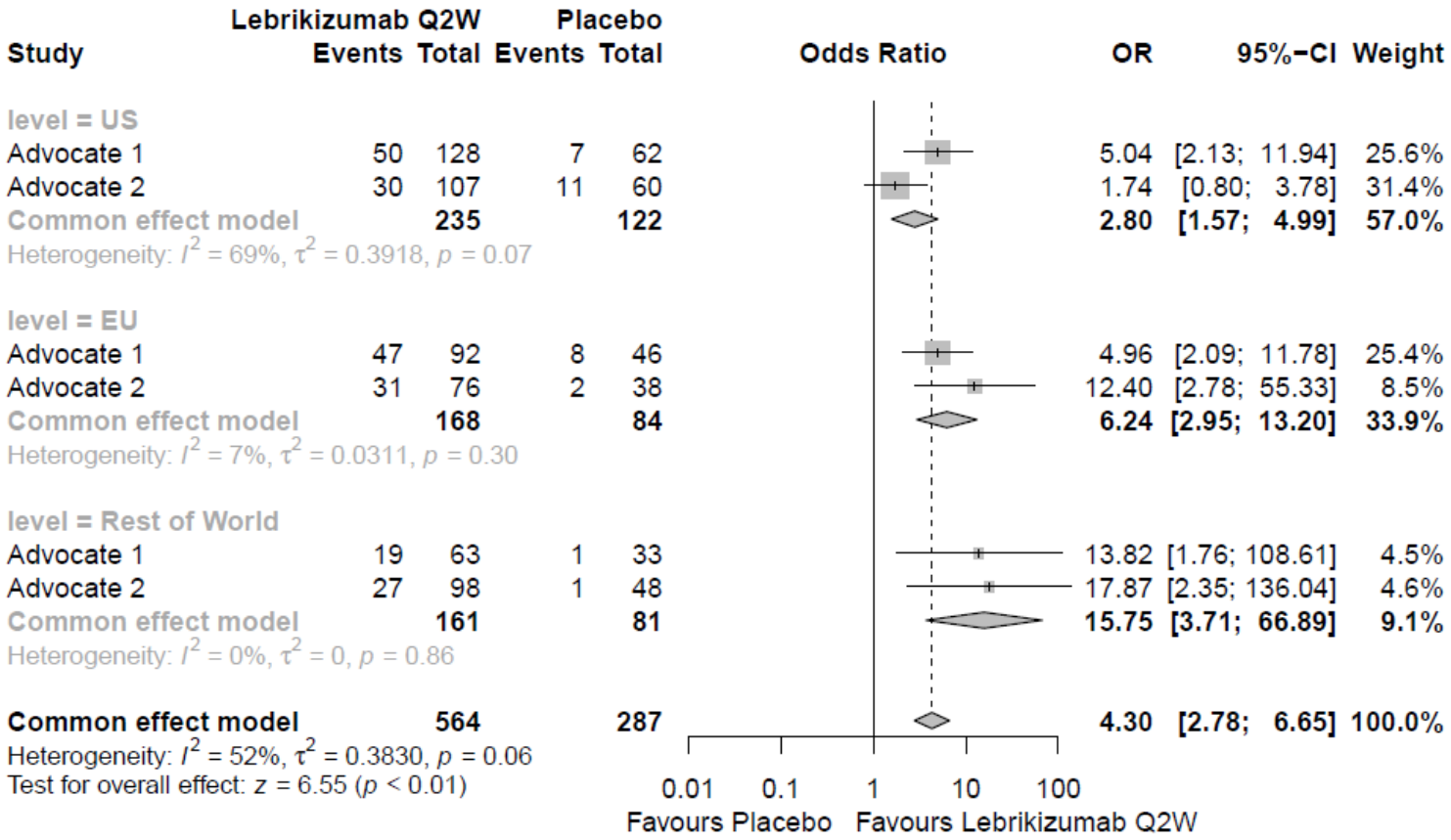


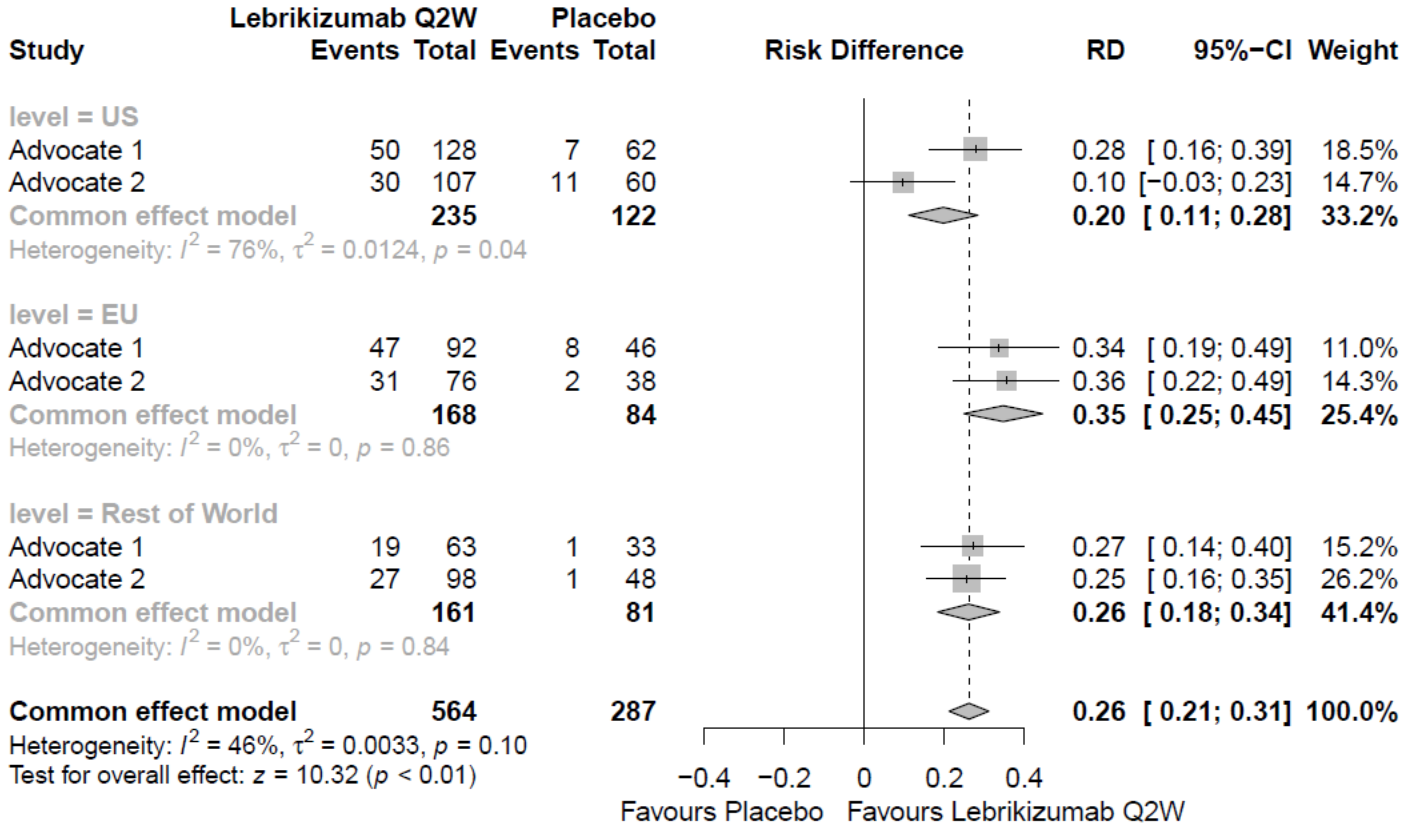

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Asian
Advocate 1 10 39 1 31 10.34 [1.24; 86.02] 4.0%
Advocate 2 19 78 2 44 6.76 [1.49; 30.61] 7.8%
Common effect model 117 75 7.80 [2.28; 26.68] 11.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.75
level = Black or African American
Advocate 1 12 33 1 16 8.57 [1.00; 73.21] 3.9%
Advocate 2 6 25 2 10 1.26 [0.21; 7.65] 5.5%
Common effect model 58 26 2.79 [0.70; 11.07] 9.3%
Heterogeneity: I^2 = 44%, τ^2 = 0.8123, p = 0.18
level = White
Advocate 1 88 196 14 93 4.60 [2.44; 8.67] 44.1%
Advocate 2 61 168 9 85 4.81 [2.25; 10.28] 30.8%
Common effect model 364 178 4.69 [2.88; 7.62] 74.8%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.93
level = Other
Advocate 1 6 15 0 1 2.05 [0.07; 58.65] 1.6%
Advocate 2 2 10 1 7 1.50 [0.11; 20.68] 2.6%
Common effect model 25 8 1.69 [0.21; 13.34] 4.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.89
Common effect model 564 287 4.54 [2.98; 6.92] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.77
Test for overall effect: z = 7.05 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Asian
Advocate 1 10 39 1 31 0.22 [0.07; 0.37] 11.9%
Advocate 2 19 78 2 44 0.20 [0.08; 0.31] 21.0%
Common effect model 117 75 0.21 [0.12; 0.30] 32.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.79
level = Black or African American
Advocate 1 12 33 1 16 0.30 [0.10; 0.50] 6.6%
Advocate 2 6 25 2 10 0.04 [−0.26; 0.34] 3.0%
Common effect model 58 26 0.22 [0.05; 0.39] 9.6%
Heterogeneity: I^2 = 50%, τ^2 = 0.0171, p = 0.16
level = White
Advocate 1 88 196 14 93 0.30 [0.20; 0.40] 26.6%
Advocate 2 61 168 9 85 0.26 [0.16; 0.36] 28.2%
Common effect model 364 178 0.28 [0.21; 0.35] 54.8%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.56
level = Other
Advocate 1 6 15 0 1 0.40 [−0.25; 1.05] 0.6%
Advocate 2 2 10 1 7 0.06 [−0.30; 0.42] 2.1%
Common effect model 25 8 0.14 [−0.18; 0.45] 2.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.36
Common effect model 564 287 0.24 [0.19; 0.30] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.63
Test for overall effect: z = 9.25 (p < 0.01)
−1 −0.5 0 0.5 1
Favours Placebo
Favours Lebrikizumab Q2W

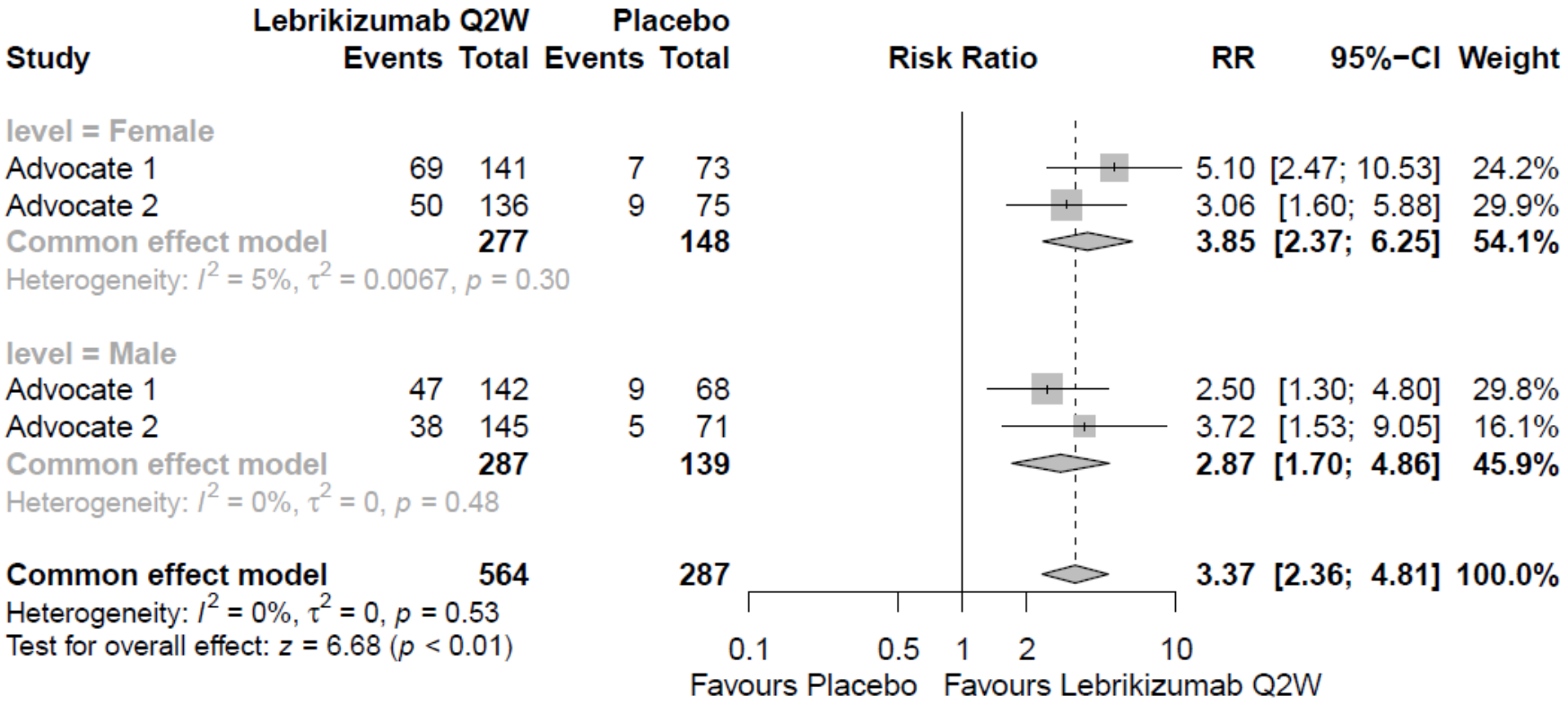
4.5.1.1.4 Region

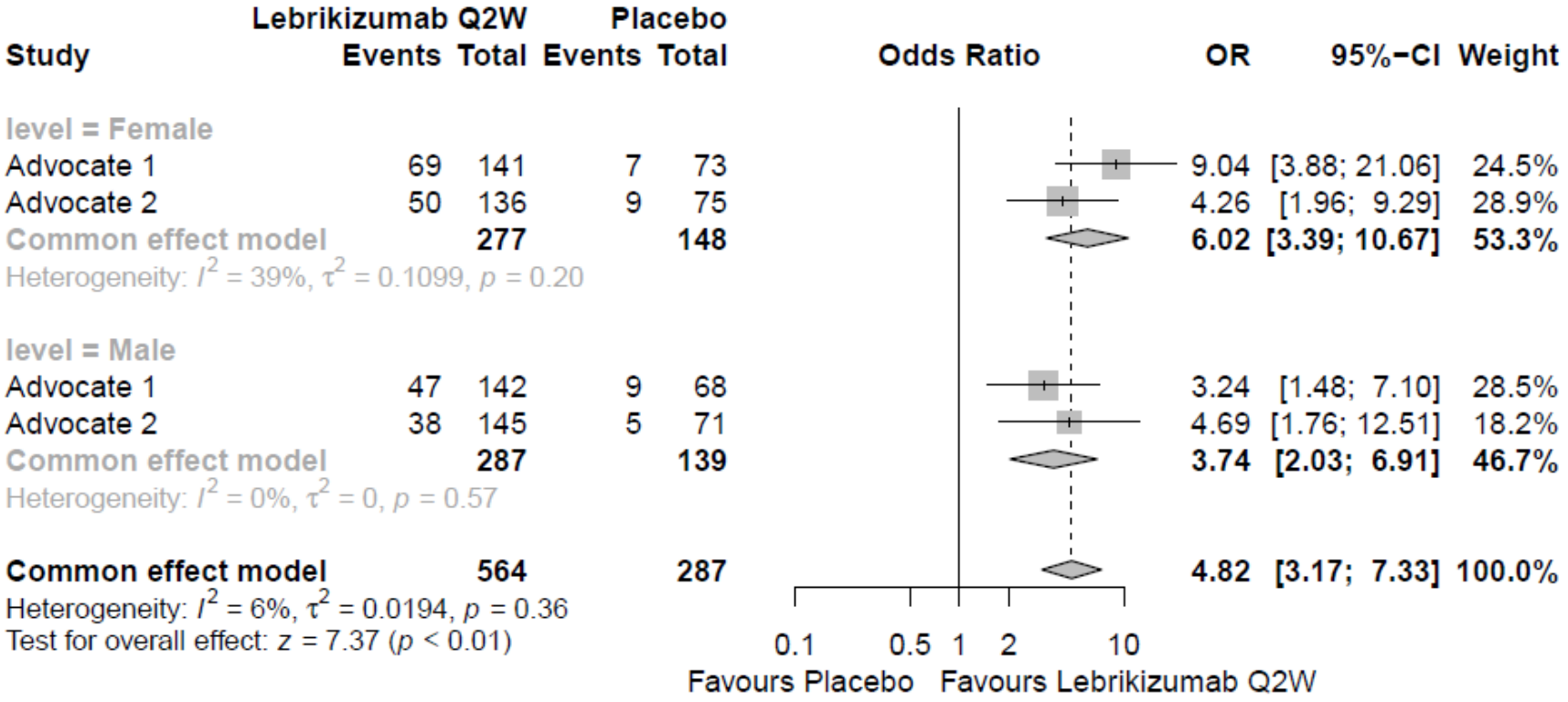


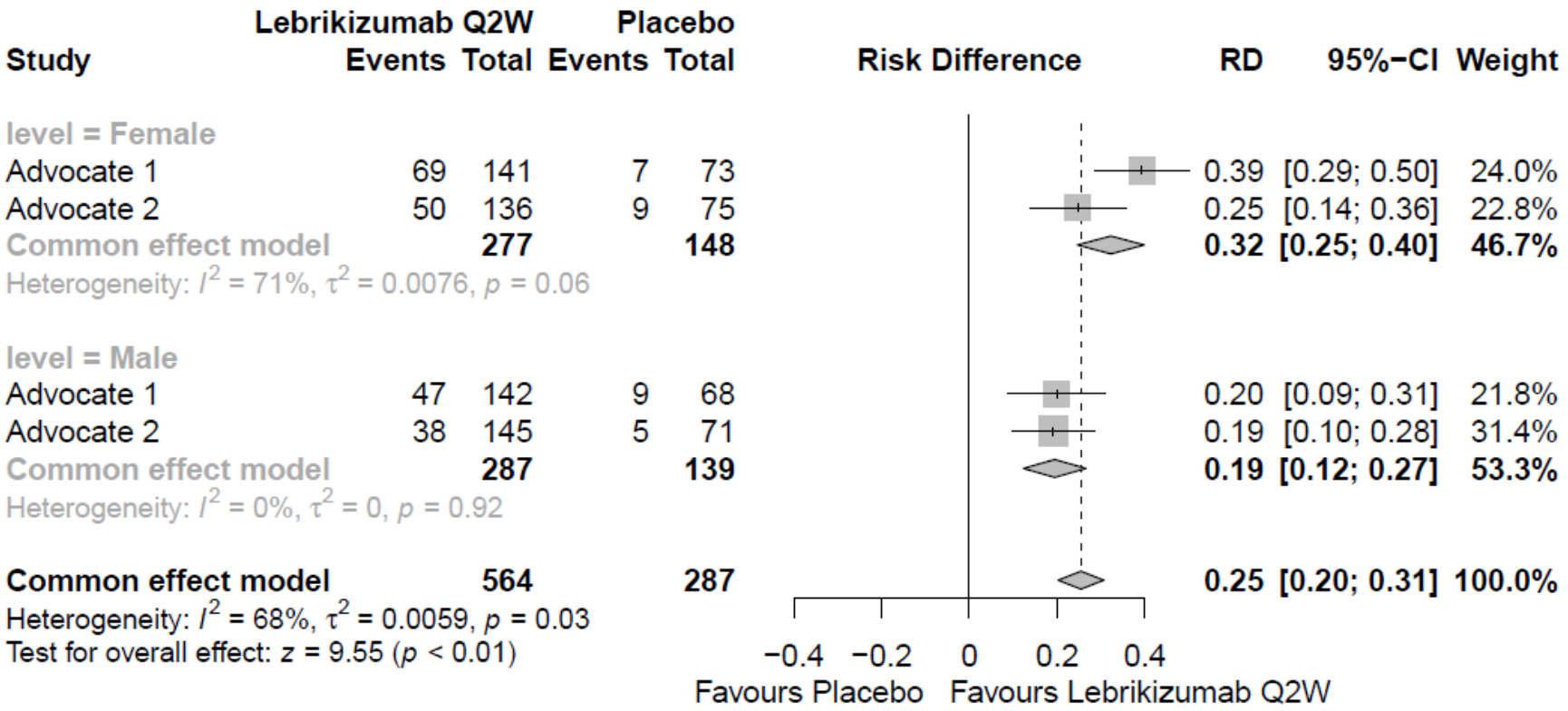

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = US
Advocate 1 50 128 7 62 5.04 [2.13; 11.94] 25.6%
Advocate 2 30 107 11 60 1.74 [0.80; 3.78] 31.4%
Common effect model 235 122 2.80 [1.57; 4.99] 57.0%
Heterogeneity: I^2 = 69%, τ^2 = 0.3918, p = 0.07
level = EU
Advocate 1 47 92 8 46 4.96 [2.09; 11.78] 25.4%
Advocate 2 31 76 2 38 12.40 [2.78; 55.33] 8.5%
Common effect model 168 84 6.24 [2.95; 13.20] 33.9%
Heterogeneity: I^2 = 7%, τ^2 = 0.0311, p = 0.30
level = Rest of World
Advocate 1 19 63 1 33 13.82 [1.76; 108.61] 4.5%
Advocate 2 27 98 1 48 17.87 [2.35; 136.04] 4.6%
Common effect model 161 81 15.75 [3.71; 66.89] 9.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.86
Common effect model 564 287 4.30 [2.78; 6.65] 100.0%
Heterogeneity: I^2 = 52%, τ^2 = 0.3830, p = 0.06
Test for overall effect: z = 6.55 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = US
Advocate 1 50 128 7 62 0.28 [0.16; 0.39] 18.5%
Advocate 2 30 107 11 60 0.10 [−0.03; 0.23] 14.7%
Common effect model 235 122 0.20 [0.11; 0.28] 33.2%
Heterogeneity: I^2 = 76%, τ^2 = 0.0124, p = 0.04
level = EU
Advocate 1 47 92 8 46 0.34 [0.19; 0.49] 11.0%
Advocate 2 31 76 2 38 0.36 [0.22; 0.49] 14.3%
Common effect model 168 84 0.35 [0.25; 0.45] 25.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.86
level = Rest of World
Advocate 1 19 63 1 33 0.27 [0.14; 0.40] 15.2%
Advocate 2 27 98 1 48 0.25 [0.16; 0.35] 26.2%
Common effect model 161 81 0.26 [0.18; 0.34] 41.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.84
Common effect model 564 287 0.26 [0.21; 0.31] 100.0%
Heterogeneity: I^2 = 46%, τ^2 = 0.0033, p = 0.10
Test for overall effect: z = 10.32 (p < 0.01)
−0.4 −0.2 0 0.2 0.4
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.1.5 Geschlecht

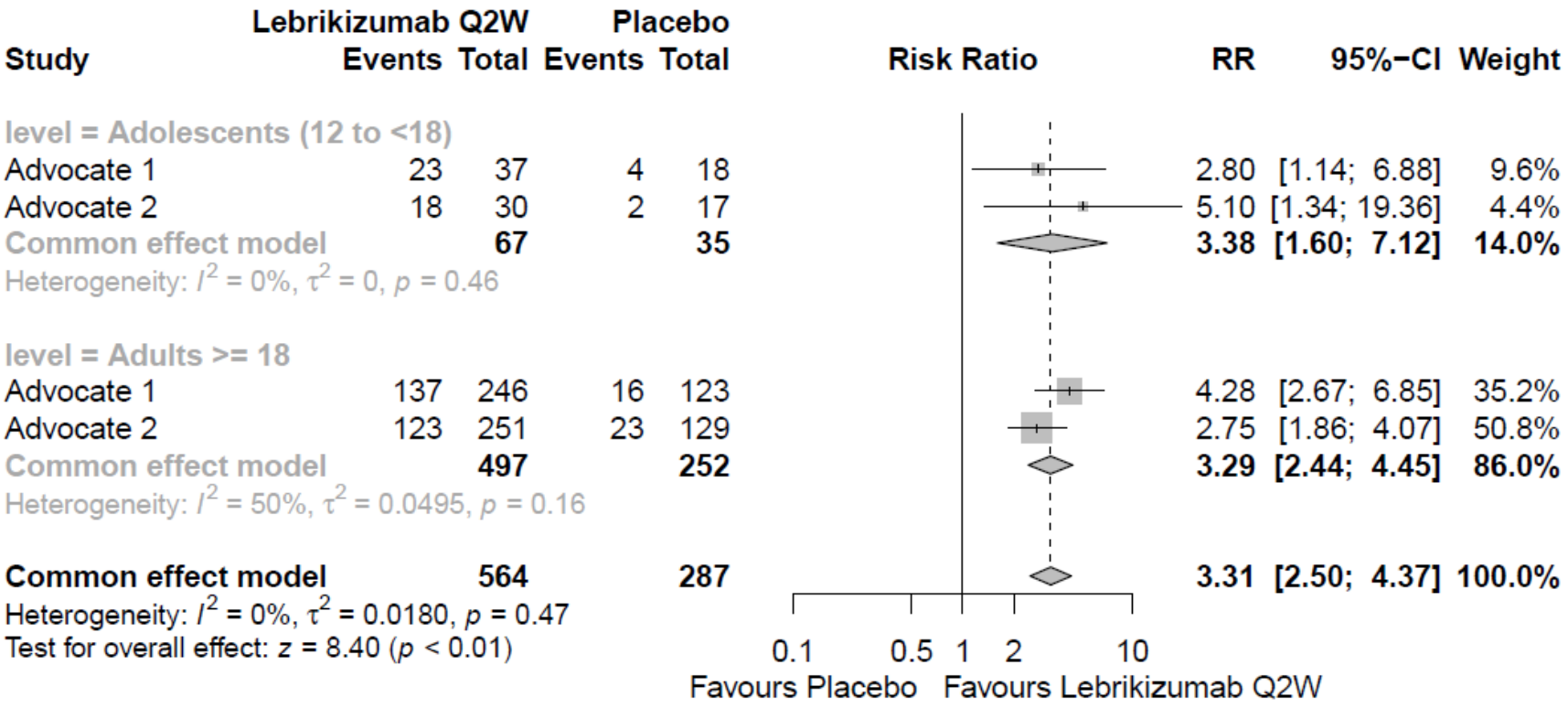


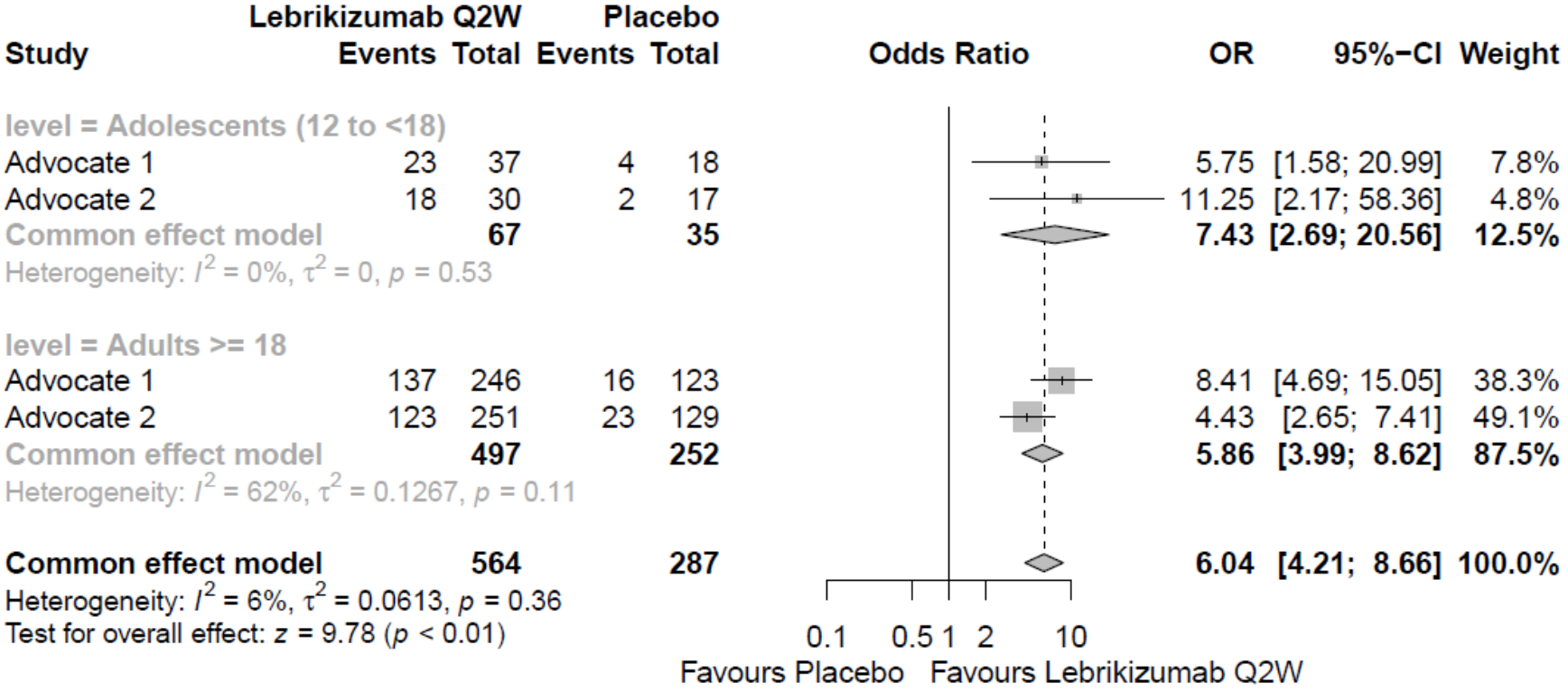

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Female
Advocate 1 69 141 7 73 9.04 [3.88; 21.06] 24.5%
Advocate 2 50 136 9 75 4.26 [1.96; 9.29] 28.9%
Common effect model 277 148 6.02 [3.39; 10.67] 53.3%
Heterogeneity: I^2 = 39%, τ^2 = 0.1099, p = 0.20
level = Male
Advocate 1 47 142 9 68 3.24 [1.48; 7.10] 28.5%
Advocate 2 38 145 5 71 4.69 [1.76; 12.51] 18.2%
Common effect model 287 139 3.74 [2.03; 6.91] 46.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.57
Common effect model 564 287 4.82 [3.17; 7.33] 100.0%
Heterogeneity: I^2 = 6%, τ^2 = 0.0194, p = 0.36
Test for overall effect: z = 7.37 (p < 0.01)
0.1
0.5
1
2
10
Favours Placebo
Favours Lebrikizumab Q2W

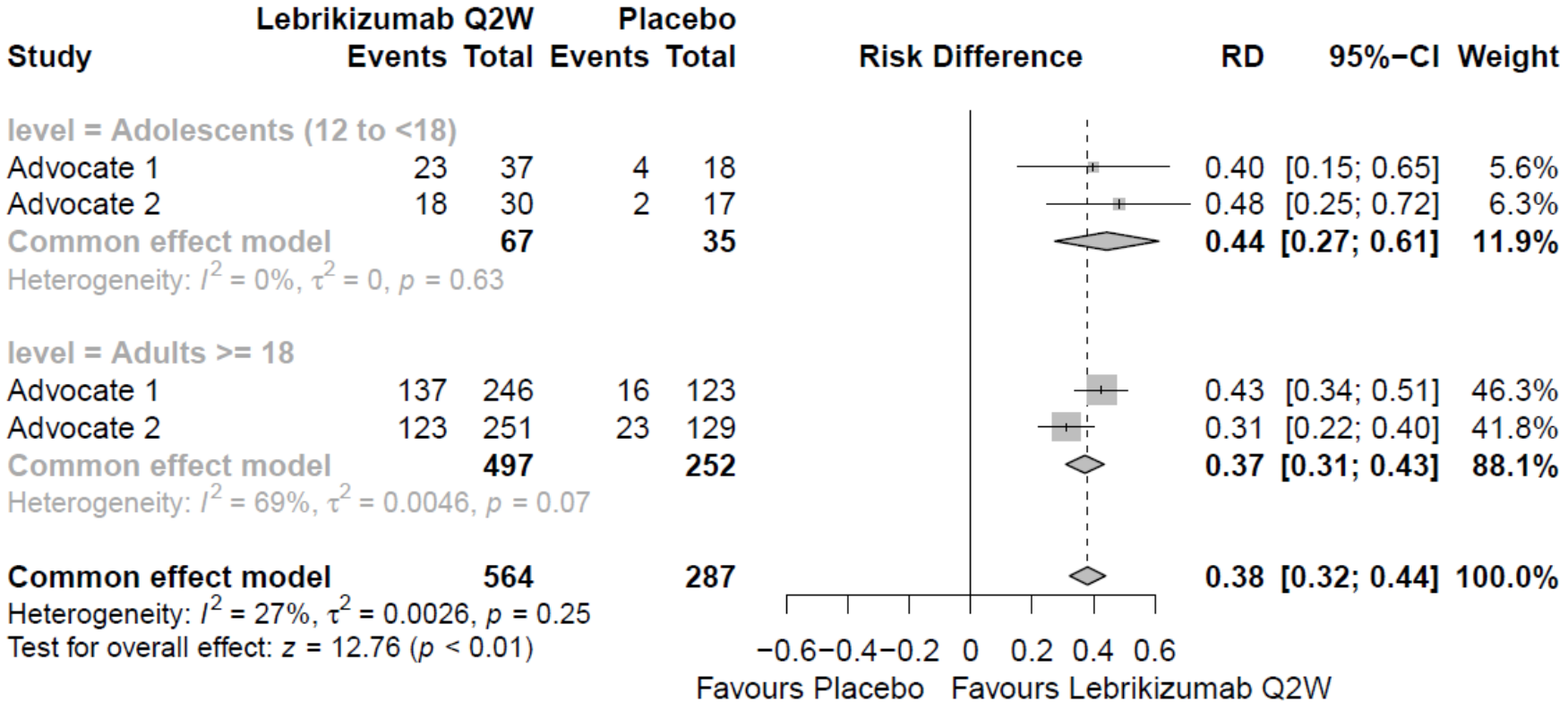

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Female
Advocate 1 69 141 7 73 0.39 [0.29; 0.50] 24.0%
Advocate 2 50 136 9 75 0.25 [0.14; 0.36] 22.8%
Common effect model 277 148 0.32 [0.25; 0.40] 46.7%
Heterogeneity: I^2 = 71%, τ^2 = 0.0076, p = 0.06
level = Male
Advocate 1 47 142 9 68 0.20 [0.09; 0.31] 21.8%
Advocate 2 38 145 5 71 0.19 [0.10; 0.28] 31.4%
Common effect model 287 139 0.19 [0.12; 0.27] 53.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.92
Common effect model 564 287 0.25 [0.20; 0.31] 100.0%
Heterogeneity: I^2 = 68%, τ^2 = 0.0059, p = 0.03
Test for overall effect: z = 9.55 (p < 0.01)
−0.4 −0.2 0 0.2 0.4
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.2 EASI-75

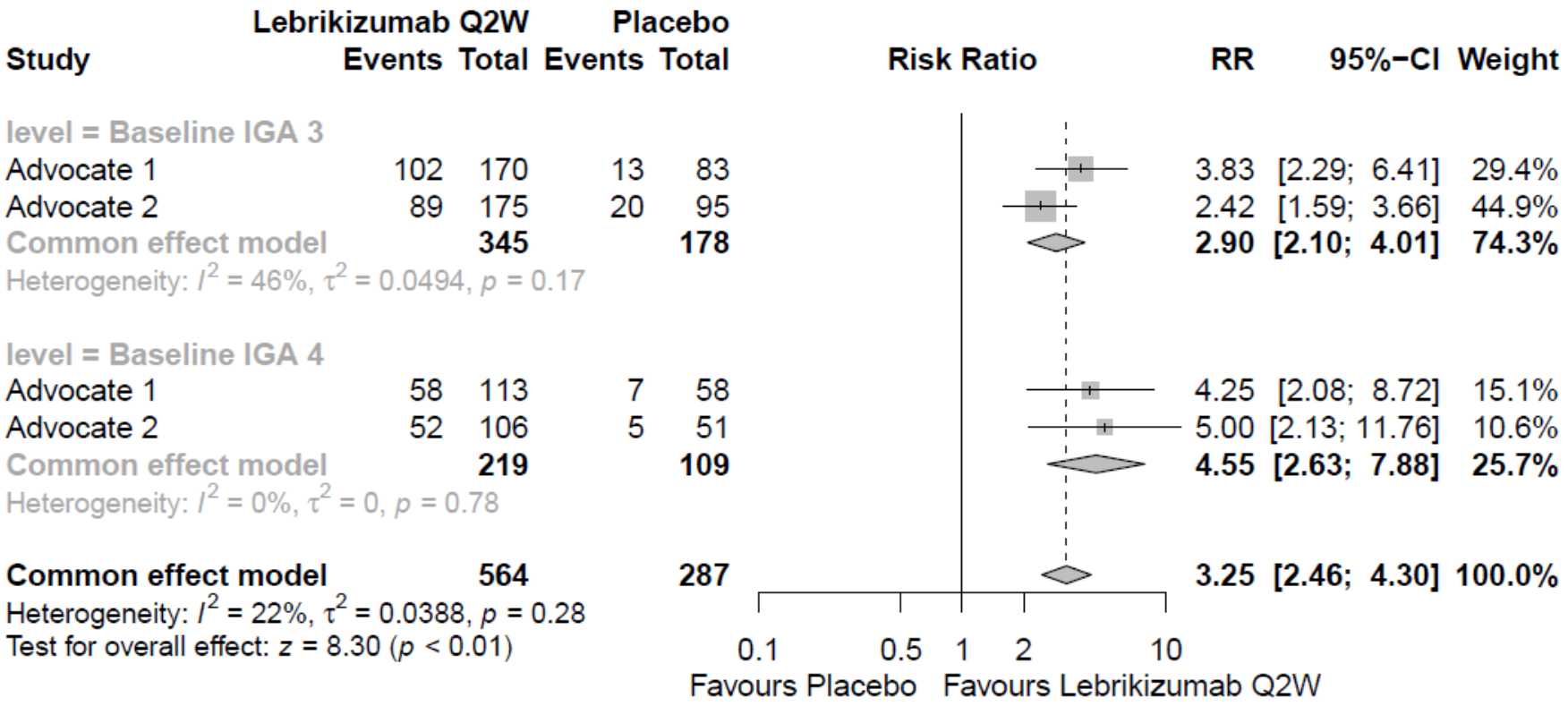
4.5.1.2.1 Altersgruppe

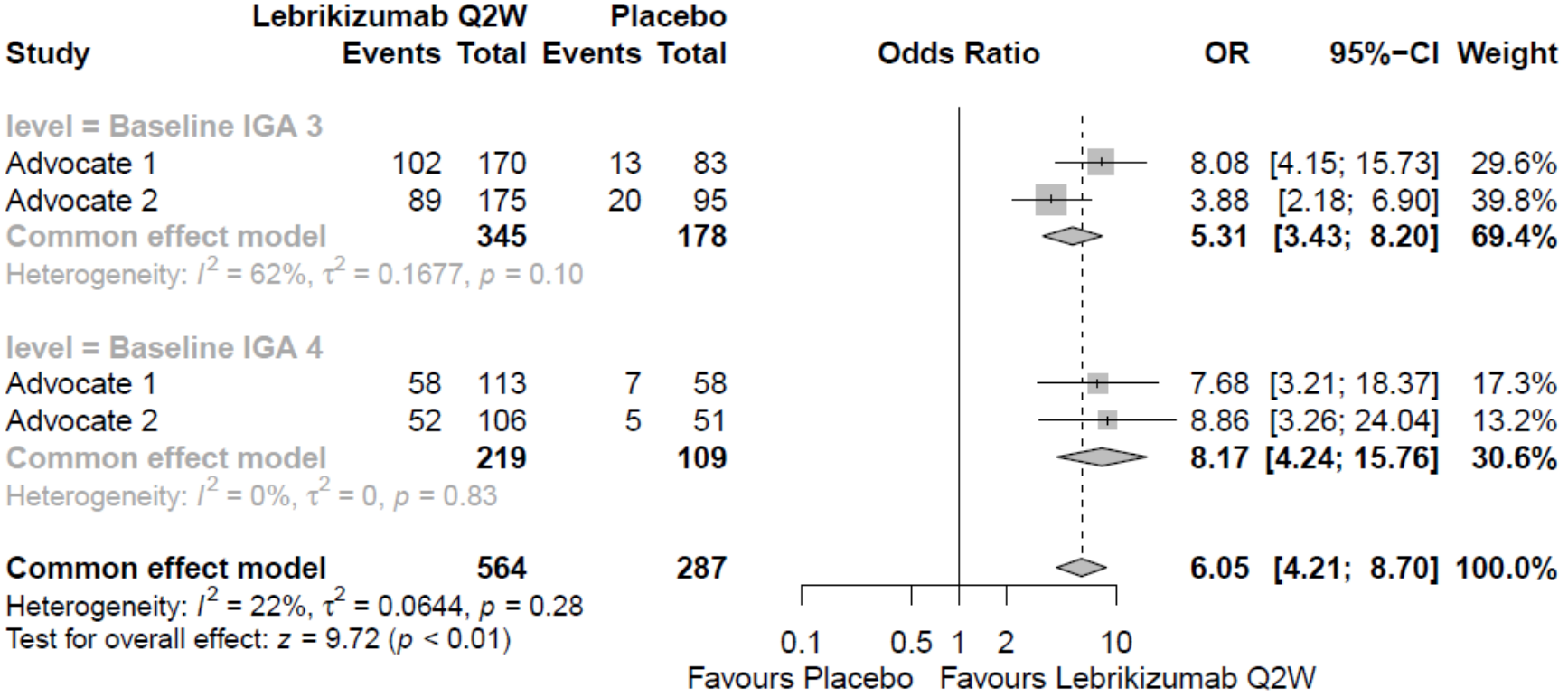


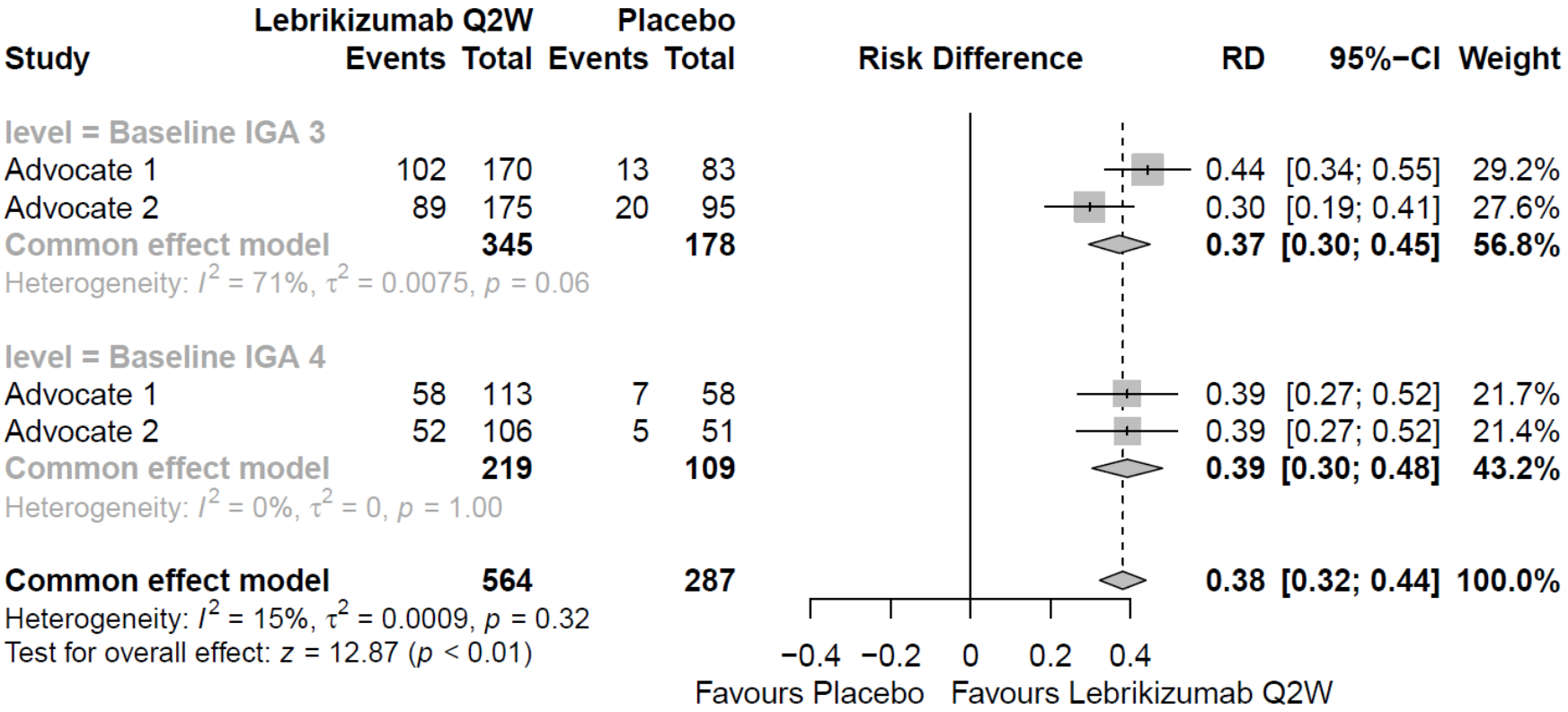

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 23 37 4 18 5.75 [1.58; 20.99] 7.8%
Advocate 2 18 30 2 17 11.25 [2.17; 58.36] 4.8%
Common effect model 67 35 7.43 [2.69; 20.56] 12.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.53
level = Adults >= 18
Advocate 1 137 246 16 123 8.41 [4.69; 15.05] 38.3%
Advocate 2 123 251 23 129 4.43 [2.65; 7.41] 49.1%
Common effect model 497 252 5.86 [3.99; 8.62] 87.5%
Heterogeneity: I^2 = 62%, τ^2 = 0.1267, p = 0.11
Common effect model 564 287 6.04 [4.21; 8.66] 100.0%
Heterogeneity: I^2 = 6%, τ^2 = 0.0613, p = 0.36
Test for overall effect: z = 9.78 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 23 37 4 18 0.40 [0.15; 0.65] 5.6%
Advocate 2 18 30 2 17 0.48 [0.25; 0.72] 6.3%
Common effect model 67 35 0.44 [0.27; 0.61] 11.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.63
level = Adults >= 18
Advocate 1 137 246 16 123 0.43 [0.34; 0.51] 46.3%
Advocate 2 123 251 23 129 0.31 [0.22; 0.40] 41.8%
Common effect model 497 252 0.37 [0.31; 0.43] 88.1%
Heterogeneity: I^2 = 69%, τ^2 = 0.0046, p = 0.07
Common effect model 564 287 0.38 [0.32; 0.44] 100.0%
Heterogeneity: I^2 = 27%, τ^2 = 0.0026, p = 0.25
Test for overall effect: z = 12.76 (p < 0.01)
−0.6 −0.4 −0.2 0 0.2 0.4 0.6
Favours Placebo
Favours Lebrikizumab Q2W

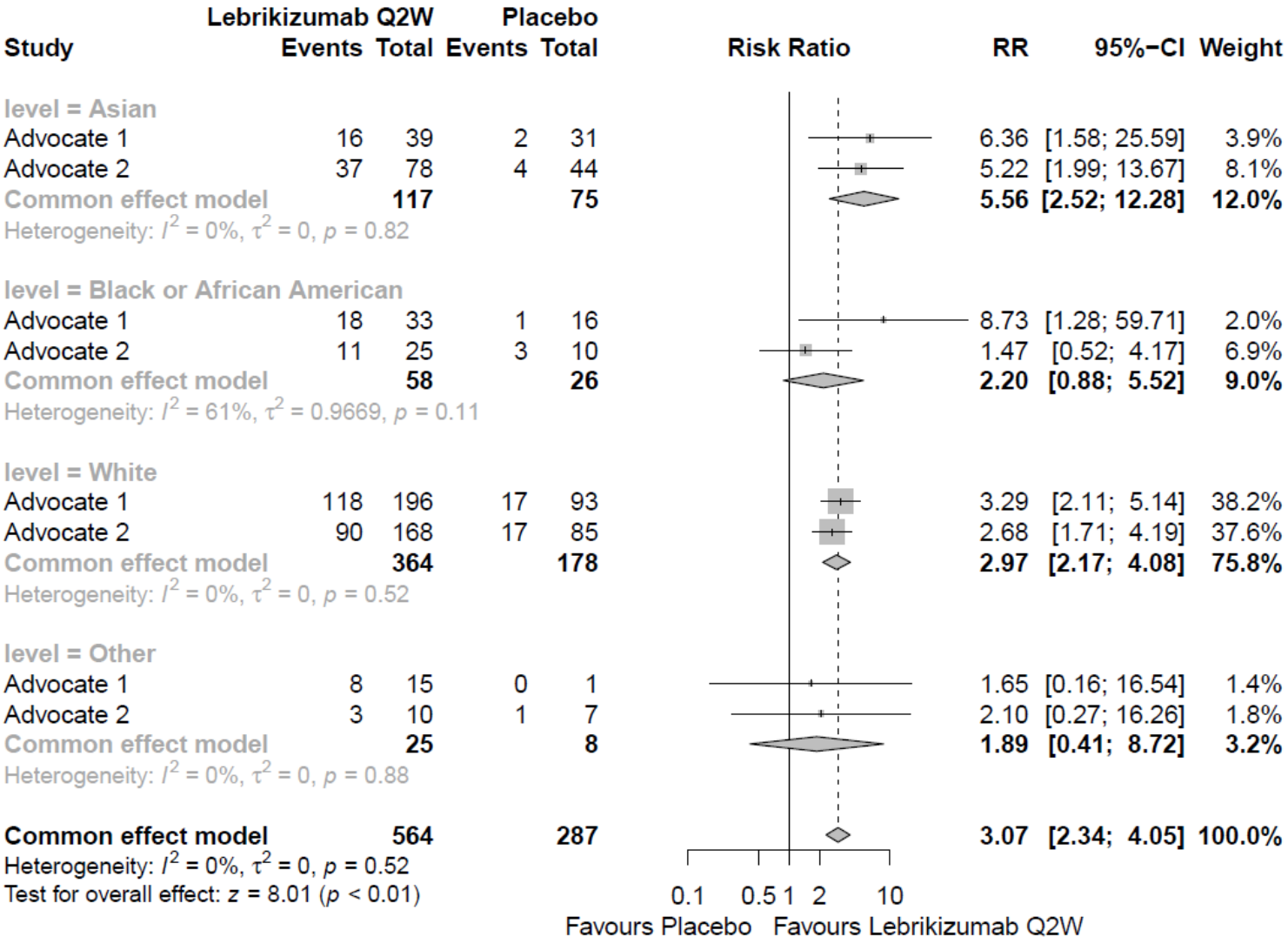
4.5.1.2.2 Krankheitsschwere

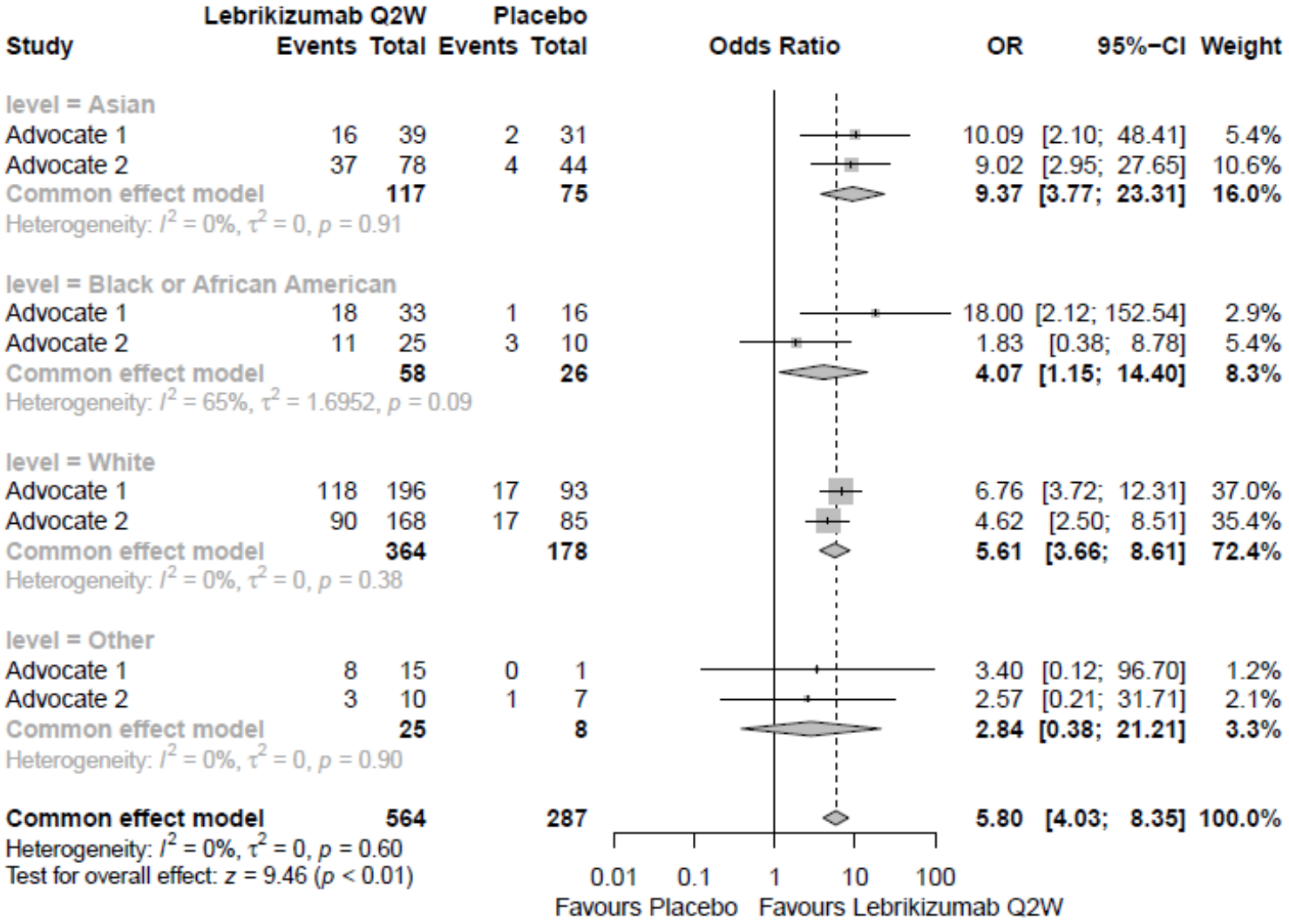


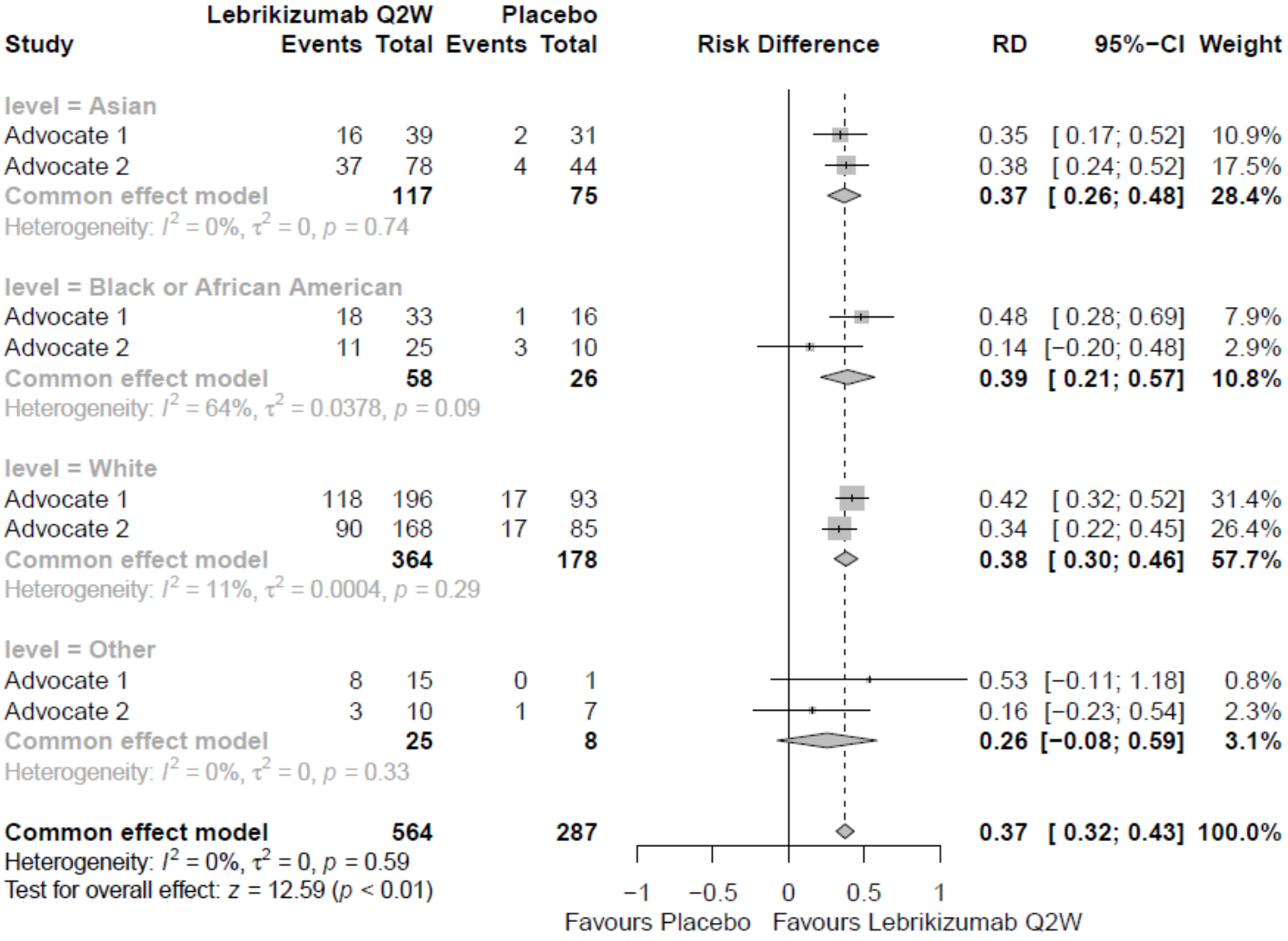

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Baseline IGA 3
Advocate 1 102 170 13 83 8.08 [4.15; 15.73] 29.6%
Advocate 2 89 175 20 95 3.88 [2.18; 6.90] 39.8%
Common effect model 345 178 5.31 [3.43; 8.20] 69.4%
Heterogeneity: I^2 = 62%, τ^2 = 0.1677, p = 0.10
level = Baseline IGA 4
Advocate 1 58 113 7 58 7.68 [3.21; 18.37] 17.3%
Advocate 2 52 106 5 51 8.86 [3.26; 24.04] 13.2%
Common effect model 219 109 8.17 [4.24; 15.76] 30.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.83
Common effect model 564 287 6.05 [4.21; 8.70] 100.0%
Heterogeneity: I^2 = 22%, τ^2 = 0.0644, p = 0.28
Test for overall effect: z = 9.72 (p < 0.01)
0.1
0.5
1
2
10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Baseline IGA 3
Advocate 1 102 170 13 83 0.44 [0.34; 0.55] 29.2%
Advocate 2 89 175 20 95 0.30 [0.19; 0.41] 27.6%
Common effect model 345 178 0.37 [0.30; 0.45] 56.8%
Heterogeneity: I^2 = 71%, τ^2 = 0.0075, p = 0.06
level = Baseline IGA 4
Advocate 1 58 113 7 58 0.39 [0.27; 0.52] 21.7%
Advocate 2 52 106 5 51 0.39 [0.27; 0.52] 21.4%
Common effect model 219 109 0.39 [0.30; 0.48] 43.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 1.00
Common effect model 564 287 0.38 [0.32; 0.44] 100.0%
Heterogeneity: I^2 = 15%, τ^2 = 0.0009, p = 0.32
Test for overall effect: z = 12.87 (p < 0.01)
−0.4 −0.2 0 0.2 0.4
Favours Placebo
Favours Lebrikizumab Q2W

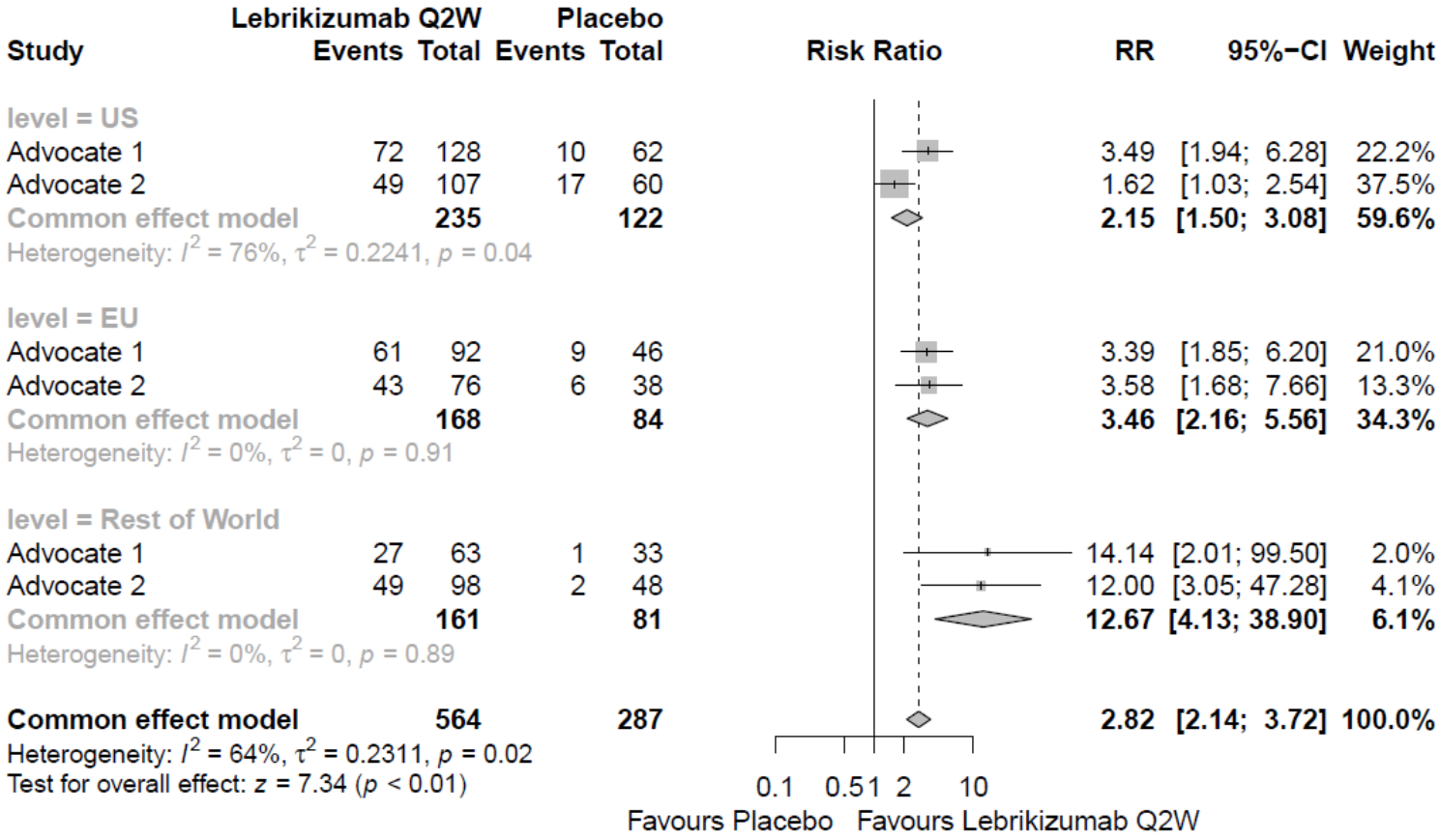
4.5.1.2.3 Ethnie

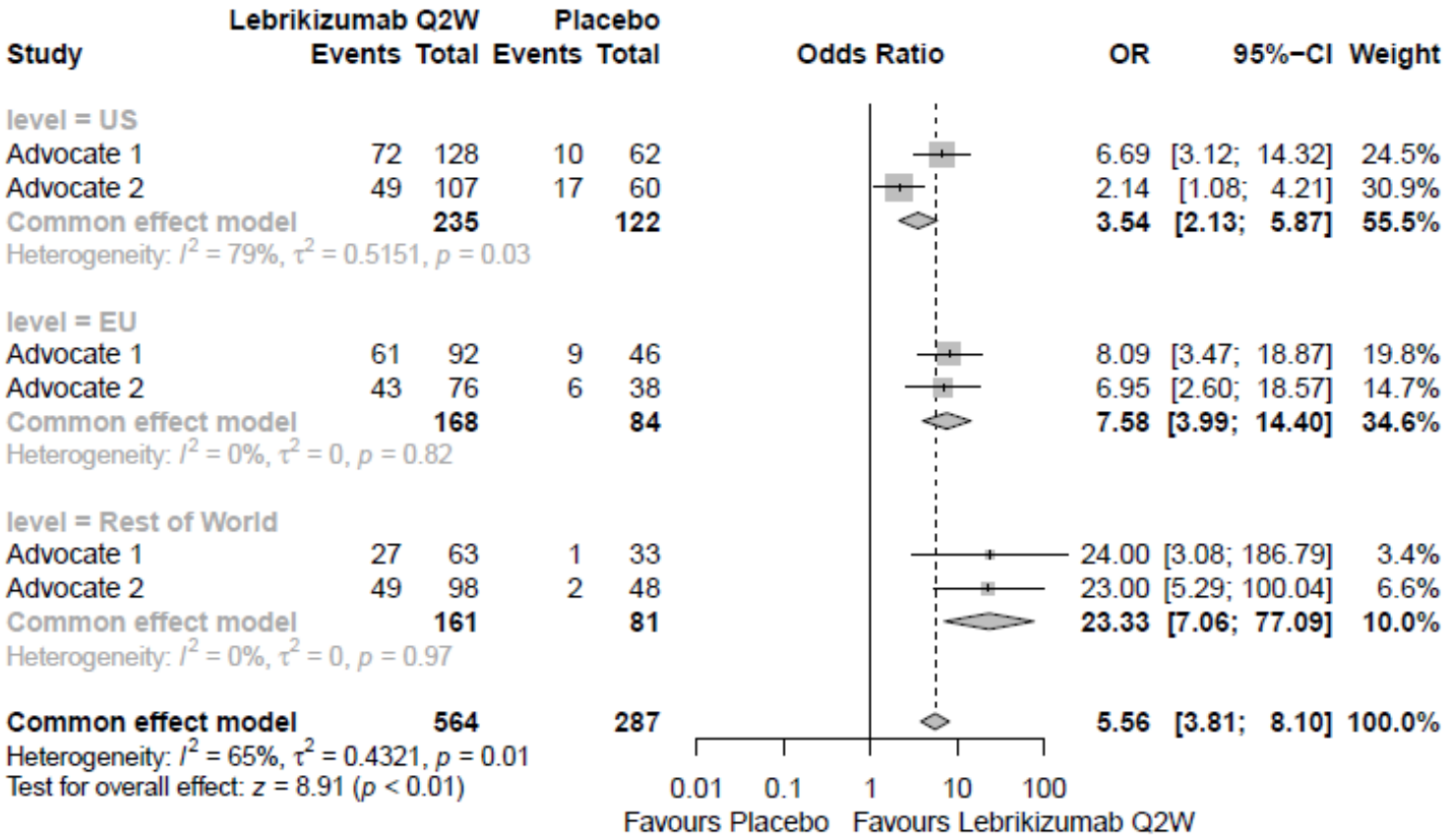


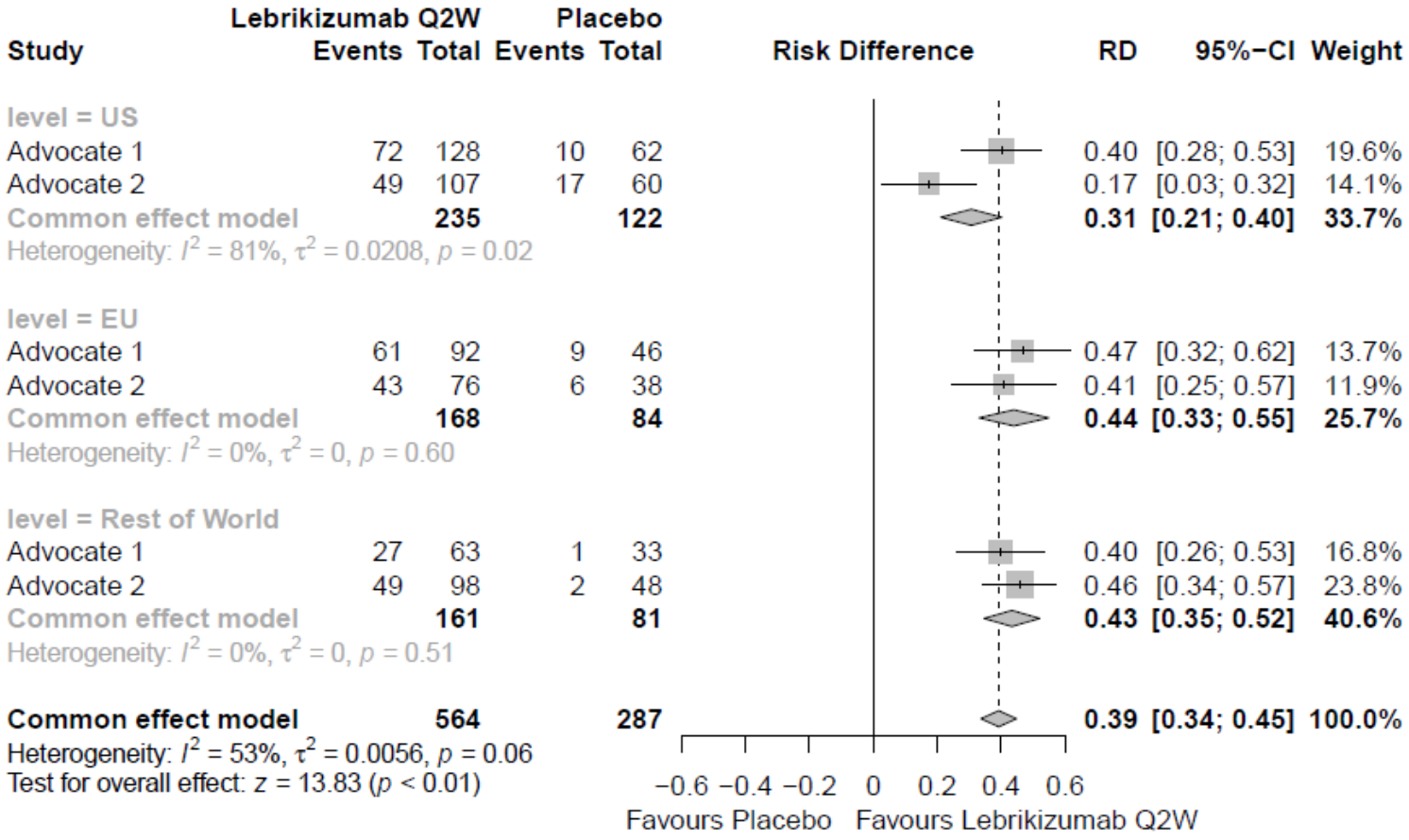

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Asian
Advocate 1 16 39 2 31 10.09 [2.10; 48.41] 5.4%
Advocate 2 37 78 4 44 9.02 [2.95; 27.65] 10.6%
Common effect model 117 75 9.37 [3.77; 23.31] 16.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.91
level = Black or African American
Advocate 1 18 33 1 16 18.00 [2.12; 152.54] 2.9%
Advocate 2 11 25 3 10 1.83 [0.38; 8.78] 5.4%
Common effect model 58 26 4.07 [1.15; 14.40] 8.3%
Heterogeneity: I^2 = 65%, τ^2 = 1.6952, p = 0.09
level = White
Advocate 1 118 196 17 93 6.76 [3.72; 12.31] 37.0%
Advocate 2 90 168 17 85 4.62 [2.50; 8.51] 35.4%
Common effect model 364 178 5.61 [3.66; 8.61] 72.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.38
level = Other
Advocate 1 8 15 0 1 3.40 [0.12; 96.70] 1.2%
Advocate 2 3 10 1 7 2.57 [0.21; 31.71] 2.1%
Common effect model 25 8 2.84 [0.38; 21.21] 3.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.90
Common effect model 564 287 5.80 [4.03; 8.35] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.60
Test for overall effect: z = 9.46 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Asian
Advocate 1 16 39 2 31 0.35 [0.17; 0.52] 10.9%
Advocate 2 37 78 4 44 0.38 [0.24; 0.52] 17.5%
Common effect model 117 75 0.37 [0.26; 0.48] 28.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.74
level = Black or African American
Advocate 1 18 33 1 16 0.48 [0.28; 0.69] 7.9%
Advocate 2 11 25 3 10 0.14 [−0.20; 0.48] 2.9%
Common effect model 58 26 0.39 [0.21; 0.57] 10.8%
Heterogeneity: I^2 = 64%, τ^2 = 0.0378, p = 0.09
level = White
Advocate 1 118 196 17 93 0.42 [0.32; 0.52] 31.4%
Advocate 2 90 168 17 85 0.34 [0.22; 0.45] 26.4%
Common effect model 364 178 0.38 [0.30; 0.46] 57.7%
Heterogeneity: I^2 = 11%, τ^2 = 0.0004, p = 0.29
level = Other
Advocate 1 8 15 0 1 0.53 [−0.11; 1.18] 0.8%
Advocate 2 3 10 1 7 0.16 [−0.23; 0.54] 2.3%
Common effect model 25 8 0.26 [−0.08; 0.59] 3.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.33
Common effect model 564 287 0.37 [0.32; 0.43] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.59
Test for overall effect: z = 12.59 (p < 0.01)
−1 −0.5 0 0.5 1
Favours Placebo
Favours Lebrikizumab Q2W

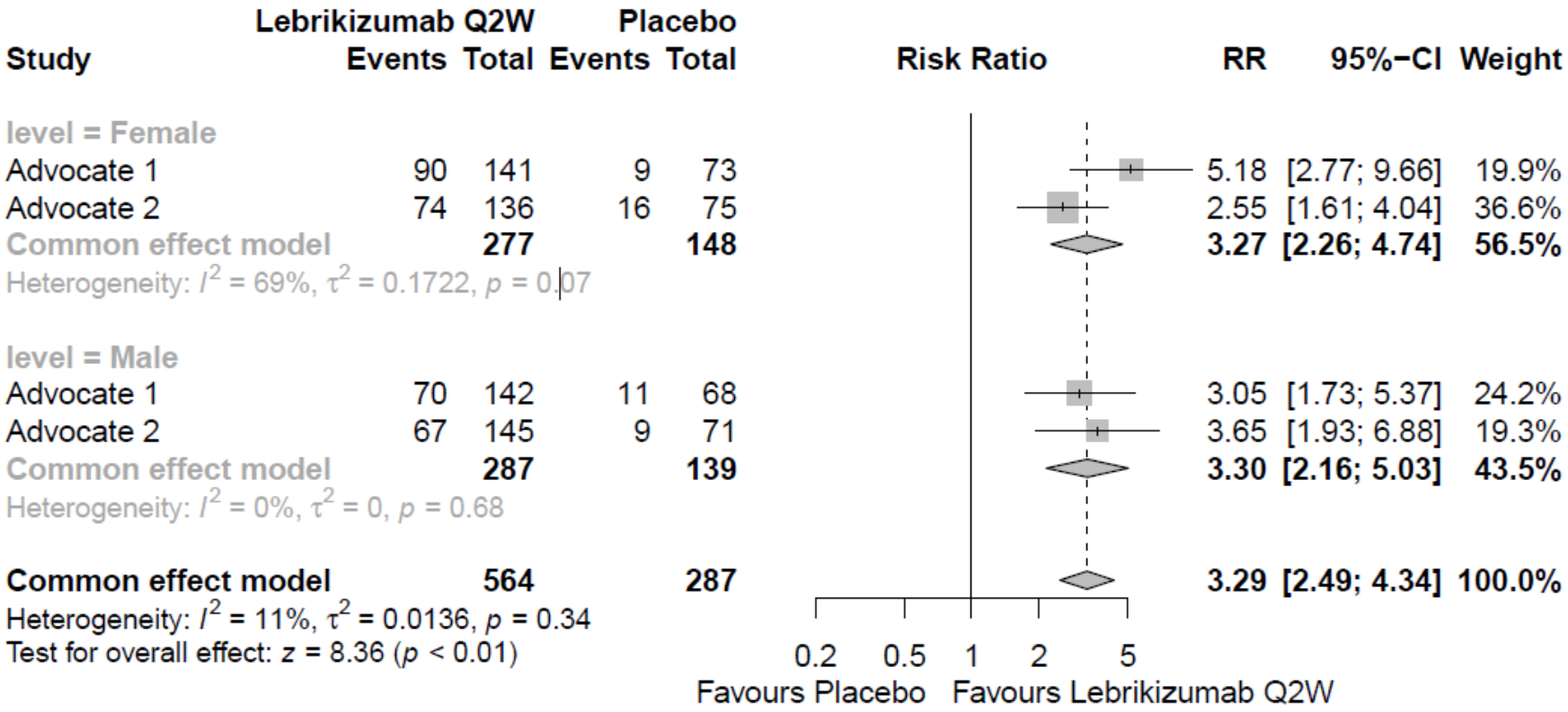
4.5.1.2.4 Region

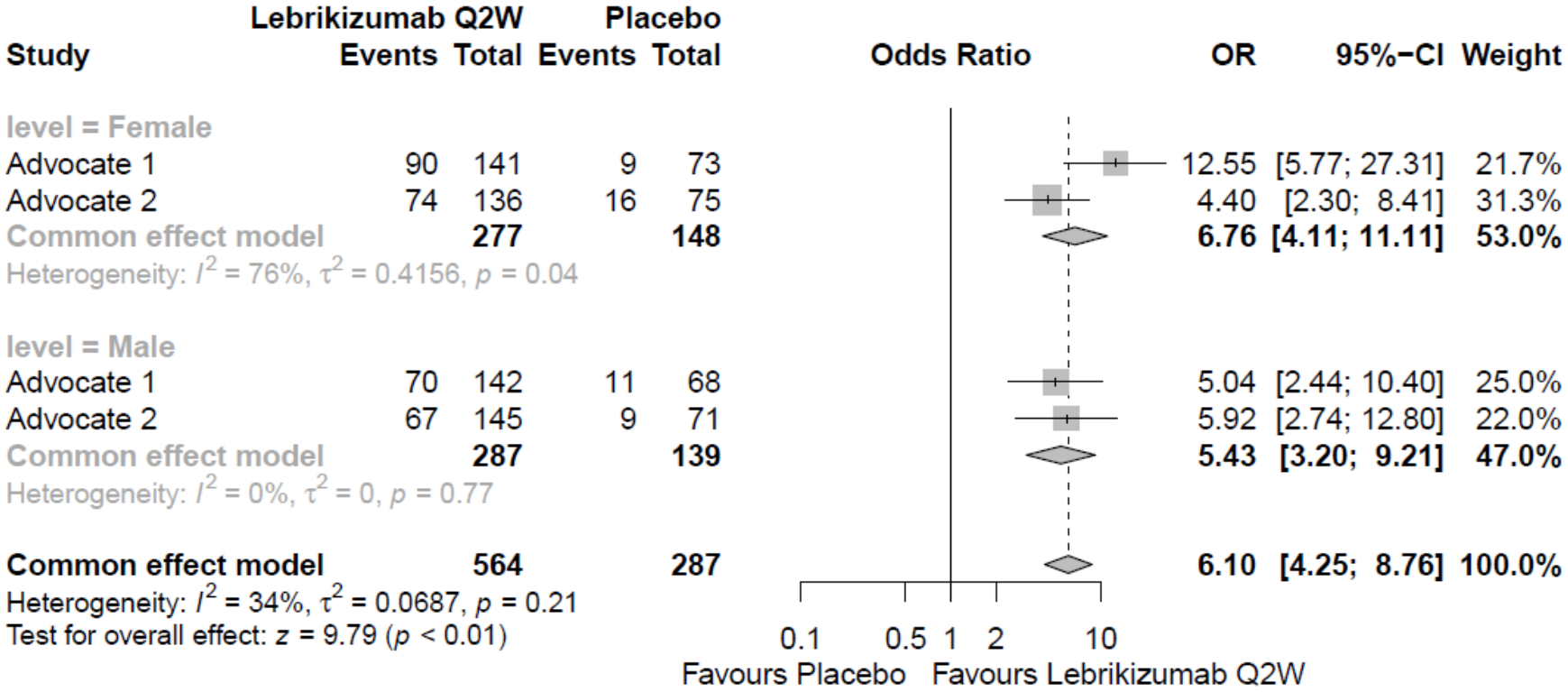


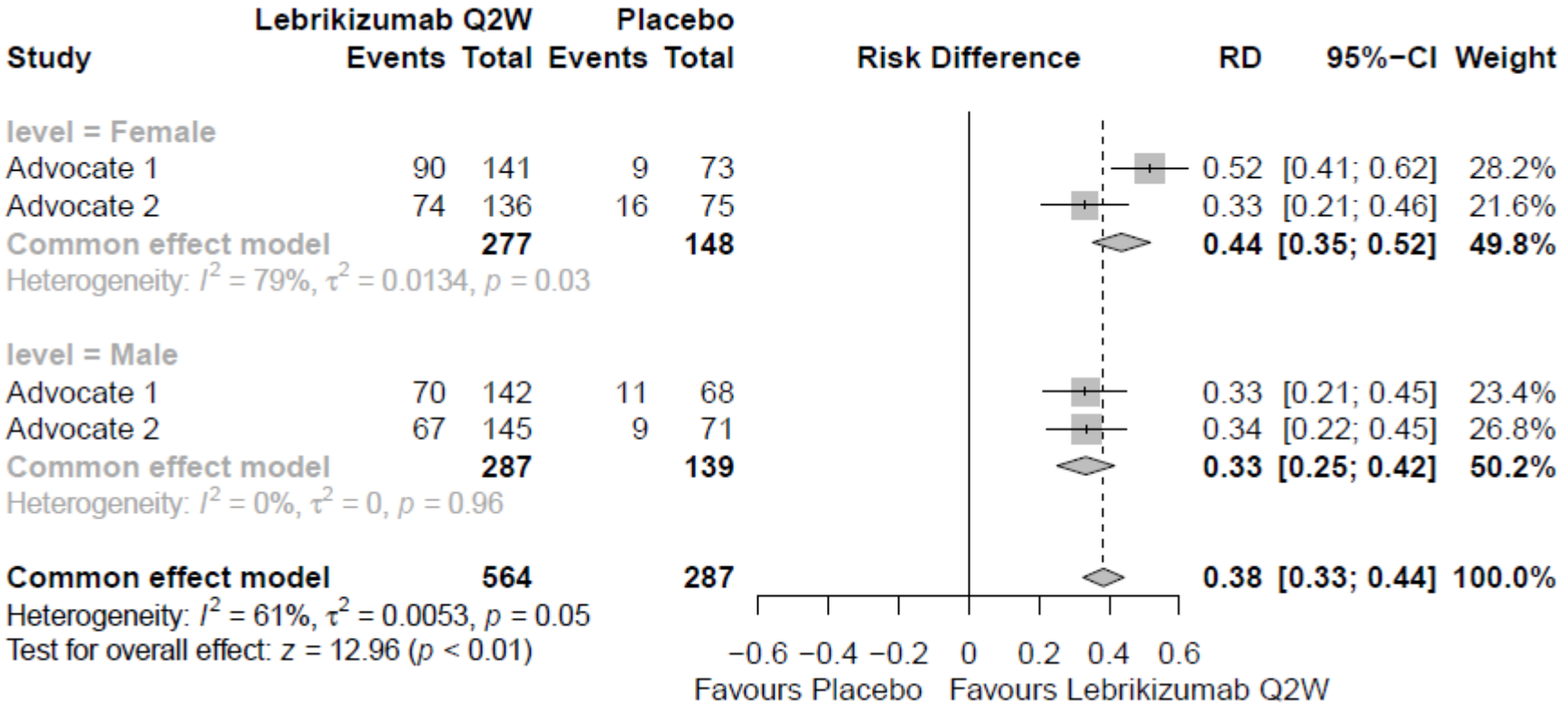

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = US
Advocate 1 72 128 10 62 6.69 [3.12; 14.32] 24.5%
Advocate 2 49 107 17 60 2.14 [1.08; 4.21] 30.9%
Common effect model 235 122 3.54 [2.13; 5.87] 55.5%
Heterogeneity: I^2 = 79%, τ^2 = 0.5151, p = 0.03
level = EU
Advocate 1 61 92 9 46 8.09 [3.47; 18.87] 19.8%
Advocate 2 43 76 6 38 6.95 [2.60; 18.57] 14.7%
Common effect model 168 84 7.58 [3.99; 14.40] 34.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.82
level = Rest of World
Advocate 1 27 63 1 33 24.00 [3.08; 186.79] 3.4%
Advocate 2 49 98 2 48 23.00 [5.29; 100.04] 6.6%
Common effect model 161 81 23.33 [7.06; 77.09] 10.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.97
Common effect model 564 287 5.56 [3.81; 8.10] 100.0%
Heterogeneity: I^2 = 65%, τ^2 = 0.4321, p = 0.01
Test for overall effect: z = 8.91 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = US
Advocate 1 72 128 10 62 0.40 [0.28; 0.53] 19.6%
Advocate 2 49 107 17 60 0.17 [0.03; 0.32] 14.1%
Common effect model 235 122 0.31 [0.21; 0.40] 33.7%
Heterogeneity: I^2 = 81%, τ^2 = 0.0208, p = 0.02
level = EU
Advocate 1 61 92 9 46 0.47 [0.32; 0.62] 13.7%
Advocate 2 43 76 6 38 0.41 [0.25; 0.57] 11.9%
Common effect model 168 84 0.44 [0.33; 0.55] 25.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.60
level = Rest of World
Advocate 1 27 63 1 33 0.40 [0.26; 0.53] 16.8%
Advocate 2 49 98 2 48 0.46 [0.34; 0.57] 23.8%
Common effect model 161 81 0.43 [0.35; 0.52] 40.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.51
Common effect model 564 287 0.39 [0.34; 0.45] 100.0%
Heterogeneity: I^2 = 53%, τ^2 = 0.0056, p = 0.06
Test for overall effect: z = 13.83 (p < 0.01)
−0.6 −0.4 −0.2 0 0.2 0.4 0.6
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.2.5 Geschlecht

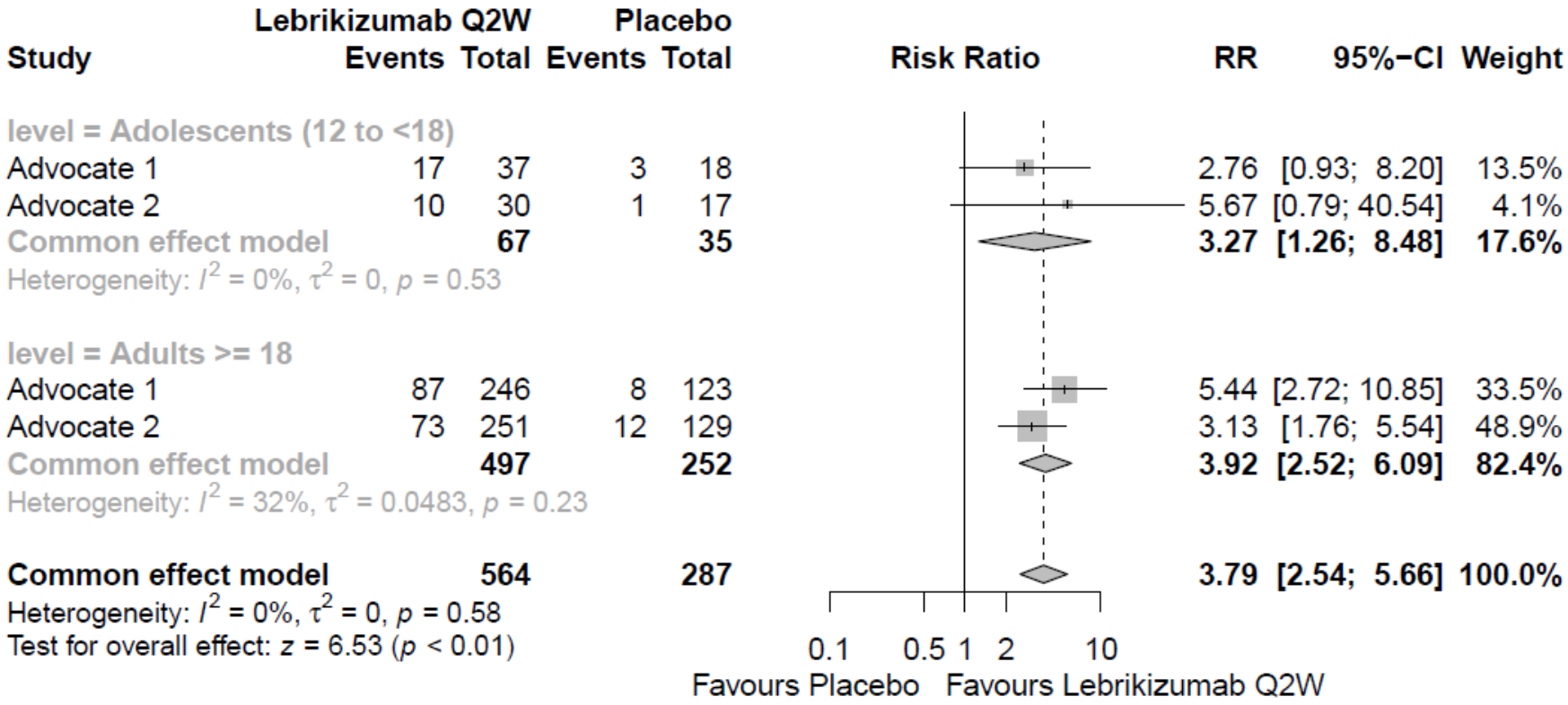


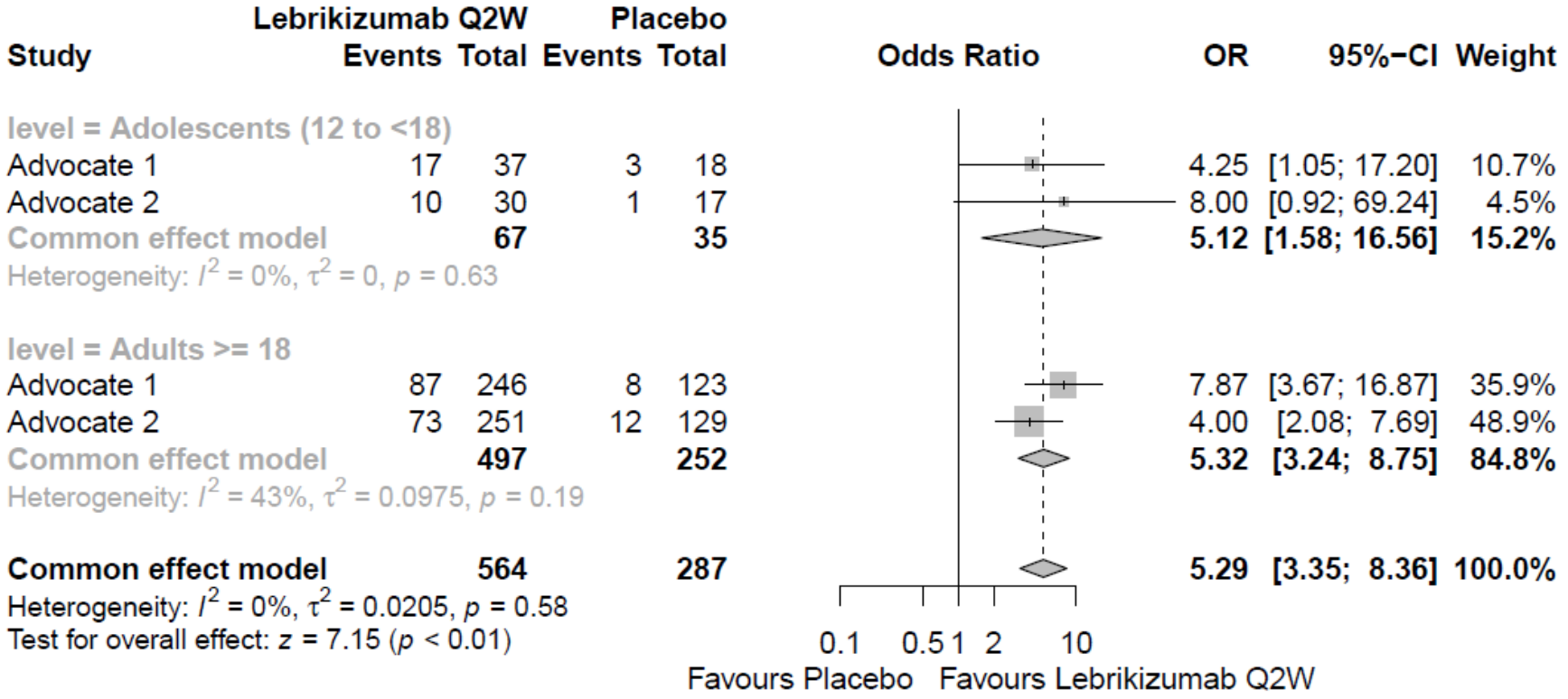

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Female
Advocate 1 90 141 9 73 12.55 [5.77; 27.31] 21.7%
Advocate 2 74 136 16 75 4.40 [2.30; 8.41] 31.3%
Common effect model 277 148 6.76 [4.11; 11.11] 53.0%
Heterogeneity: I^2 = 76%, τ^2 = 0.4156, p = 0.04
level = Male
Advocate 1 70 142 11 68 5.04 [2.44; 10.40] 25.0%
Advocate 2 67 145 9 71 5.92 [2.74; 12.80] 22.0%
Common effect model 287 139 5.43 [3.20; 9.21] 47.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.77
Common effect model 564 287 6.10 [4.25; 8.76] 100.0%
Heterogeneity: I^2 = 34%, τ^2 = 0.0687, p = 0.21
Test for overall effect: z = 9.79 (p < 0.01)
0.1
0.5
1
2
10
Favours Placebo
Favours Lebrikizumab Q2W

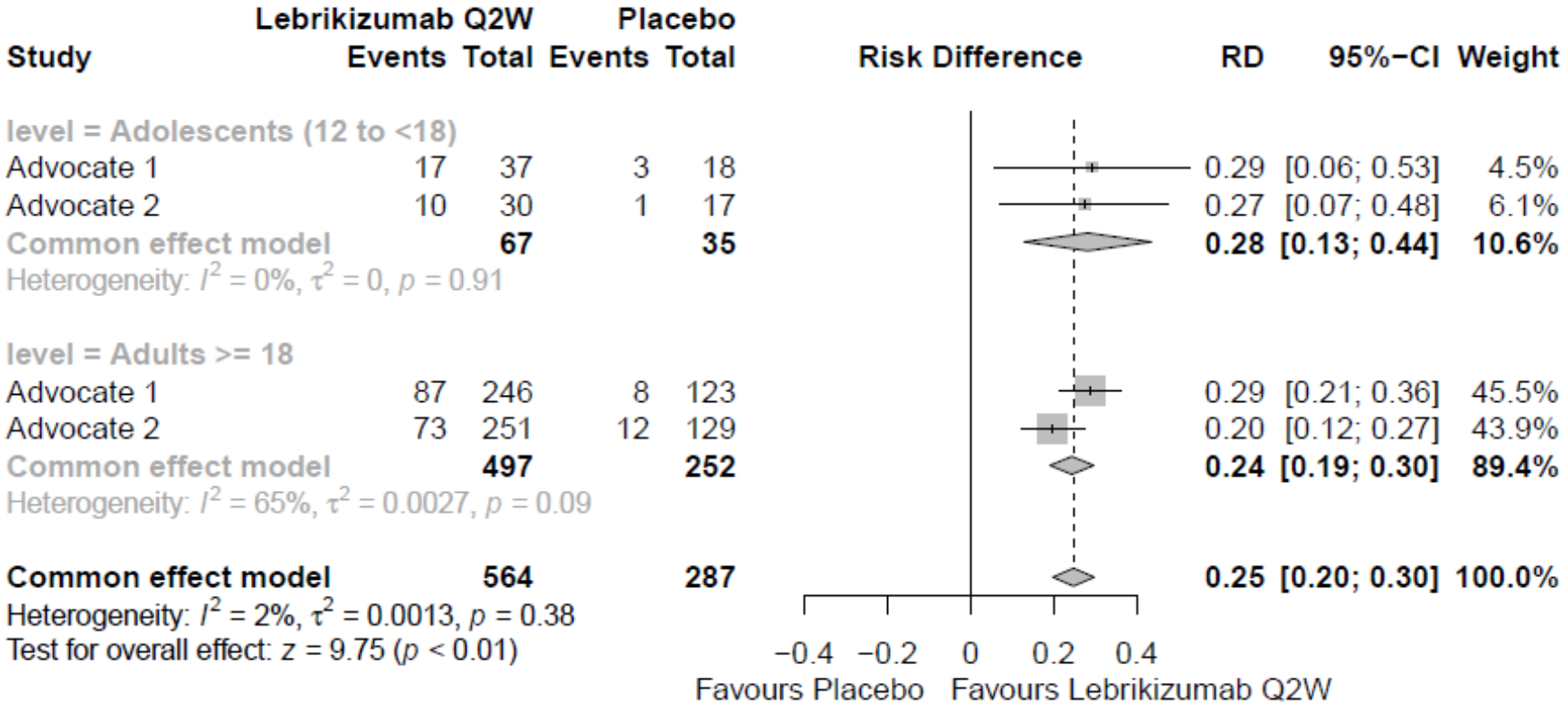

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Female
Advocate 1 90 141 9 73 0.52 [0.41; 0.62] 28.2%
Advocate 2 74 136 16 75 0.33 [0.21; 0.46] 21.6%
Common effect model 277 148 0.44 [0.35; 0.52] 49.8%
Heterogeneity: I^2 = 79%, τ^2 = 0.0134, p = 0.03
level = Male
Advocate 1 70 142 11 68 0.33 [0.21; 0.45] 23.4%
Advocate 2 67 145 9 71 0.34 [0.22; 0.45] 26.8%
Common effect model 287 139 0.33 [0.25; 0.42] 50.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.96
Common effect model 564 287 0.38 [0.33; 0.44] 100.0%
Heterogeneity: I^2 = 61%, τ^2 = 0.0053, p = 0.05
Test for overall effect: z = 12.96 (p < 0.01)
−0.6 −0.4 −0.2 0 0.2 0.4 0.6
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.3 EASI-90

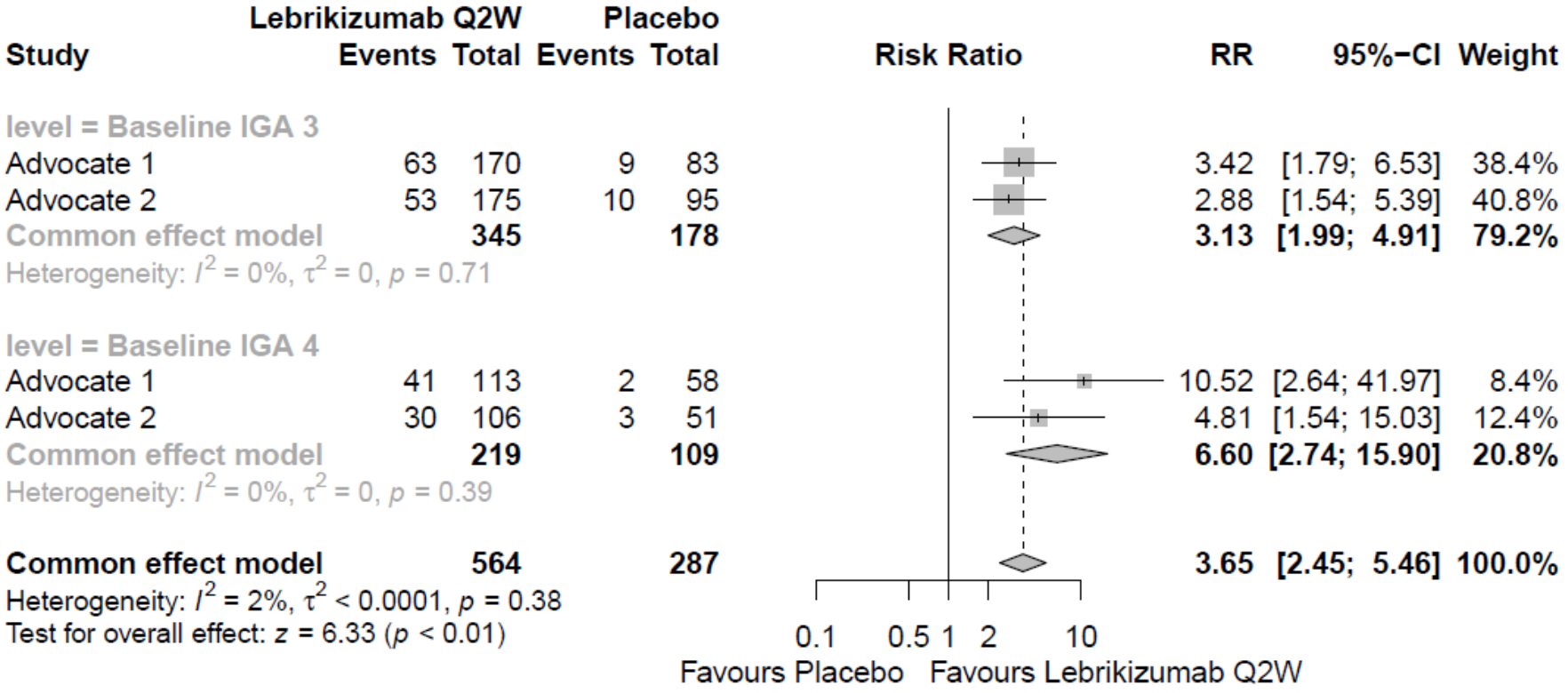
4.5.1.3.1 Altersgruppe

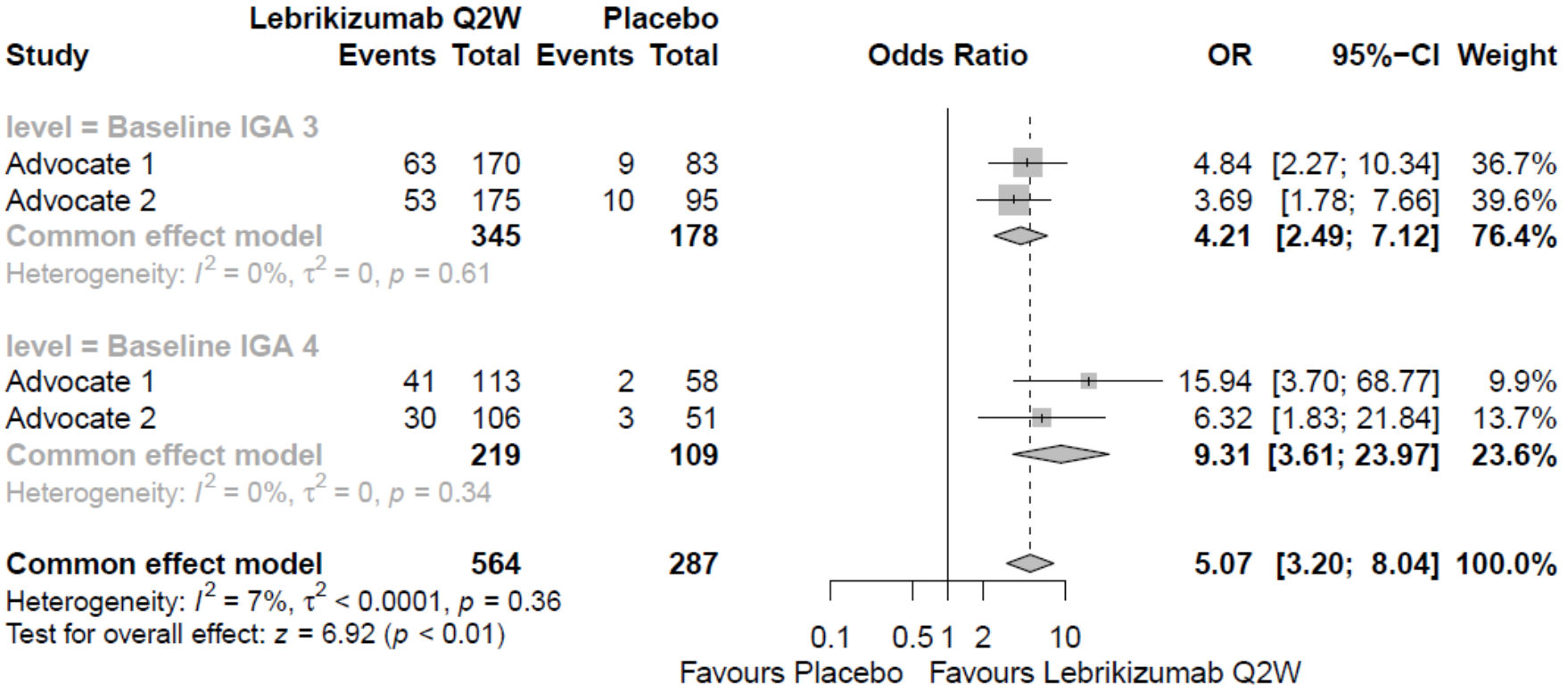


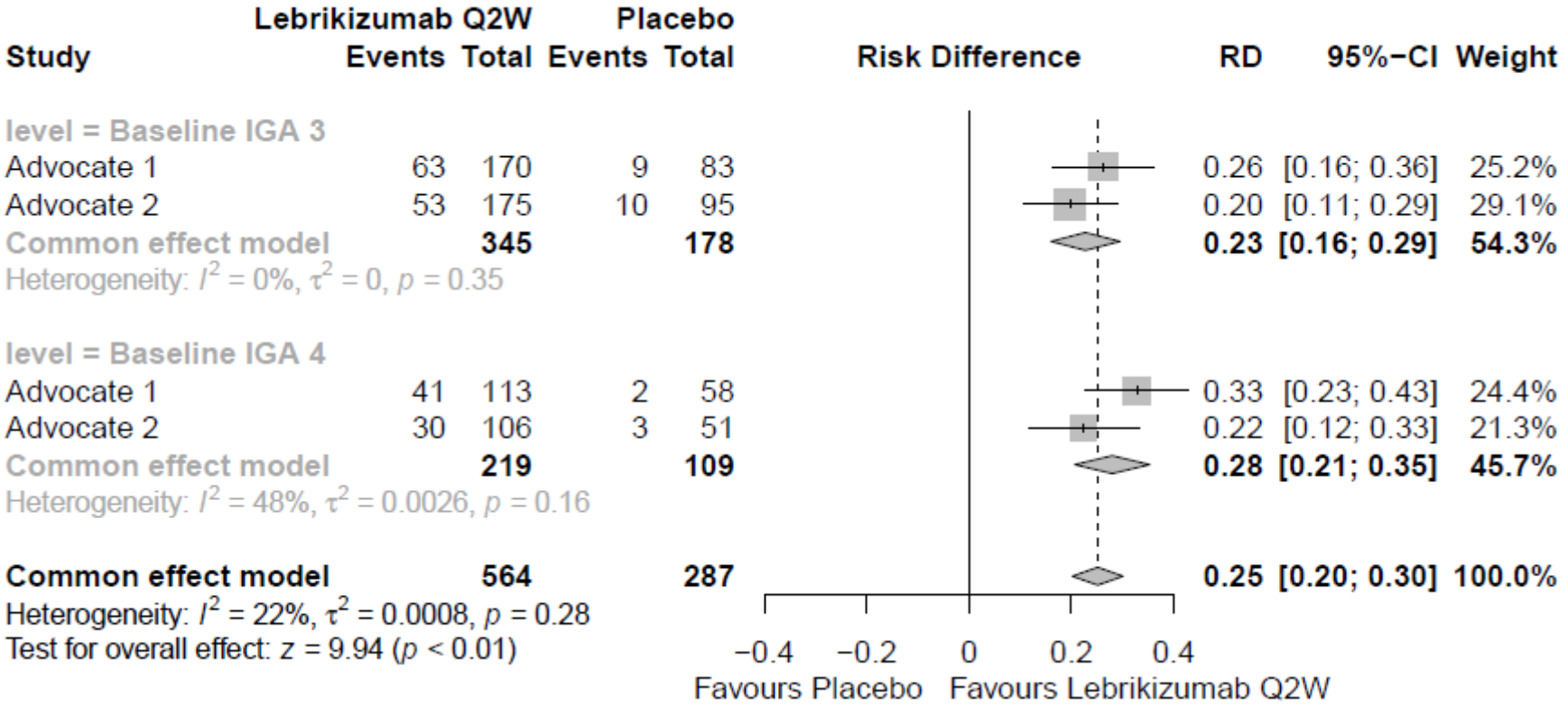

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 17 37 3 18 4.25 [1.05; 17.20] 10.7%
Advocate 2 10 30 1 17 8.00 [0.92; 69.24] 4.5%
Common effect model 67 35 5.12 [1.58; 16.56] 15.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.63
level = Adults >= 18
Advocate 1 87 246 8 123 7.87 [3.67; 16.87] 35.9%
Advocate 2 73 251 12 129 4.00 [2.08; 7.69] 48.9%
Common effect model 497 252 5.32 [3.24; 8.75] 84.8%
Heterogeneity: I^2 = 43%, τ^2 = 0.0975, p = 0.19
Common effect model 564 287 5.29 [3.35; 8.36] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0.0205, p = 0.58
Test for overall effect: z = 7.15 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 17 37 3 18 0.29 [0.06; 0.53] 4.5%
Advocate 2 10 30 1 17 0.27 [0.07; 0.48] 6.1%
Common effect model 67 35 0.28 [0.13; 0.44] 10.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.91
level = Adults >= 18
Advocate 1 87 246 8 123 0.29 [0.21; 0.36] 45.5%
Advocate 2 73 251 12 129 0.20 [0.12; 0.27] 43.9%
Common effect model 497 252 0.24 [0.19; 0.30] 89.4%
Heterogeneity: I^2 = 65%, τ^2 = 0.0027, p = 0.09
Common effect model 564 287 0.25 [0.20; 0.30] 100.0%
Heterogeneity: I^2 = 2%, τ^2 = 0.0013, p = 0.38
Test for overall effect: z = 9.75 (p < 0.01)
−0.4 −0.2 0 0.2 0.4
Favours Placebo
Favours Lebrikizumab Q2W

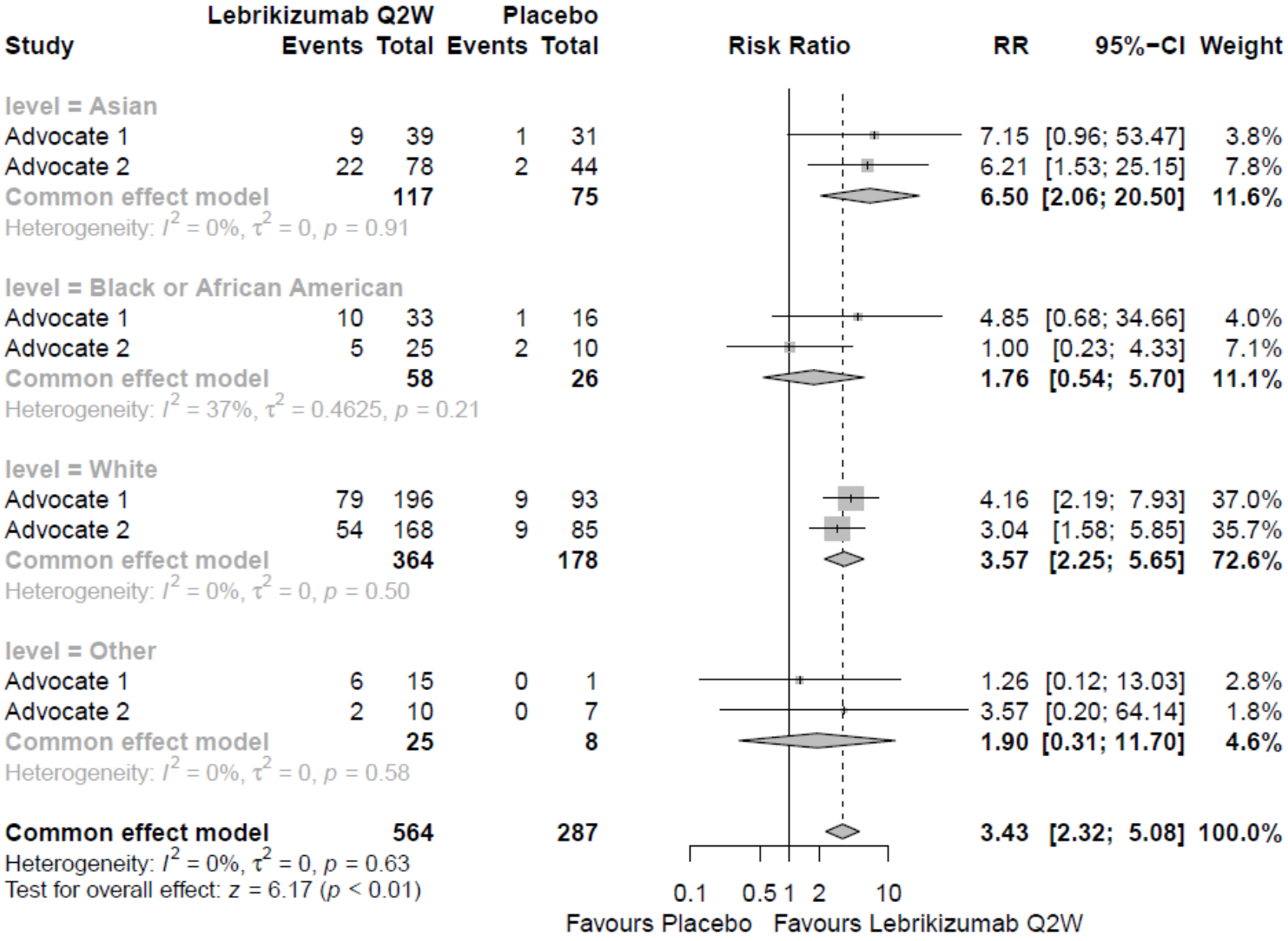
4.5.1.3.2 Krankheitsschwere

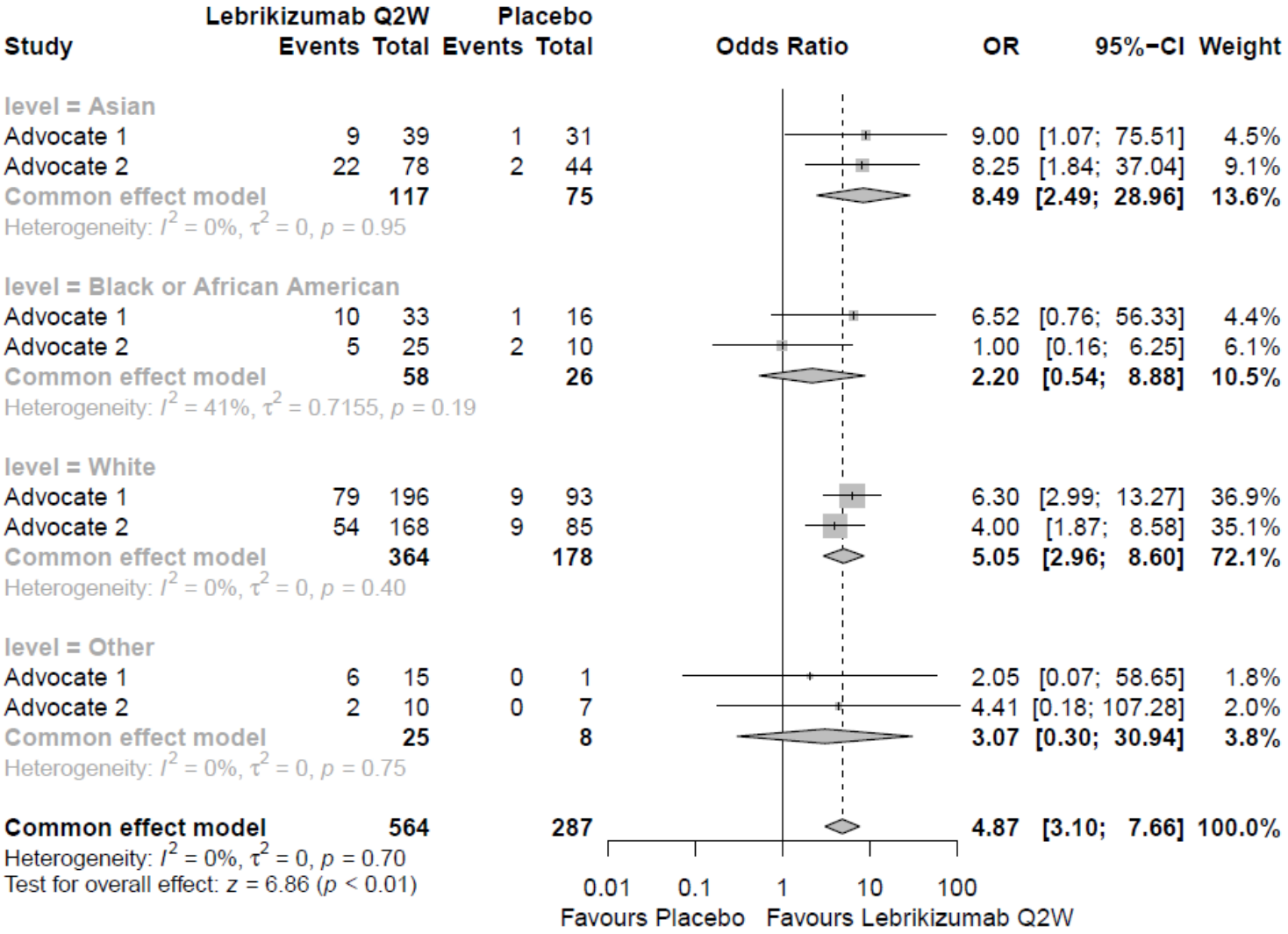


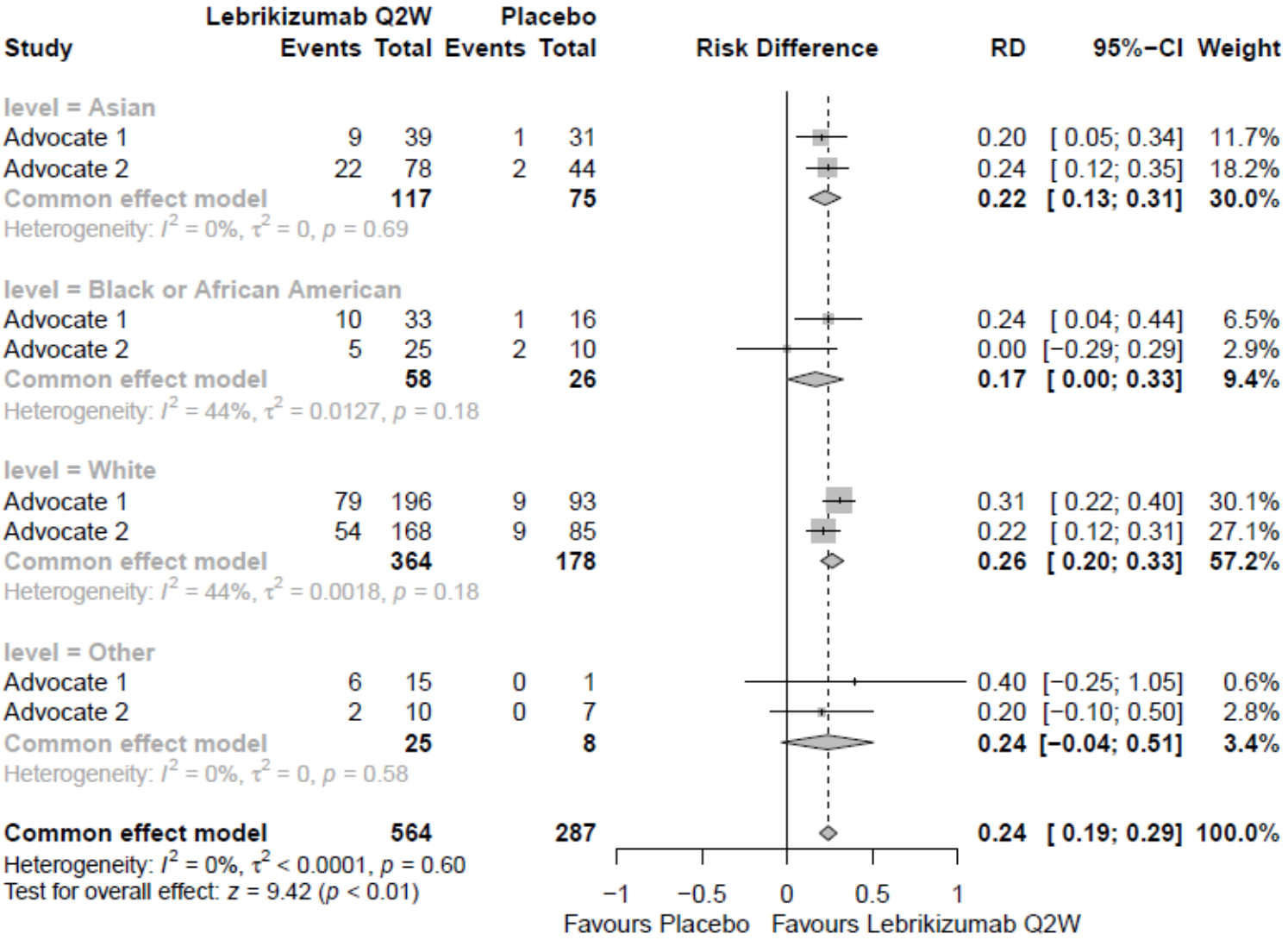

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Baseline IGA 3
Advocate 1 63 170 9 83 4.84 [2.27; 10.34] 36.7%
Advocate 2 53 175 10 95 3.69 [1.78; 7.66] 39.6%
Common effect model 345 178 4.21 [2.49; 7.12] 76.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.61
level = Baseline IGA 4
Advocate 1 41 113 2 58 15.94 [3.70; 68.77] 9.9%
Advocate 2 30 106 3 51 6.32 [1.83; 21.84] 13.7%
Common effect model 219 109 9.31 [3.61; 23.97] 23.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.34
Common effect model 564 287 5.07 [3.20; 8.04] 100.0%
Heterogeneity: I^2 = 7%, τ^2 < 0.0001, p = 0.36
Test for overall effect: z = 6.92 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Baseline IGA 3
Advocate 1 63 170 9 83 0.26 [0.16; 0.36] 25.2%
Advocate 2 53 175 10 95 0.20 [0.11; 0.29] 29.1%
Common effect model 345 178 0.23 [0.16; 0.29] 54.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.35
level = Baseline IGA 4
Advocate 1 41 113 2 58 0.33 [0.23; 0.43] 24.4%
Advocate 2 30 106 3 51 0.22 [0.12; 0.33] 21.3%
Common effect model 219 109 0.28 [0.21; 0.35] 45.7%
Heterogeneity: I^2 = 48%, τ^2 = 0.0026, p = 0.16
Common effect model 564 287 0.25 [0.20; 0.30] 100.0%
Heterogeneity: I^2 = 22%, τ^2 = 0.0008, p = 0.28
Test for overall effect: z = 9.94 (p < 0.01)
−0.4
−0.2
0
0.2
0.4
Favours Placebo
Favours Lebrikizumab Q2W

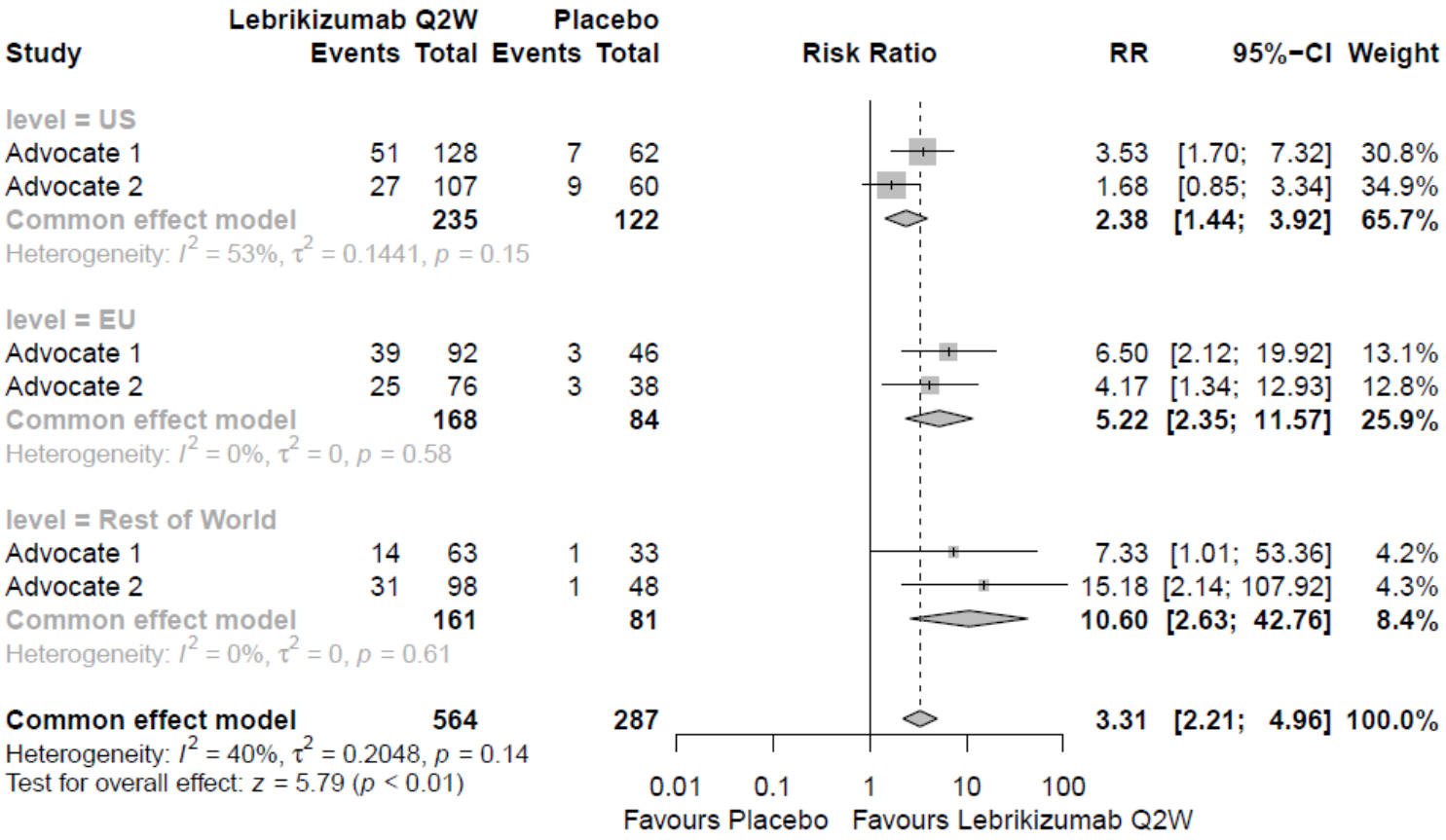
4.5.1.3.3 Ethnie

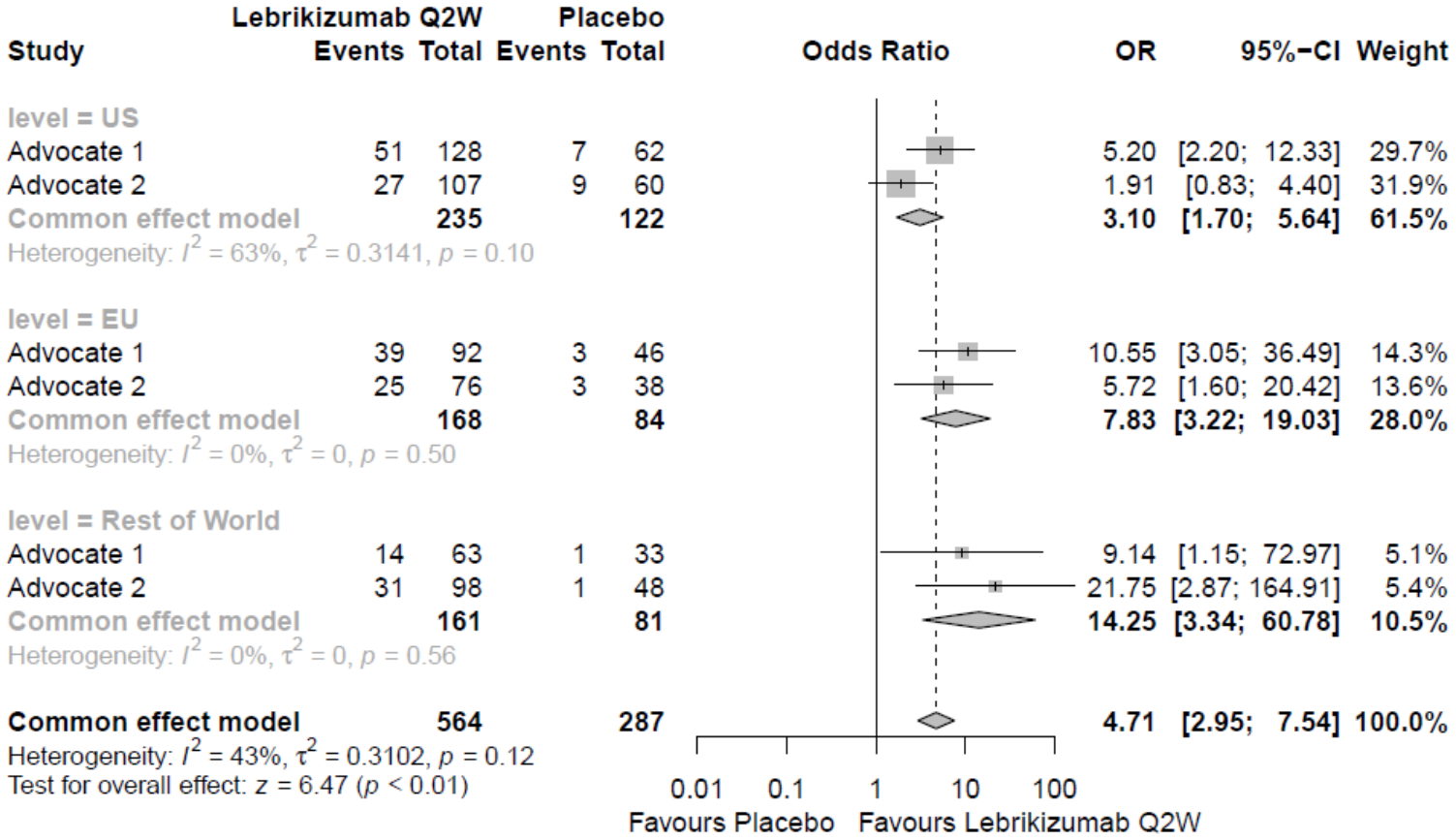


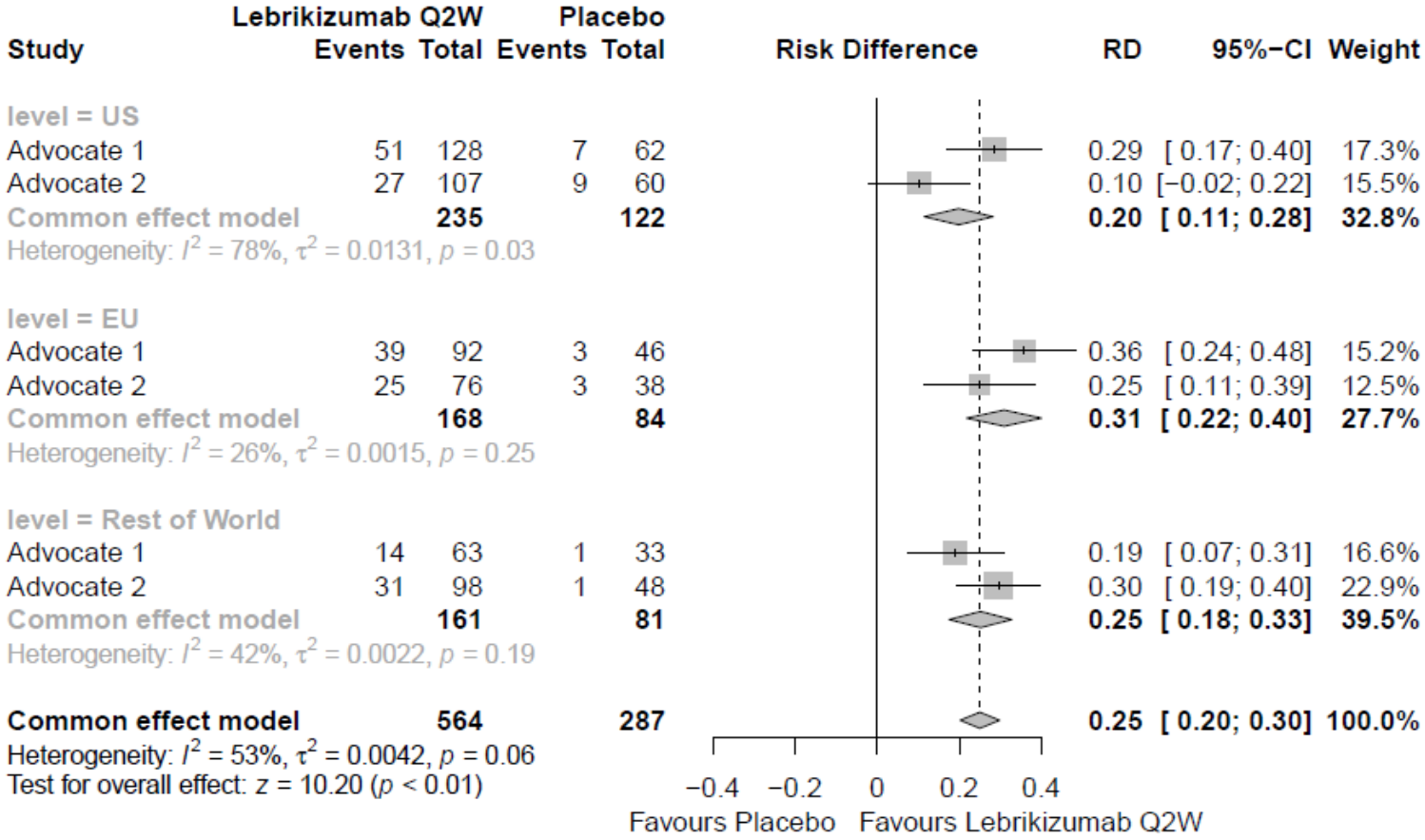

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Asian
Advocate 1 9 39 1 31 9.00 [1.07; 75.51] 4.5%
Advocate 2 22 78 2 44 8.25 [1.84; 37.04] 9.1%
Common effect model 117 75 8.49 [2.49; 28.96] 13.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.95
level = Black or African American
Advocate 1 10 33 1 16 6.52 [0.76; 56.33] 4.4%
Advocate 2 5 25 2 10 1.00 [0.16; 6.25] 6.1%
Common effect model 58 26 2.20 [0.54; 8.88] 10.5%
Heterogeneity: I^2 = 41%, τ^2 = 0.7155, p = 0.19
level = White
Advocate 1 79 196 9 93 6.30 [2.99; 13.27] 36.9%
Advocate 2 54 168 9 85 4.00 [1.87; 8.58] 35.1%
Common effect model 364 178 5.05 [2.96; 8.60] 72.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.40
level = Other
Advocate 1 6 15 0 1 2.05 [0.07; 58.65] 1.8%
Advocate 2 2 10 0 7 4.41 [0.18; 107.28] 2.0%
Common effect model 25 8 3.07 [0.30; 30.94] 3.8%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.75
Common effect model 564 287 4.87 [3.10; 7.66] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.70
Test for overall effect: z = 6.86 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Asian
Advocate 1 9 39 1 31 0.20 [0.05; 0.34] 11.7%
Advocate 2 22 78 2 44 0.24 [0.12; 0.35] 18.2%
Common effect model 117 75 0.22 [0.13; 0.31] 30.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.69
level = Black or African American
Advocate 1 10 33 1 16 0.24 [0.04; 0.44] 6.5%
Advocate 2 5 25 2 10 0.00 [−0.29; 0.29] 2.9%
Common effect model 58 26 0.17 [0.00; 0.33] 9.4%
Heterogeneity: I^2 = 44%, τ^2 = 0.0127, p = 0.18
level = White
Advocate 1 79 196 9 93 0.31 [0.22; 0.40] 30.1%
Advocate 2 54 168 9 85 0.22 [0.12; 0.31] 27.1%
Common effect model 364 178 0.26 [0.20; 0.33] 57.2%
Heterogeneity: I^2 = 44%, τ^2 = 0.0018, p = 0.18
level = Other
Advocate 1 6 15 0 1 0.40 [−0.25; 1.05] 0.6%
Advocate 2 2 10 0 7 0.20 [−0.10; 0.50] 2.8%
Common effect model 25 8 0.24 [−0.04; 0.51] 3.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.58
Common effect model 564 287 0.24 [0.19; 0.29] 100.0%
Heterogeneity: I^2 = 0%, τ^2 < 0.0001, p = 0.60
Test for overall effect: z = 9.42 (p < 0.01)
−1 −0.5 0 0.5 1
Favours Placebo
Favours Lebrikizumab Q2W

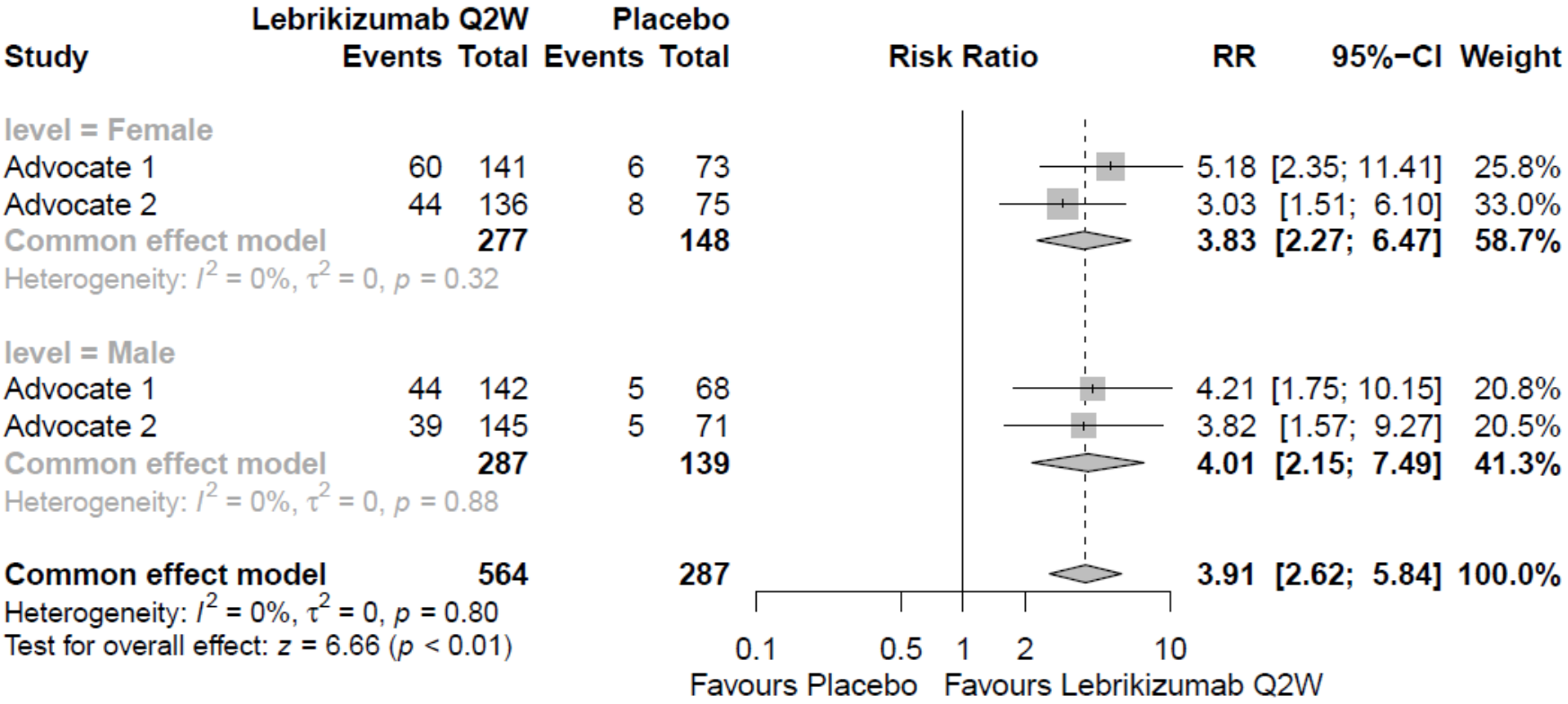
4.5.1.3.4 Region

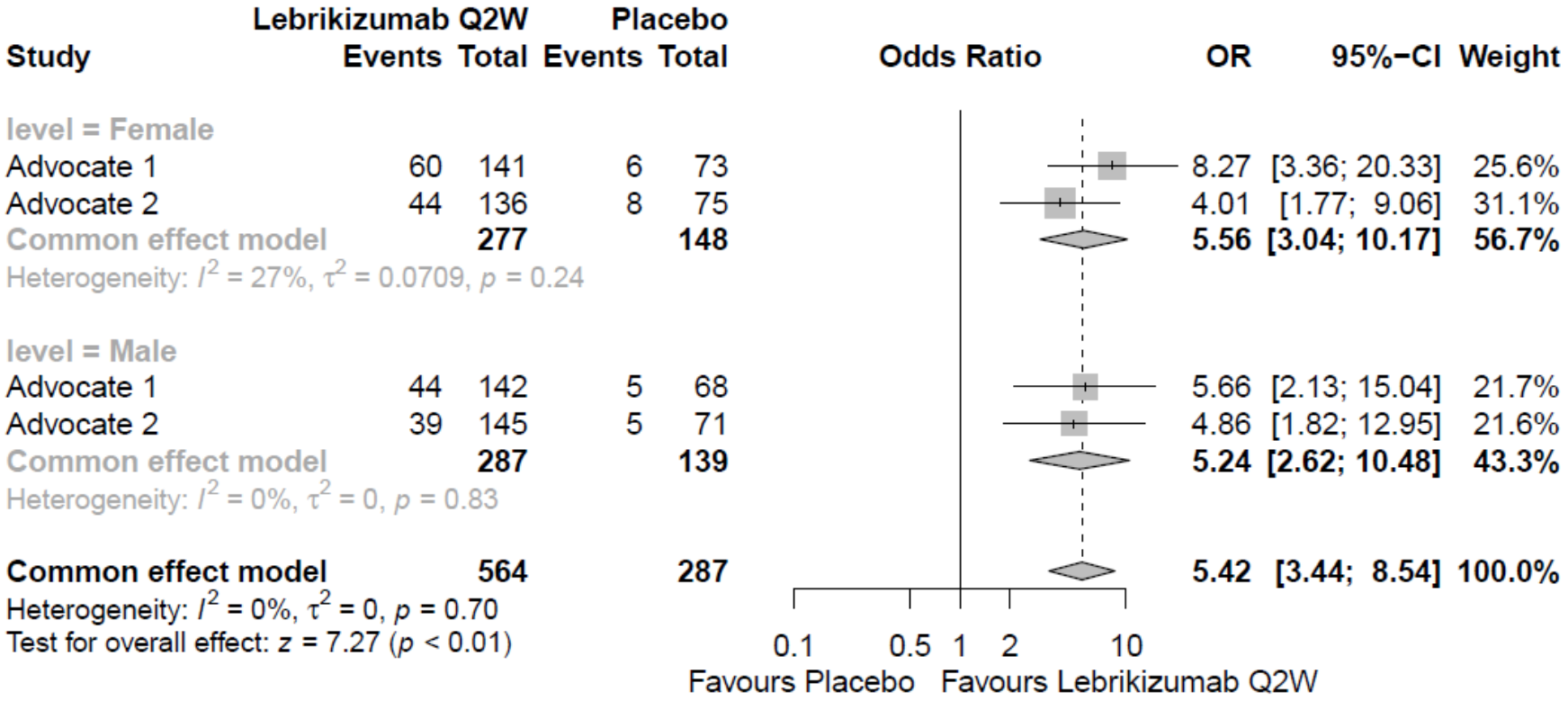


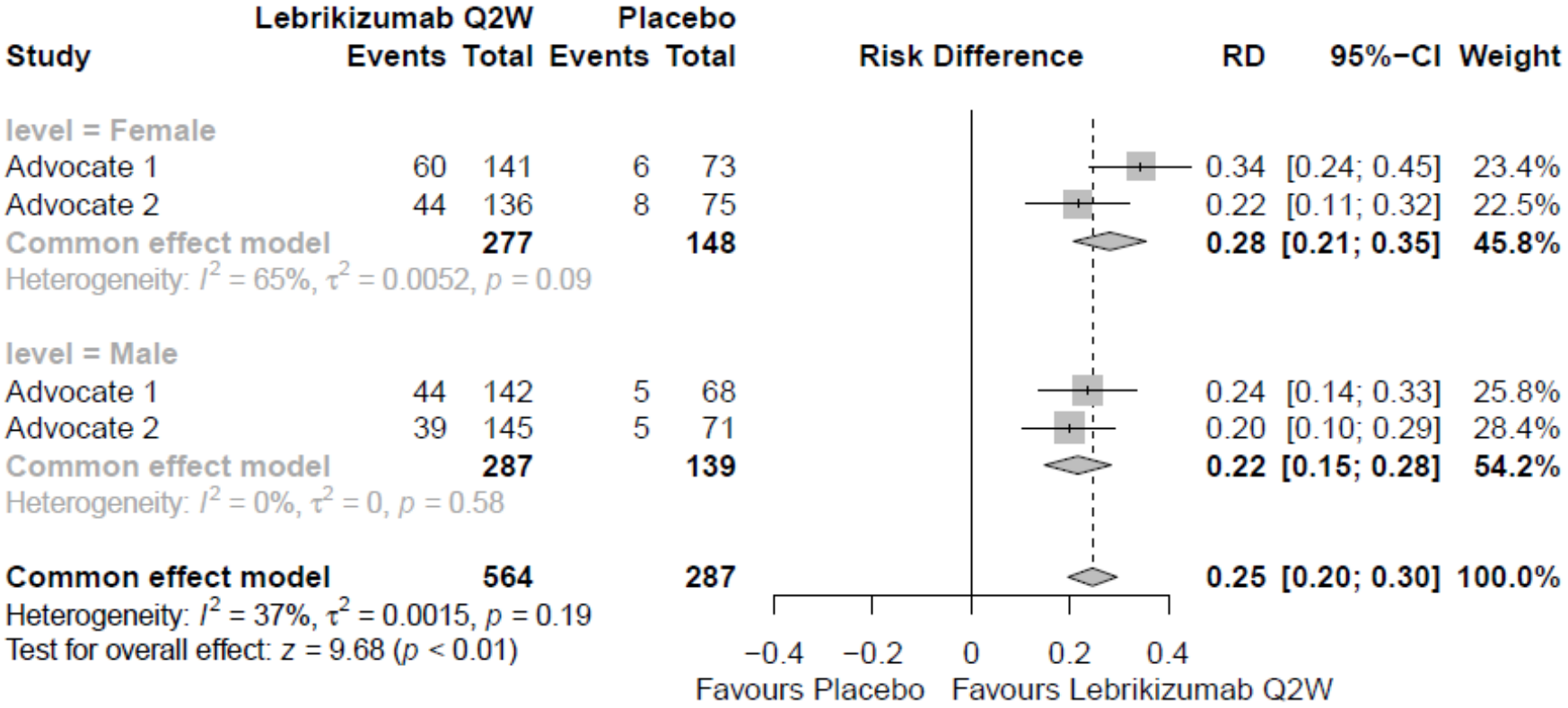

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = US
Advocate 1 51 128 7 62 5.20 [2.20; 12.33] 29.7%
Advocate 2 27 107 9 60 1.91 [0.83; 4.40] 31.9%
Common effect model 235 122 3.10 [1.70; 5.64] 61.5%
Heterogeneity: I^2 = 63%, τ^2 = 0.3141, p = 0.10
level = EU
Advocate 1 39 92 3 46 10.55 [3.05; 36.49] 14.3%
Advocate 2 25 76 3 38 5.72 [1.60; 20.42] 13.6%
Common effect model 168 84 7.83 [3.22; 19.03] 28.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.50
level = Rest of World
Advocate 1 14 63 1 33 9.14 [1.15; 72.97] 5.1%
Advocate 2 31 98 1 48 21.75 [2.87; 164.91] 5.4%
Common effect model 161 81 14.25 [3.34; 60.78] 10.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.56
Common effect model 564 287 4.71 [2.95; 7.54] 100.0%
Heterogeneity: I^2 = 43%, τ^2 = 0.3102, p = 0.12
Test for overall effect: z = 6.47 (p < 0.01)
0.01
0.1
1
10
100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = US
Advocate 1 51 128 7 62 0.29 [0.17; 0.40] 17.3%
Advocate 2 27 107 9 60 0.10 [−0.02; 0.22] 15.5%
Common effect model 235 122 0.20 [0.11; 0.28] 32.8%
Heterogeneity: I^2 = 78%, τ^2 = 0.0131, p = 0.03
level = EU
Advocate 1 39 92 3 46 0.36 [0.24; 0.48] 15.2%
Advocate 2 25 76 3 38 0.25 [0.11; 0.39] 12.5%
Common effect model 168 84 0.31 [0.22; 0.40] 27.7%
Heterogeneity: I^2 = 26%, τ^2 = 0.0015, p = 0.25
level = Rest of World
Advocate 1 14 63 1 33 0.19 [0.07; 0.31] 16.6%
Advocate 2 31 98 1 48 0.30 [0.19; 0.40] 22.9%
Common effect model 161 81 0.25 [0.18; 0.33] 39.5%
Heterogeneity: I^2 = 42%, τ^2 = 0.0022, p = 0.19
Common effect model 564 287 0.25 [0.20; 0.30] 100.0%
Heterogeneity: I^2 = 53%, τ^2 = 0.0042, p = 0.06
Test for overall effect: z = 10.20 (p < 0.01)
−0.4 −0.2 0 0.2 0.4
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.3.5 Geschlecht

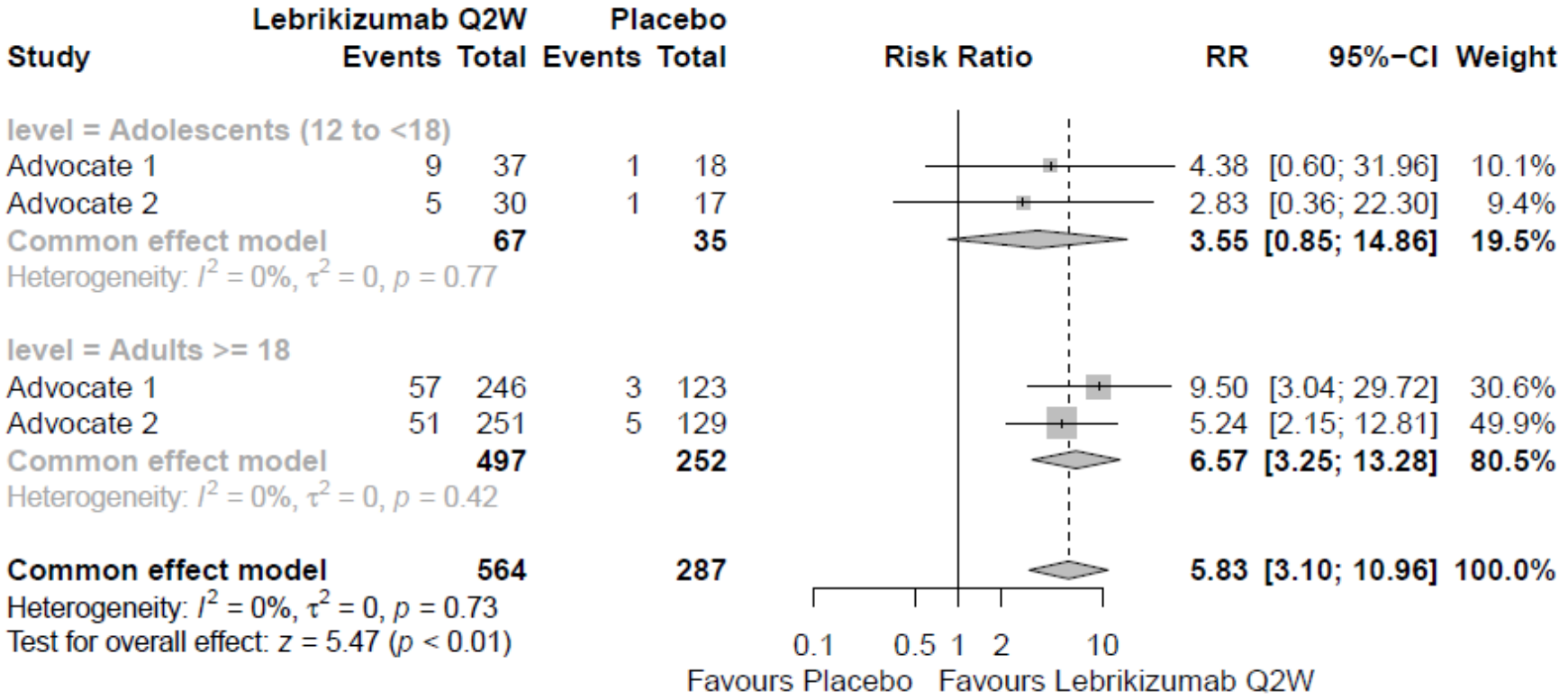


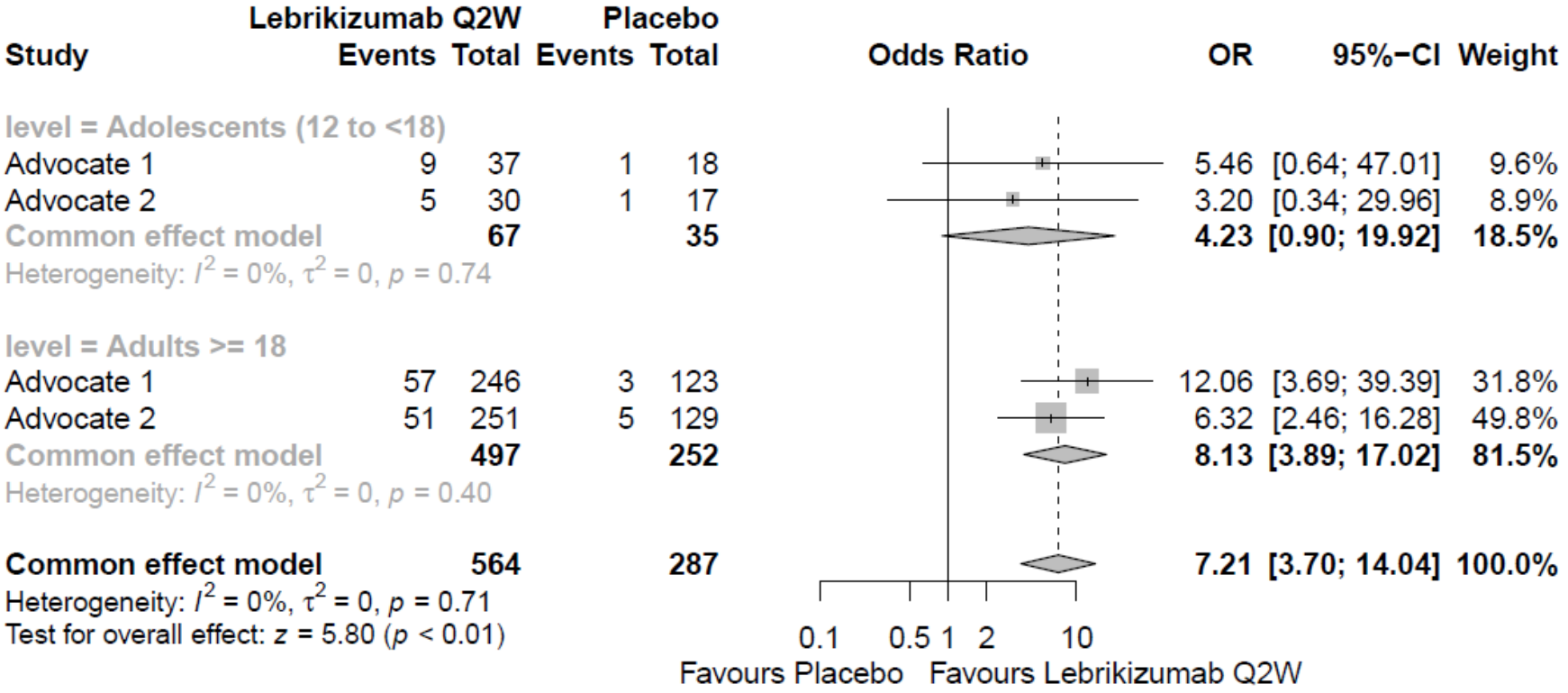

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Female
Advocate 1 60 141 6 73 8.27 [3.36; 20.33] 25.6%
Advocate 2 44 136 8 75 4.01 [1.77; 9.06] 31.1%
Common effect model 277 148 5.56 [3.04; 10.17] 56.7%
Heterogeneity: I^2 = 27%, τ^2 = 0.0709, p = 0.24
level = Male
Advocate 1 44 142 5 68 5.66 [2.13; 15.04] 21.7%
Advocate 2 39 145 5 71 4.86 [1.82; 12.95] 21.6%
Common effect model 287 139 5.24 [2.62; 10.48] 43.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.83
Common effect model 564 287 5.42 [3.44; 8.54] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.70
Test for overall effect: z = 7.27 (p < 0.01)
0.1
0.5
1
2
10
Favours Placebo
Favours Lebrikizumab Q2W

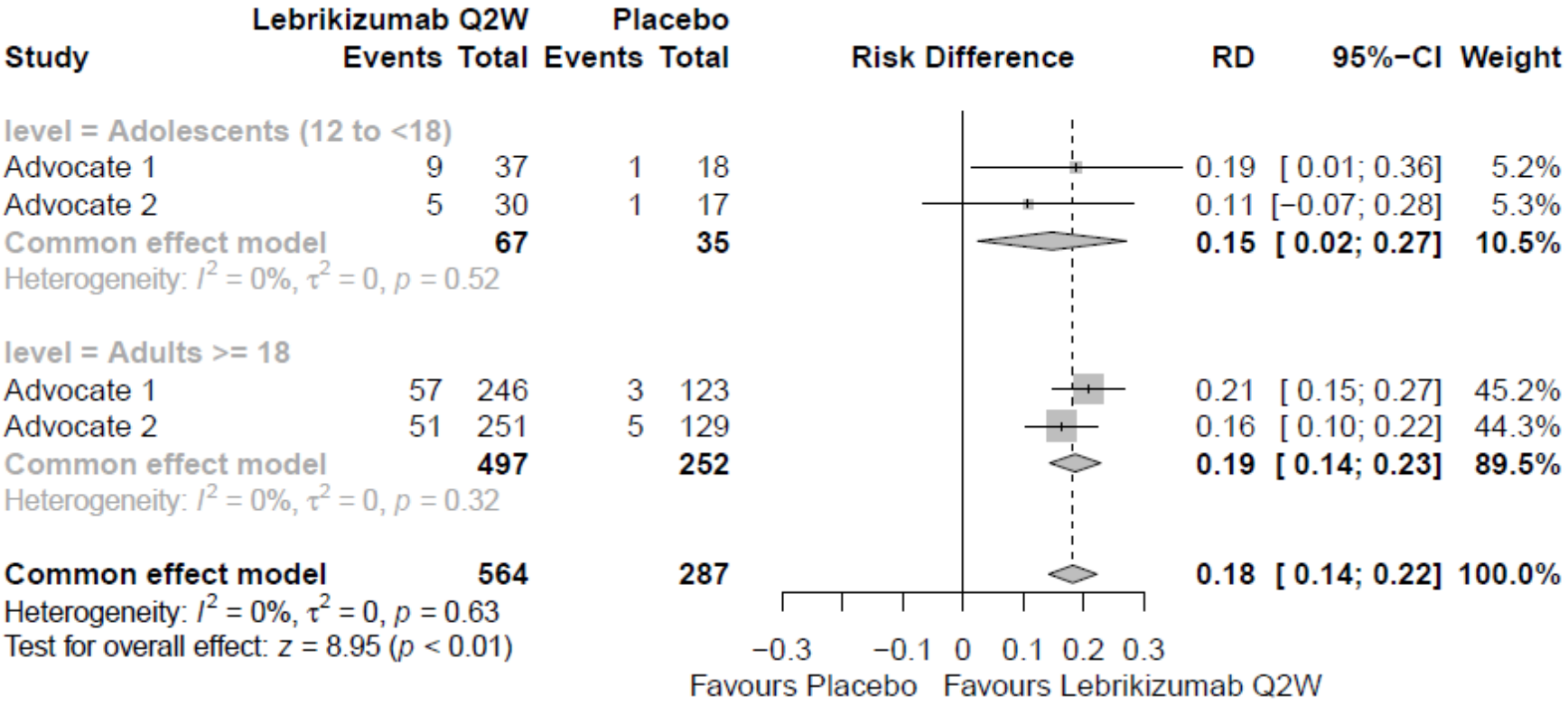

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Female
Advocate 1 60 141 6 73 0.34 [0.24; 0.45] 23.4%
Advocate 2 44 136 8 75 0.22 [0.11; 0.32] 22.5%
Common effect model 277 148 0.28 [0.21; 0.35] 45.8%
Heterogeneity: I^2 = 65%, τ^2 = 0.0052, p = 0.09
level = Male
Advocate 1 44 142 5 68 0.24 [0.14; 0.33] 25.8%
Advocate 2 39 145 5 71 0.20 [0.10; 0.29] 28.4%
Common effect model 287 139 0.22 [0.15; 0.28] 54.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.58
Common effect model 564 287 0.25 [0.20; 0.30] 100.0%
Heterogeneity: I^2 = 37%, τ^2 = 0.0015, p = 0.19
Test for overall effect: z = 9.68 (p < 0.01)
−0.4 −0.2 0 0.2 0.4
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.4 SCORAD-75

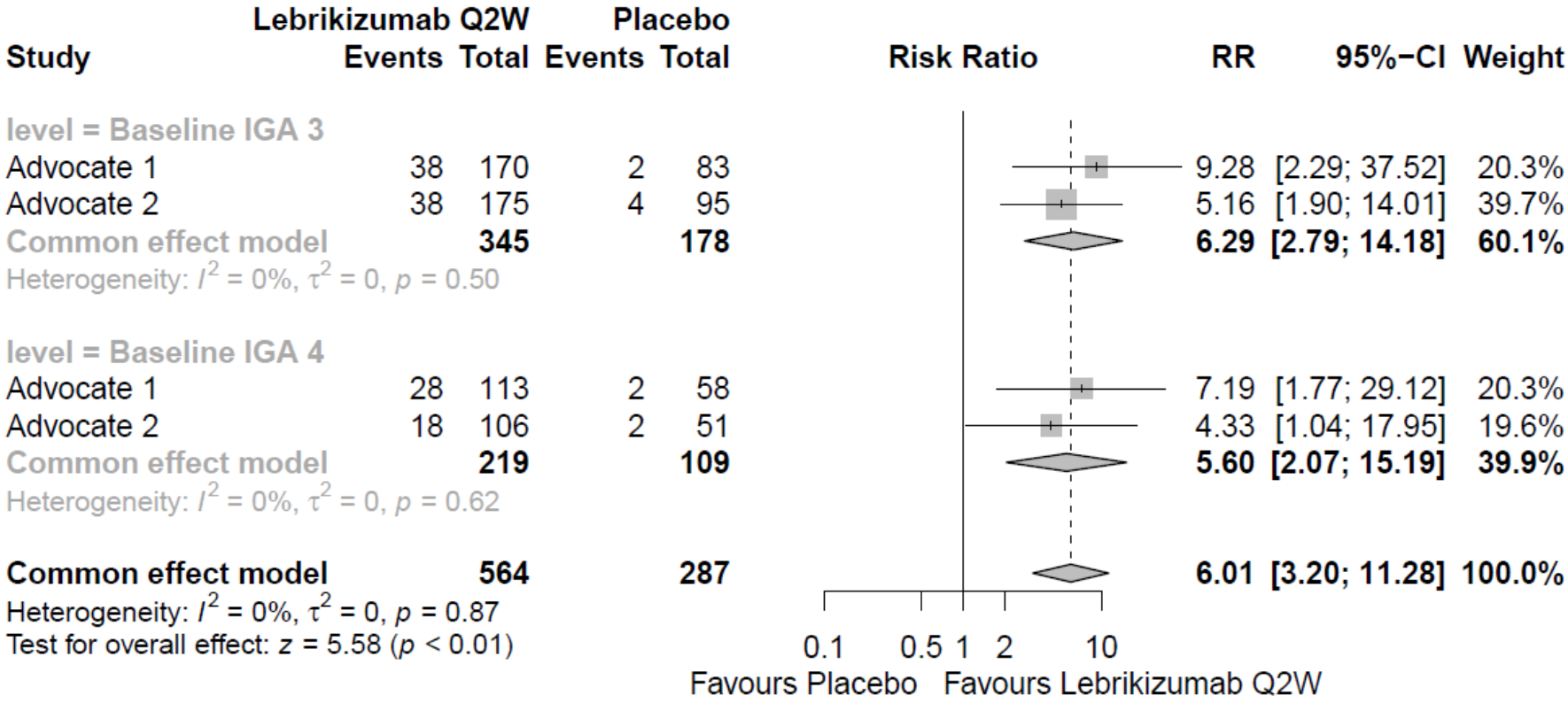
4.5.1.4.1 Altersgruppe

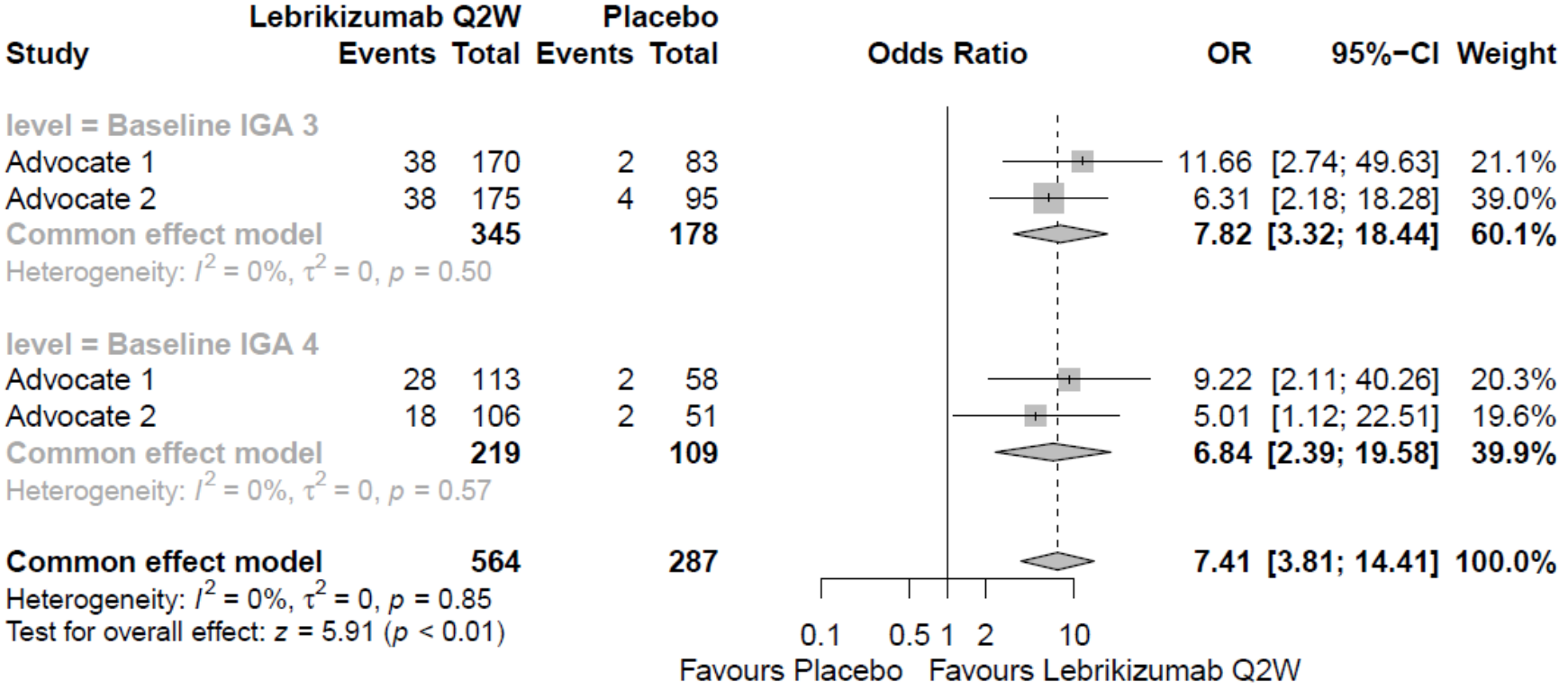


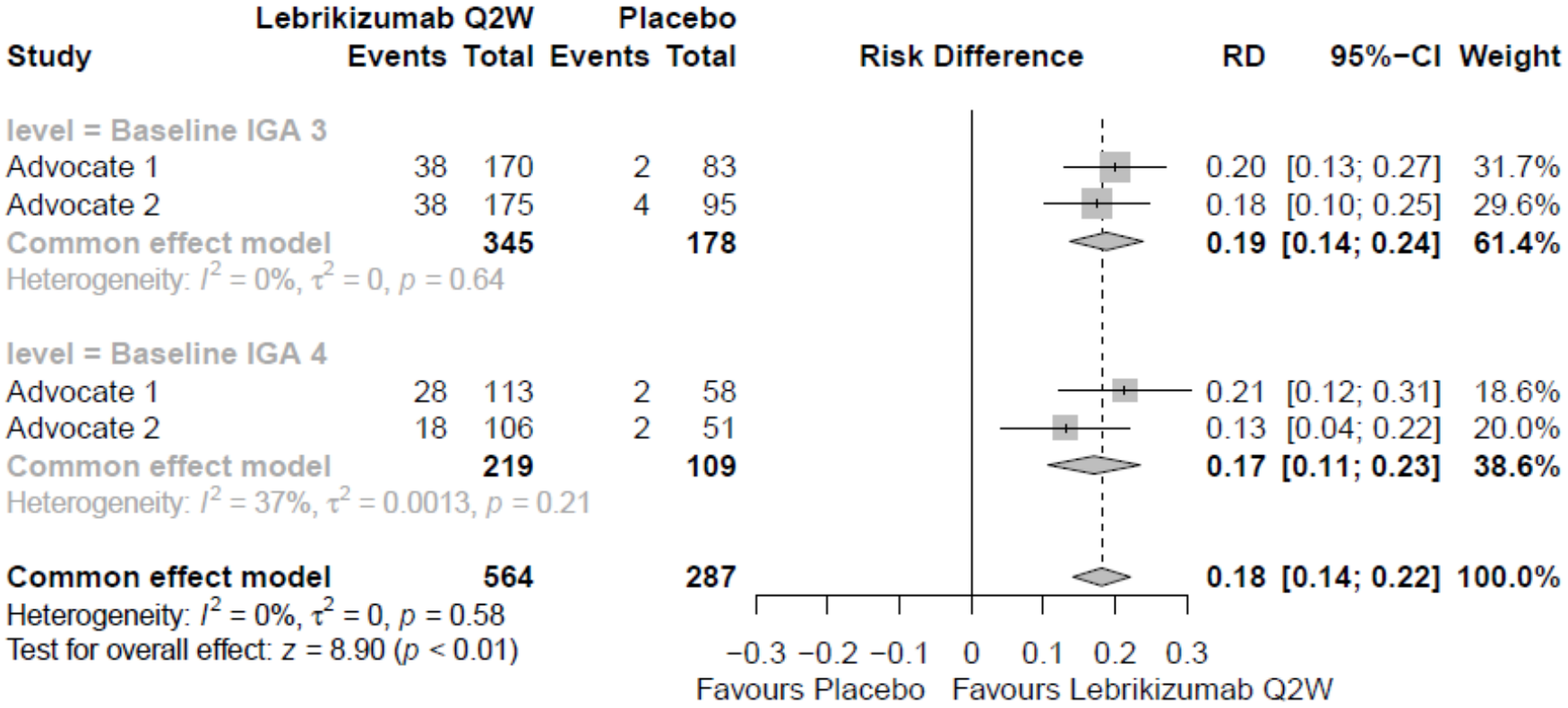

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 9 37 1 18 5.46 [0.64; 47.01] 9.6%
Advocate 2 5 30 1 17 3.20 [0.34; 29.96] 8.9%
Common effect model 67 35 4.23 [0.90; 19.92] 18.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.74
level = Adults >= 18
Advocate 1 57 246 3 123 12.06 [3.69; 39.39] 31.8%
Advocate 2 51 251 5 129 6.32 [2.46; 16.28] 49.8%
Common effect model 497 252 8.13 [3.89; 17.02] 81.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.40
Common effect model 564 287 7.21 [3.70; 14.04] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.71
Test for overall effect: z = 5.80 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 9 37 1 18 0.19 [0.01; 0.36] 5.2%
Advocate 2 5 30 1 17 0.11 [−0.07; 0.28] 5.3%
Common effect model 67 35 0.15 [0.02; 0.27] 10.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.52
level = Adults >= 18
Advocate 1 57 246 3 123 0.21 [0.15; 0.27] 45.2%
Advocate 2 51 251 5 129 0.16 [0.10; 0.22] 44.3%
Common effect model 497 252 0.19 [0.14; 0.23] 89.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.32
Common effect model 564 287 0.18 [0.14; 0.22] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.63
Test for overall effect: z = 8.95 (p < 0.01)
−0.3 −0.1 0 0.1 0.2 0.3
Favours Placebo
Favours Lebrikizumab Q2W

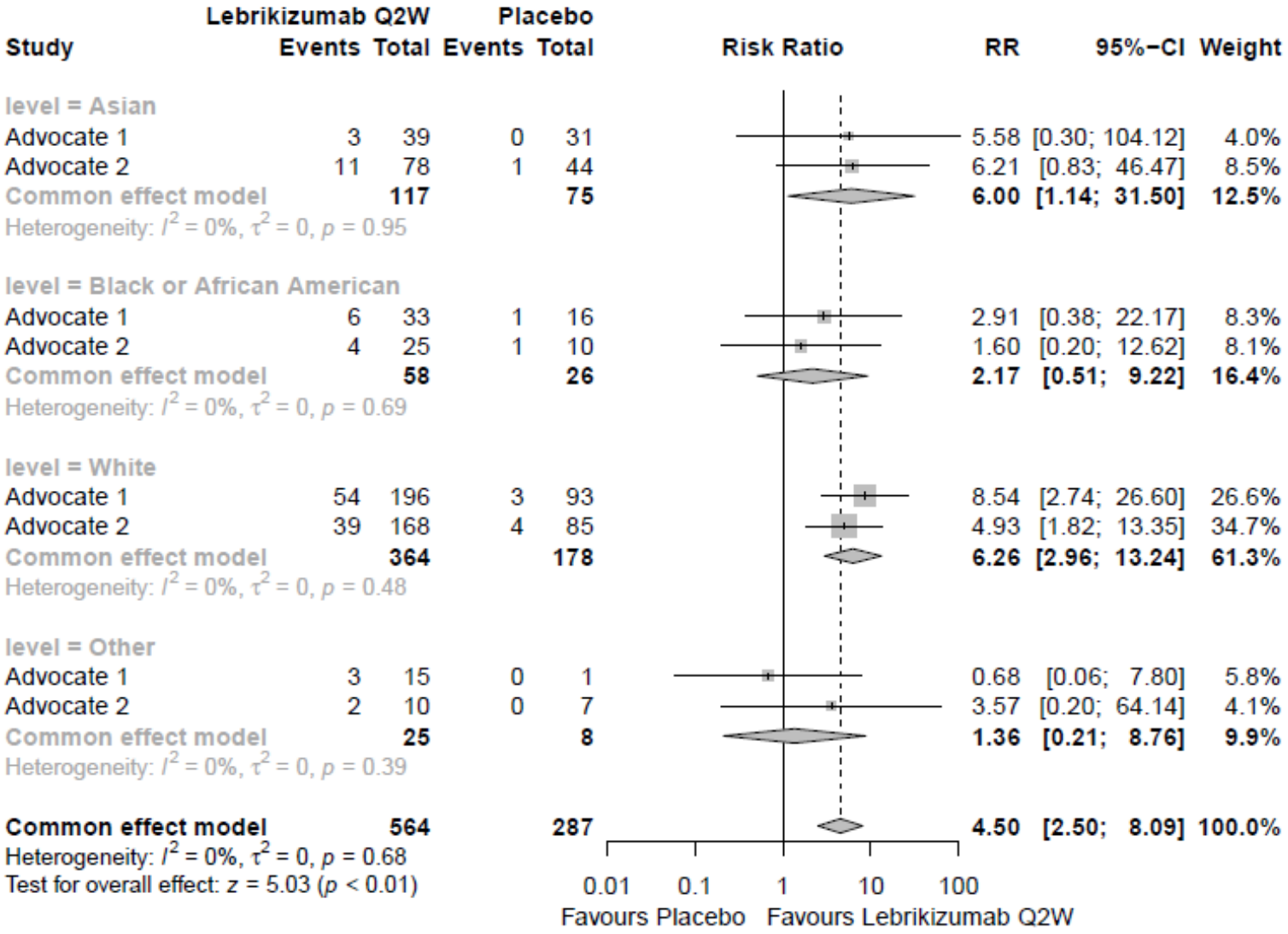
4.5.1.4.2 Krankheitsschwere

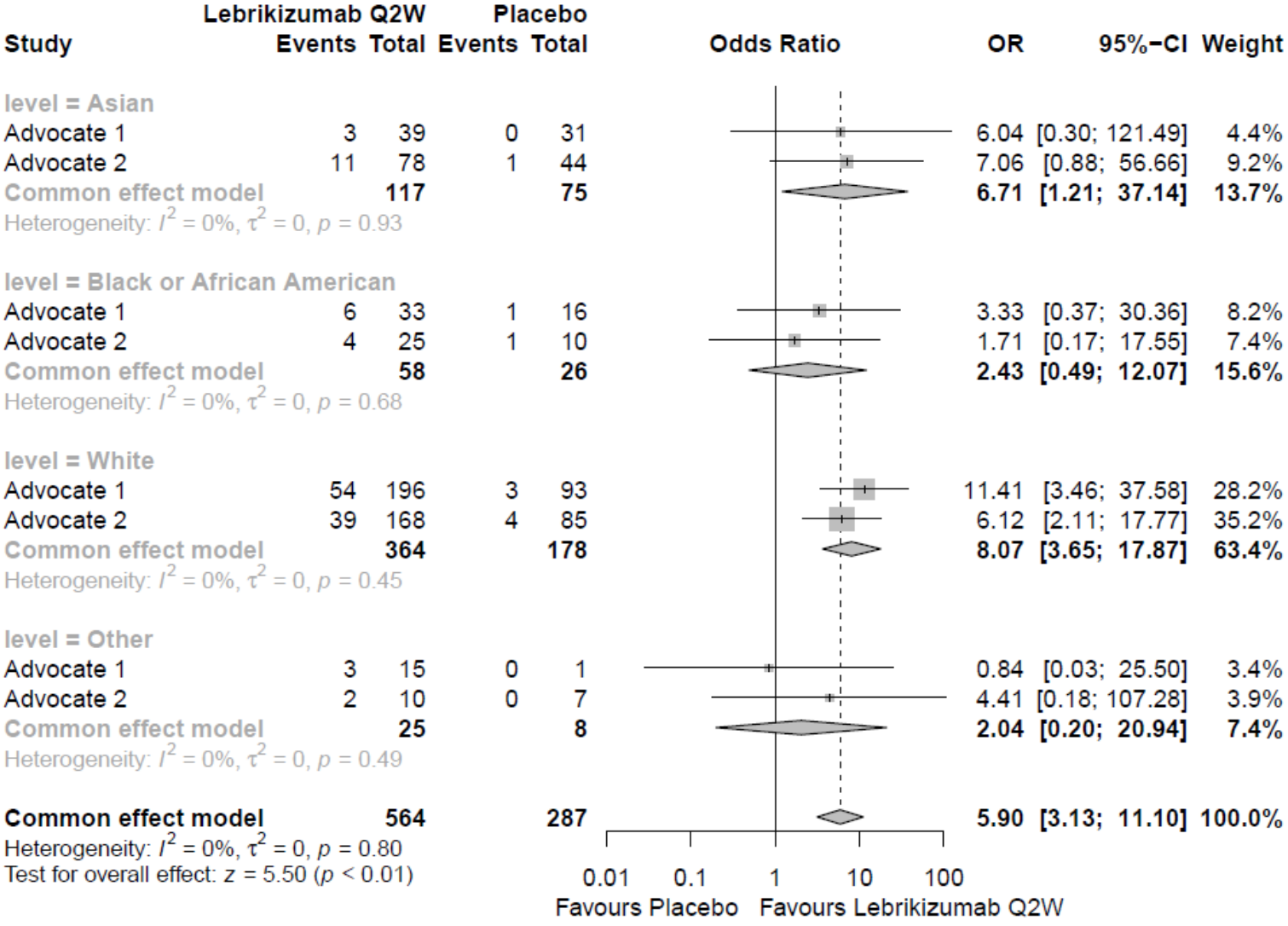


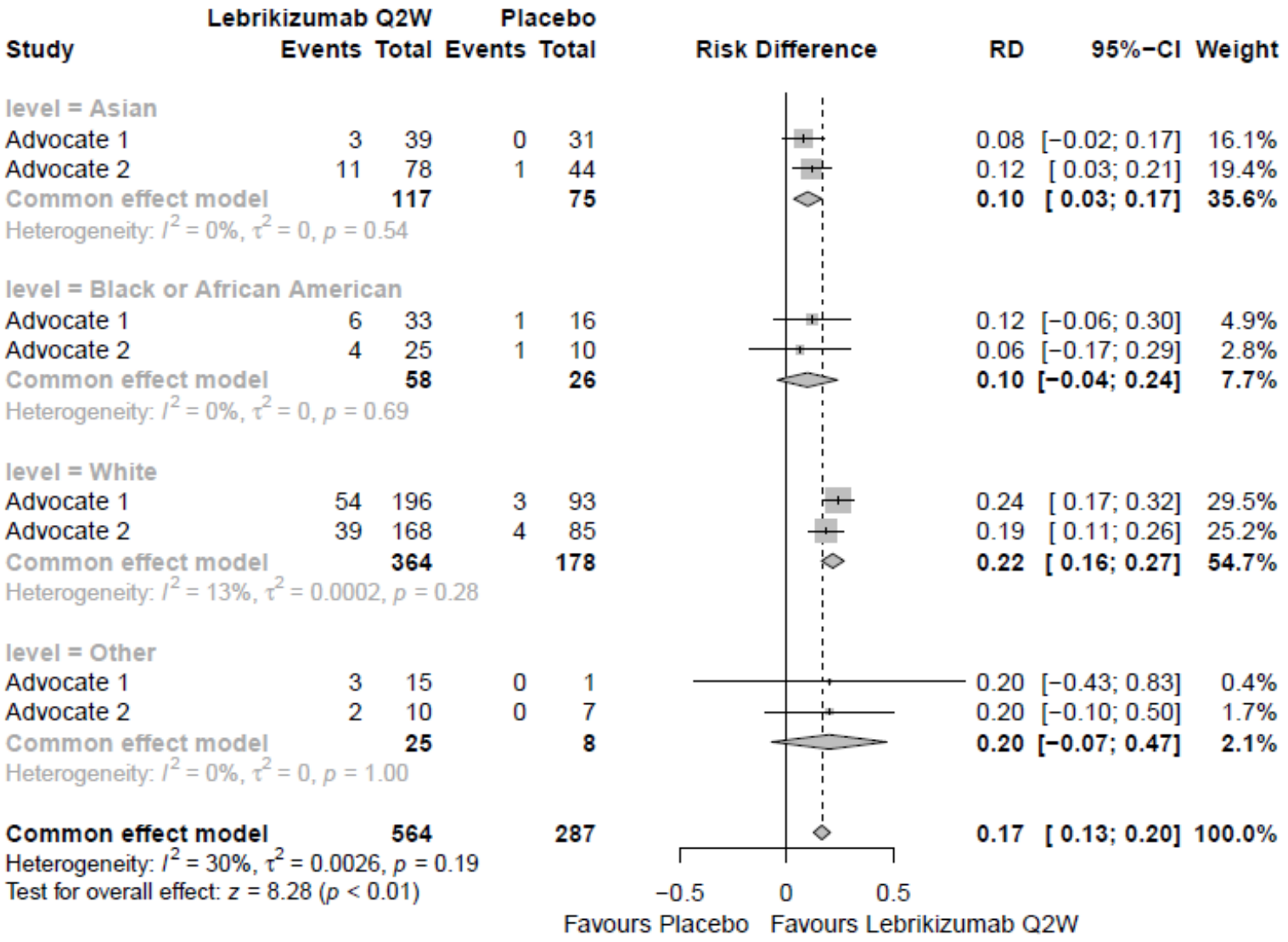

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Baseline IGA 3
Advocate 1 38 170 2 83 11.66 [2.74; 49.63] 21.1%
Advocate 2 38 175 4 95 6.31 [2.18; 18.28] 39.0%
Common effect model 345 178 7.82 [3.32; 18.44] 60.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.50
level = Baseline IGA 4
Advocate 1 28 113 2 58 9.22 [2.11; 40.26] 20.3%
Advocate 2 18 106 2 51 5.01 [1.12; 22.51] 19.6%
Common effect model 219 109 6.84 [2.39; 19.58] 39.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.57
Common effect model 564 287 7.41 [3.81; 14.41] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.85
Test for overall effect: z = 5.91 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Baseline IGA 3
Advocate 1 38 170 2 83 0.20 [0.13; 0.27] 31.7%
Advocate 2 38 175 4 95 0.18 [0.10; 0.25] 29.6%
Common effect model 345 178 0.19 [0.14; 0.24] 61.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.64
level = Baseline IGA 4
Advocate 1 28 113 2 58 0.21 [0.12; 0.31] 18.6%
Advocate 2 18 106 2 51 0.13 [0.04; 0.22] 20.0%
Common effect model 219 109 0.17 [0.11; 0.23] 38.6%
Heterogeneity: I^2 = 37%, τ^2 = 0.0013, p = 0.21
Common effect model 564 287 0.18 [0.14; 0.22] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.58
Test for overall effect: z = 8.90 (p < 0.01)
−0.3 −0.2 −0.1 0 0.1 0.2 0.3
Favours Placebo
Favours Lebrikizumab Q2W

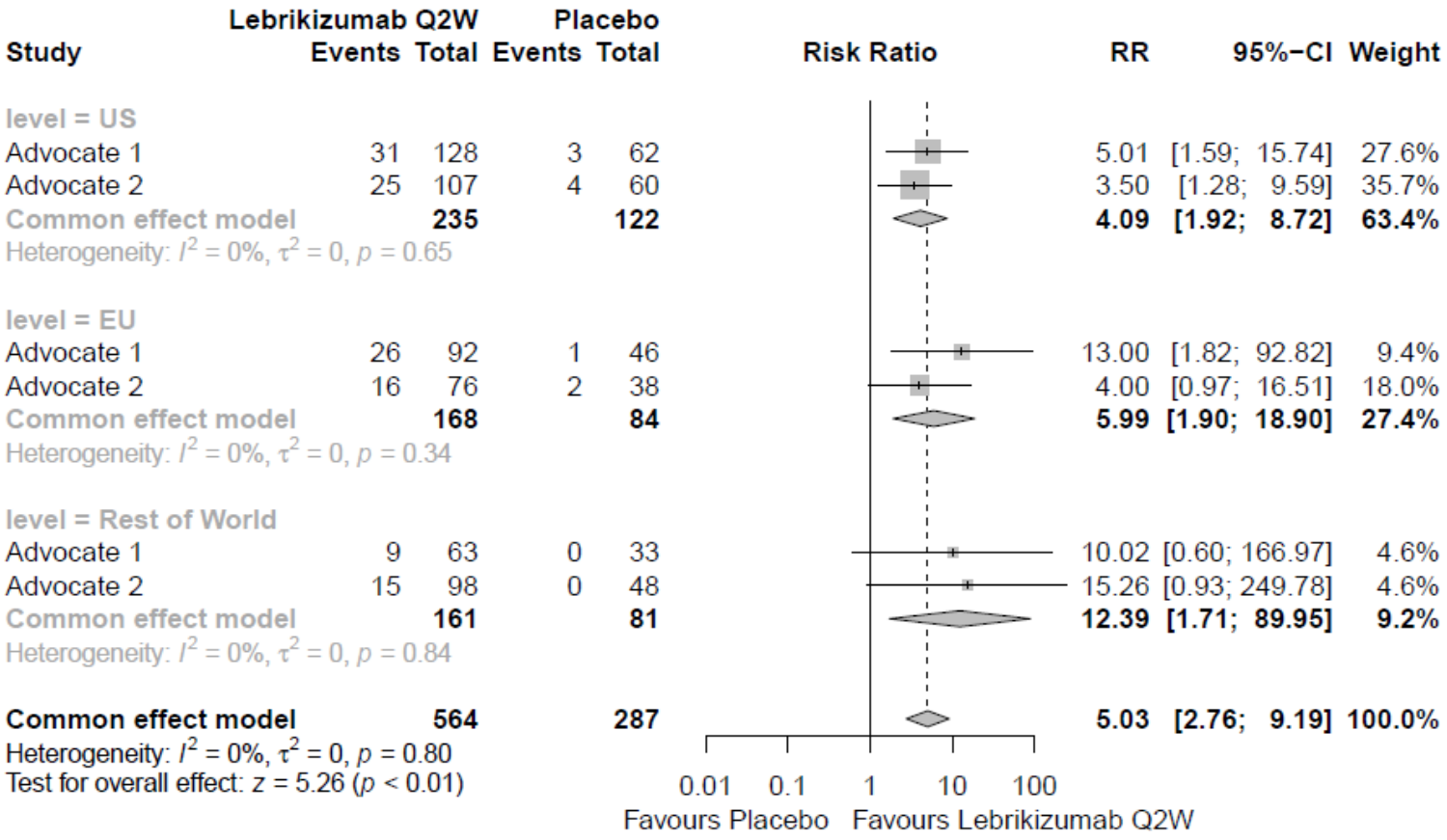
4.5.1.4.3 Ethnie

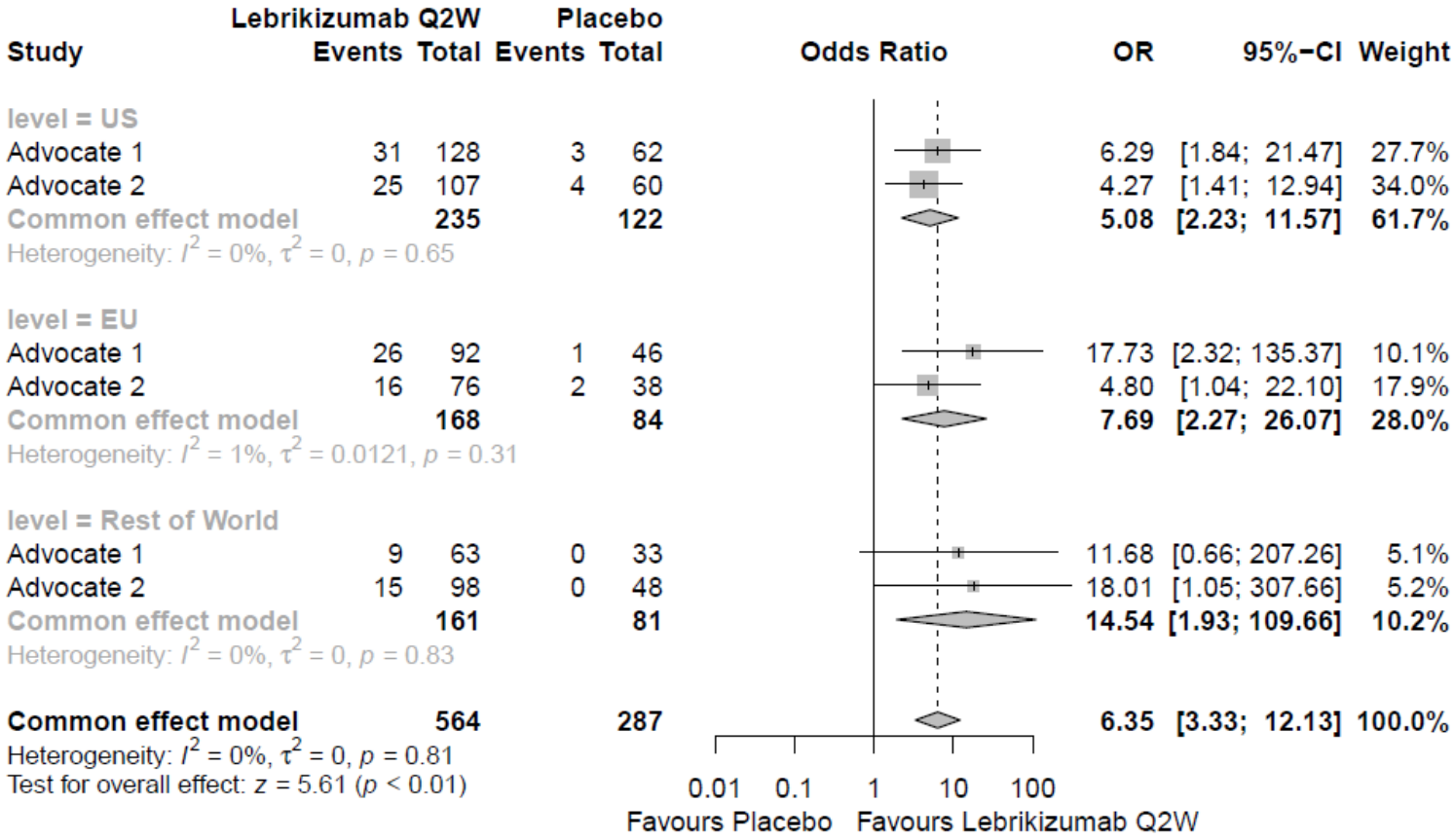


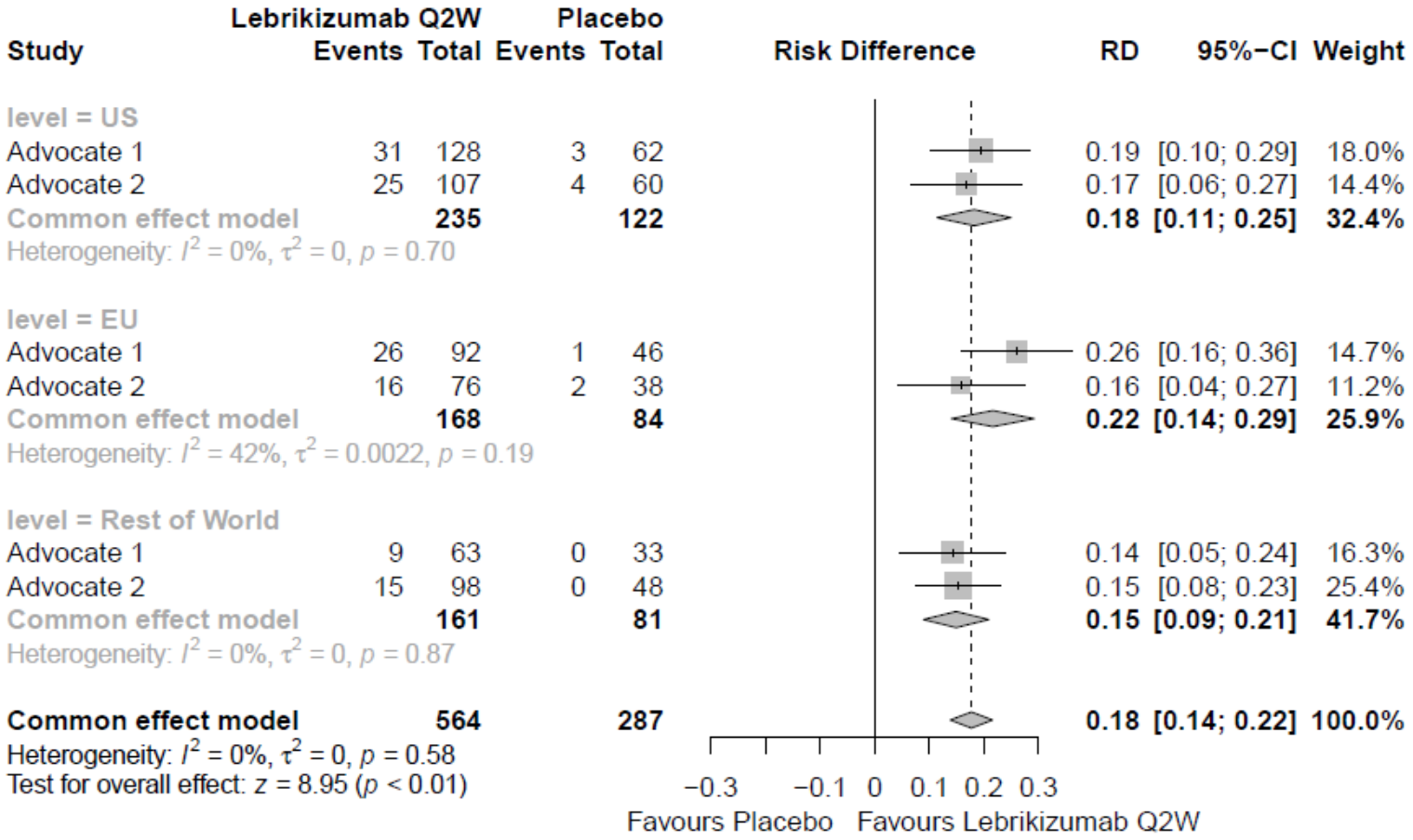

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Asian
Advocate 1 3 39 0 31 6.04 [0.30; 121.49] 4.4%
Advocate 2 11 78 1 44 7.06 [0.88; 56.66] 9.2%
Common effect model 117 75 6.71 [1.21; 37.14] 13.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.93
level = Black or African American
Advocate 1 6 33 1 16 3.33 [0.37; 30.36] 8.2%
Advocate 2 4 25 1 10 1.71 [0.17; 17.55] 7.4%
Common effect model 58 26 2.43 [0.49; 12.07] 15.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.68
level = White
Advocate 1 54 196 3 93 11.41 [3.46; 37.58] 28.2%
Advocate 2 39 168 4 85 6.12 [2.11; 17.77] 35.2%
Common effect model 364 178 8.07 [3.65; 17.87] 63.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.45
level = Other
Advocate 1 3 15 0 1 0.84 [0.03; 25.50] 3.4%
Advocate 2 2 10 0 7 4.41 [0.18; 107.28] 3.9%
Common effect model 25 8 2.04 [0.20; 20.94] 7.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.49
Common effect model 564 287 5.90 [3.13; 11.10] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.80
Test for overall effect: z = 5.50 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Asian
Advocate 1 3 39 0 31 0.08 [−0.02; 0.17] 16.1%
Advocate 2 11 78 1 44 0.12 [0.03; 0.21] 19.4%
Common effect model 117 75 0.10 [0.03; 0.17] 35.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.54
level = Black or African American
Advocate 1 6 33 1 16 0.12 [−0.06; 0.30] 4.9%
Advocate 2 4 25 1 10 0.06 [−0.17; 0.29] 2.8%
Common effect model 58 26 0.10 [−0.04; 0.24] 7.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.69
level = White
Advocate 1 54 196 3 93 0.24 [0.17; 0.32] 29.5%
Advocate 2 39 168 4 85 0.19 [0.11; 0.26] 25.2%
Common effect model 364 178 0.22 [0.16; 0.27] 54.7%
Heterogeneity: I^2 = 13%, τ^2 = 0.0002, p = 0.28
level = Other
Advocate 1 3 15 0 1 0.20 [−0.43; 0.83] 0.4%
Advocate 2 2 10 0 7 0.20 [−0.10; 0.50] 1.7%
Common effect model 25 8 0.20 [−0.07; 0.47] 2.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 1.00
Common effect model 564 287 0.17 [0.13; 0.20] 100.0%
Heterogeneity: I^2 = 30%, τ^2 = 0.0026, p = 0.19
Test for overall effect: z = 8.28 (p < 0.01)
−0.5
0
0.5
Favours Placebo
Favours Lebrikizumab Q2W

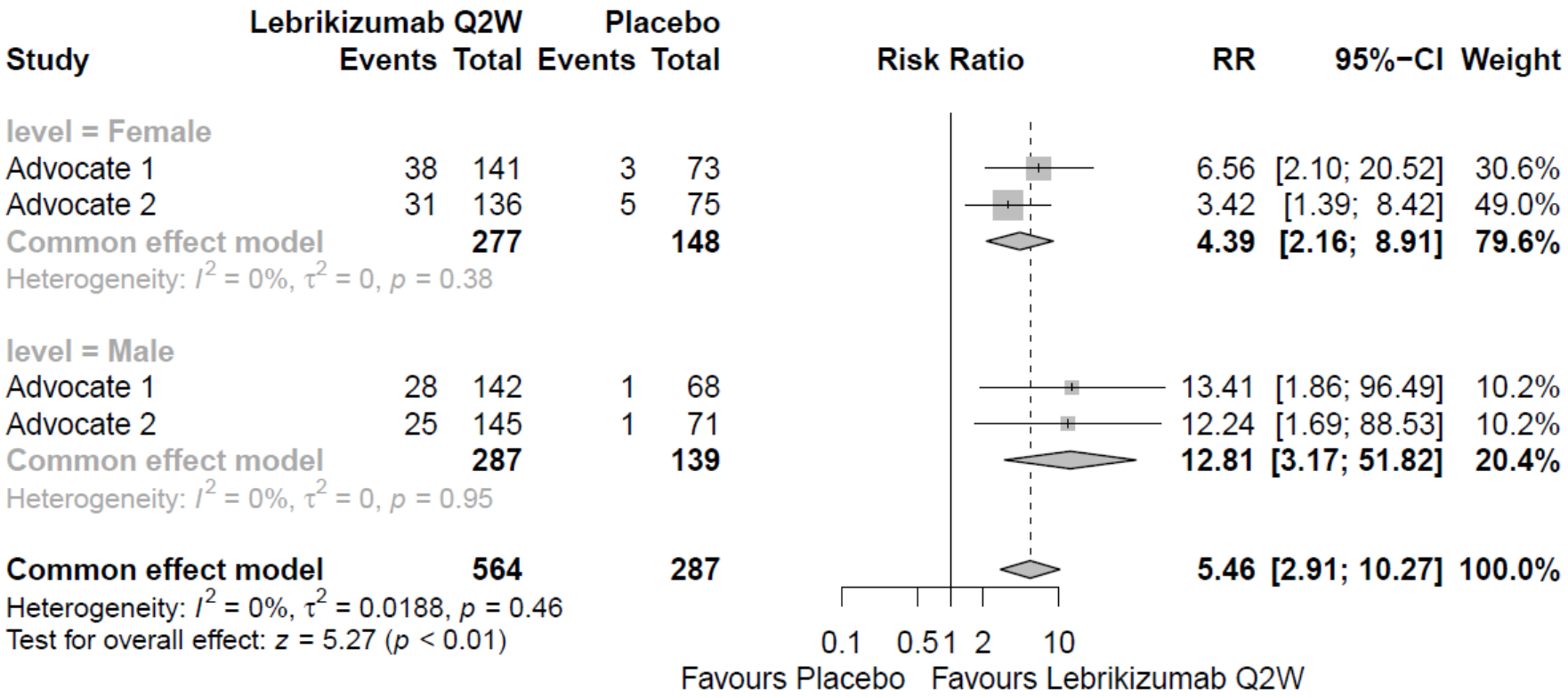
4.5.1.4.4 Region

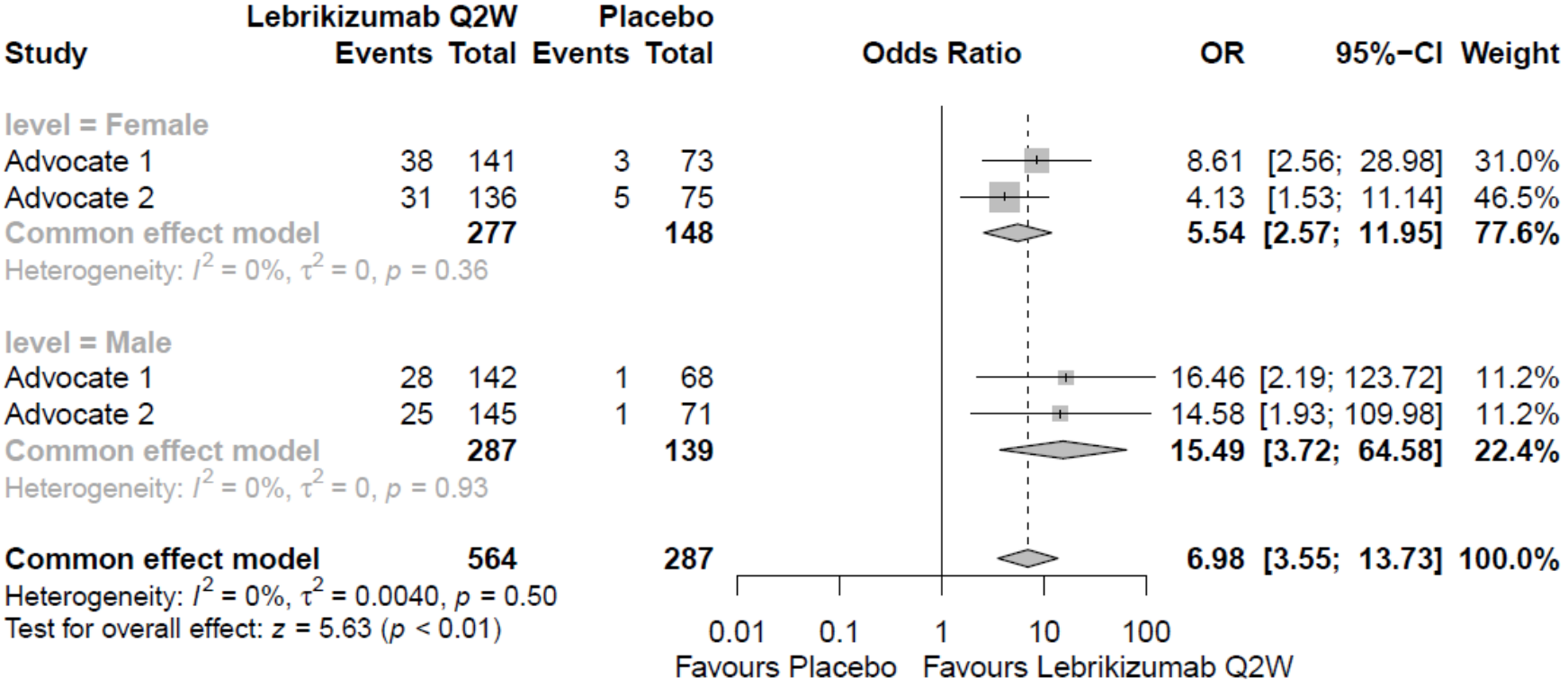


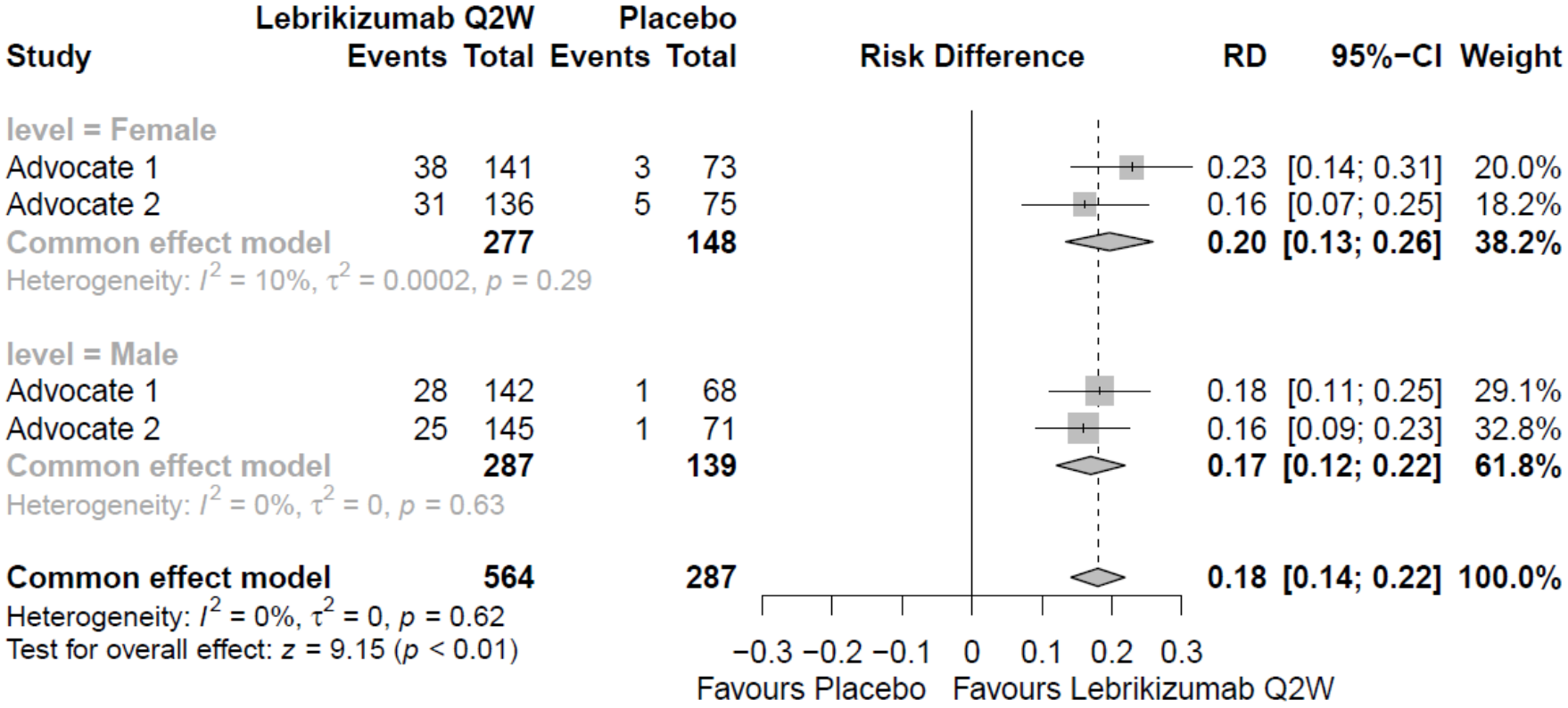

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = US
Advocate 1 31 128 3 62 6.29 [1.84; 21.47] 27.7%
Advocate 2 25 107 4 60 4.27 [1.41; 12.94] 34.0%
Common effect model 235 122 5.08 [2.23; 11.57] 61.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.65
level = EU
Advocate 1 26 92 1 46 17.73 [2.32; 135.37] 10.1%
Advocate 2 16 76 2 38 4.80 [1.04; 22.10] 17.9%
Common effect model 168 84 7.69 [2.27; 26.07] 28.0%
Heterogeneity: I^2 = 1%, τ^2 = 0.0121, p = 0.31
level = Rest of World
Advocate 1 9 63 0 33 11.68 [0.66; 207.26] 5.1%
Advocate 2 15 98 0 48 18.01 [1.05; 307.66] 5.2%
Common effect model 161 81 14.54 [1.93; 109.66] 10.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.83
Common effect model 564 287 6.35 [3.33; 12.13] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.81
Test for overall effect: z = 5.61 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = US
Advocate 1 31 128 3 62 0.19 [0.10; 0.29] 18.0%
Advocate 2 25 107 4 60 0.17 [0.06; 0.27] 14.4%
Common effect model 235 122 0.18 [0.11; 0.25] 32.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.70
level = EU
Advocate 1 26 92 1 46 0.26 [0.16; 0.36] 14.7%
Advocate 2 16 76 2 38 0.16 [0.04; 0.27] 11.2%
Common effect model 168 84 0.22 [0.14; 0.29] 25.9%
Heterogeneity: I^2 = 42%, τ^2 = 0.0022, p = 0.19
level = Rest of World
Advocate 1 9 63 0 33 0.14 [0.05; 0.24] 16.3%
Advocate 2 15 98 0 48 0.15 [0.08; 0.23] 25.4%
Common effect model 161 81 0.15 [0.09; 0.21] 41.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.87
Common effect model 564 287 0.18 [0.14; 0.22] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.58
Test for overall effect: z = 8.95 (p < 0.01)
−0.3 −0.1 0 0.1 0.2 0.3
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.4.5 Geschlecht

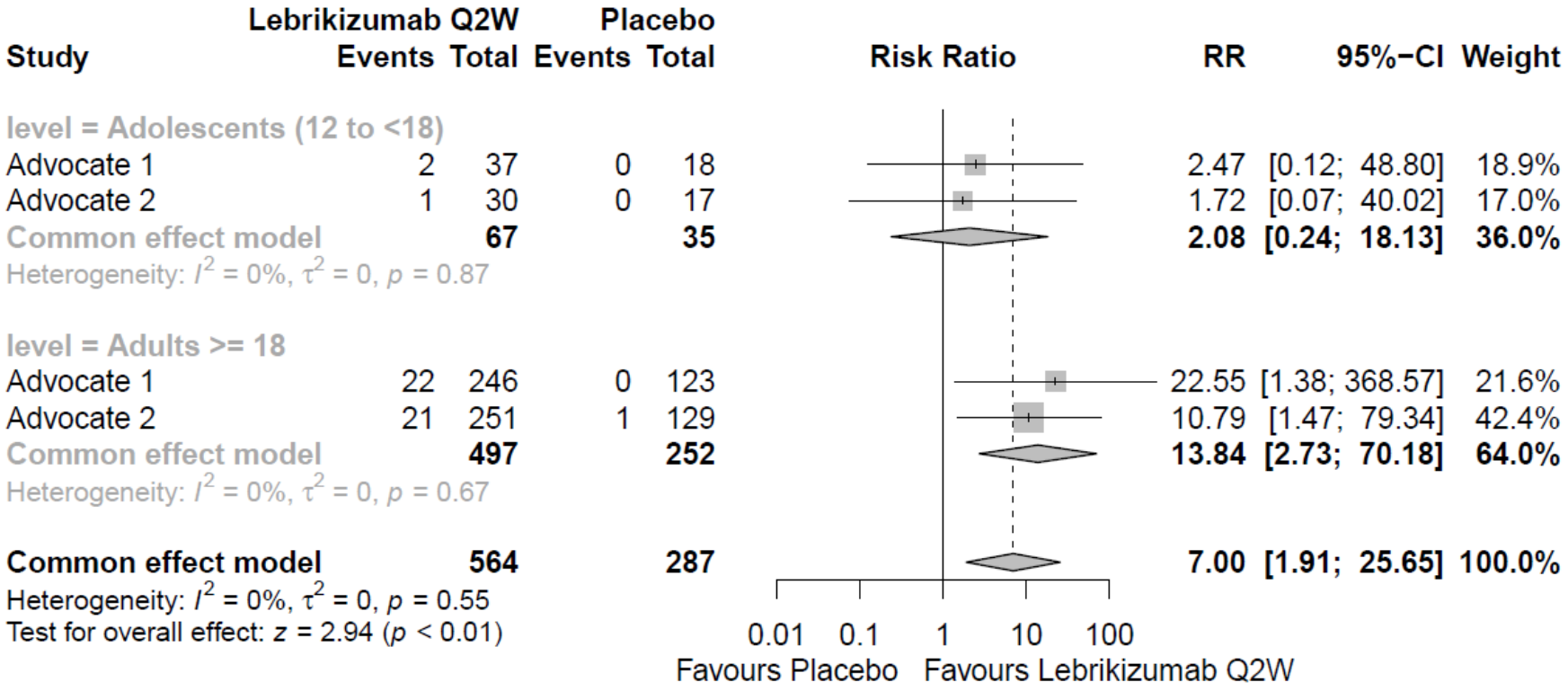


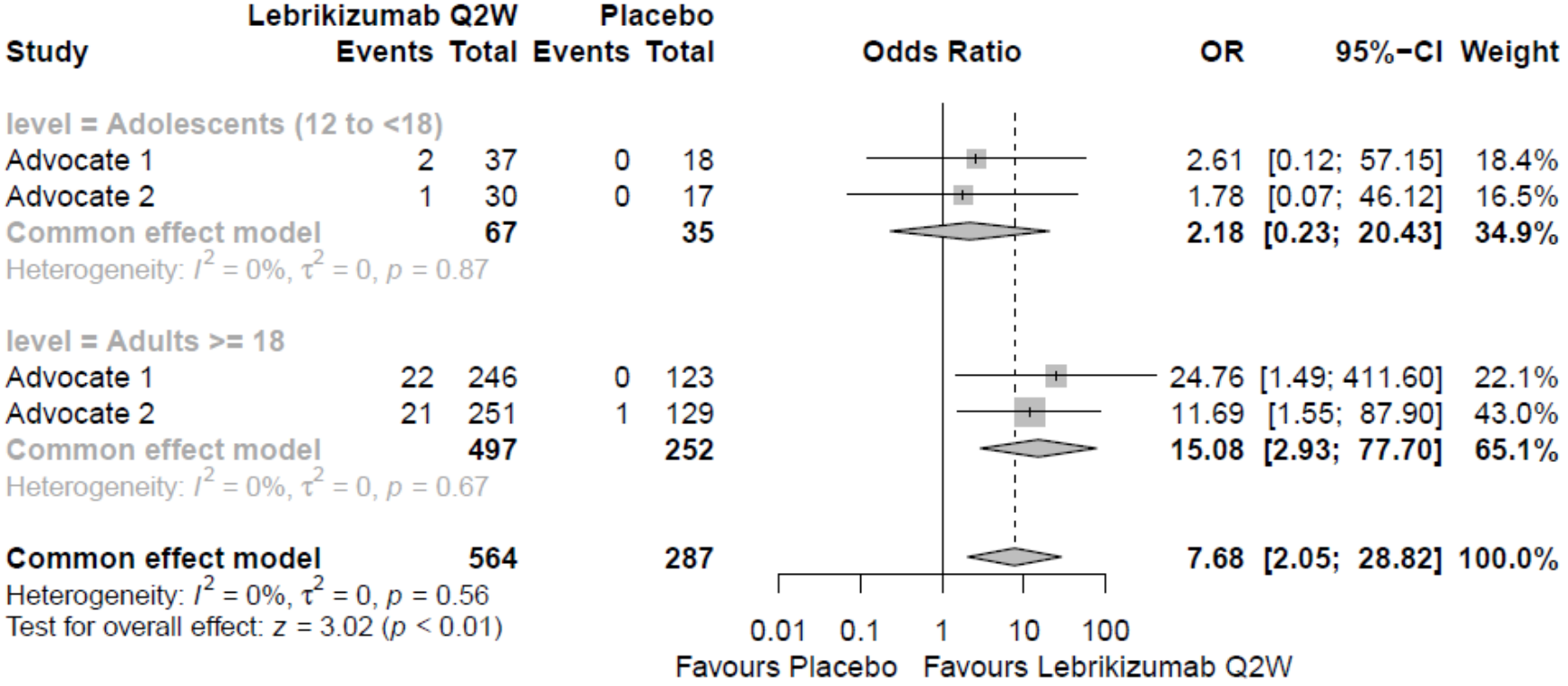

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Female
Advocate 1 38 141 3 73 8.61 [2.56; 28.98] 31.0%
Advocate 2 31 136 5 75 4.13 [1.53; 11.14] 46.5%
Common effect model 277 148 5.54 [2.57; 11.95] 77.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.36
level = Male
Advocate 1 28 142 1 68 16.46 [2.19; 123.72] 11.2%
Advocate 2 25 145 1 71 14.58 [1.93; 109.98] 11.2%
Common effect model 287 139 15.49 [3.72; 64.58] 22.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.93
Common effect model 564 287 6.98 [3.55; 13.73] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0.0040, p = 0.50
Test for overall effect: z = 5.63 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W

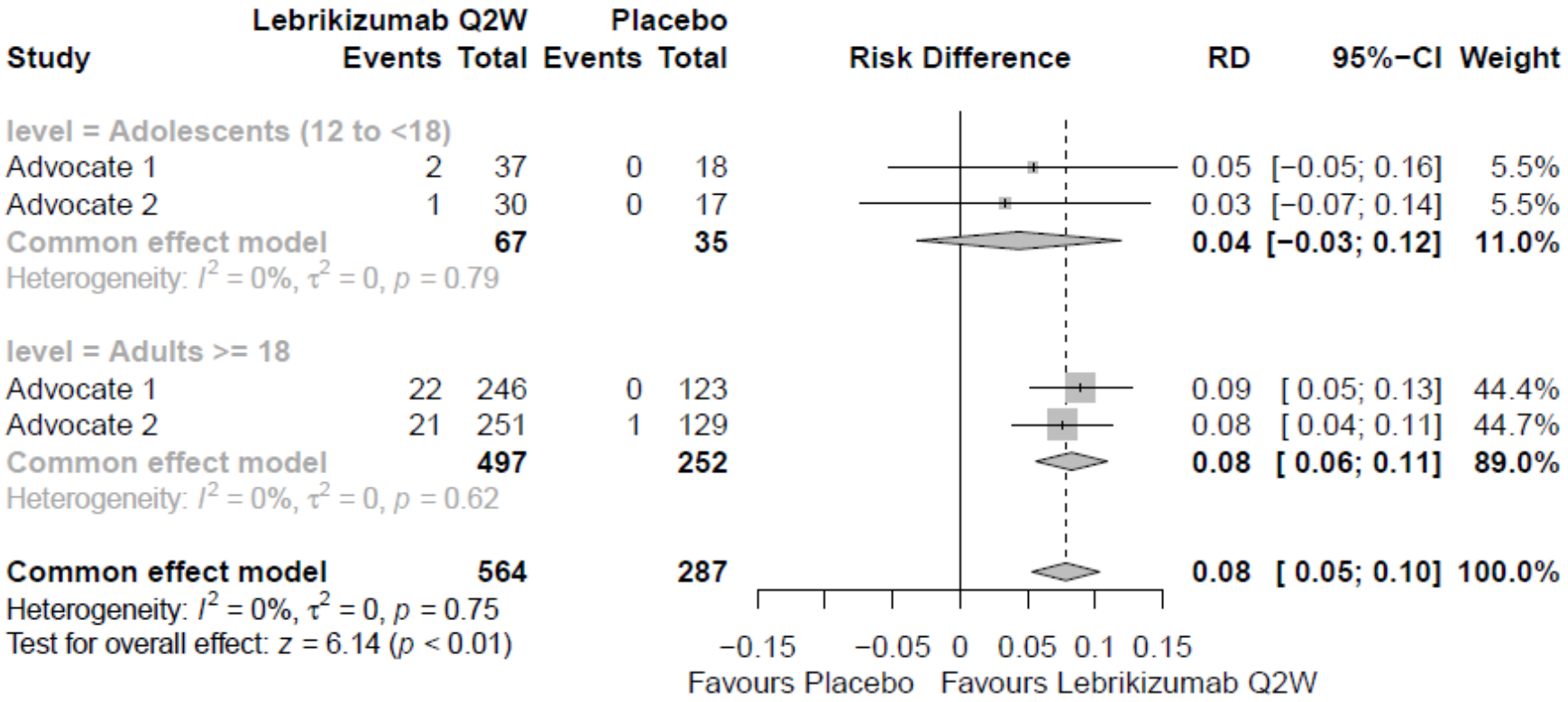

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Female
Advocate 1 38 141 3 73 0.23 [0.14; 0.31] 20.0%
Advocate 2 31 136 5 75 0.16 [0.07; 0.25] 18.2%
Common effect model 277 148 0.20 [0.13; 0.26] 38.2%
Heterogeneity: I^2 = 10%, τ^2 = 0.0002, p = 0.29
level = Male
Advocate 1 28 142 1 68 0.18 [0.11; 0.25] 29.1%
Advocate 2 25 145 1 71 0.16 [0.09; 0.23] 32.8%
Common effect model 287 139 0.17 [0.12; 0.22] 61.8%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.63
Common effect model 564 287 0.18 [0.14; 0.22] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.62
Test for overall effect: z = 9.15 (p < 0.01)
−0.3 −0.2 −0.1 0 0.1 0.2 0.3
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.5 SCORAD-90

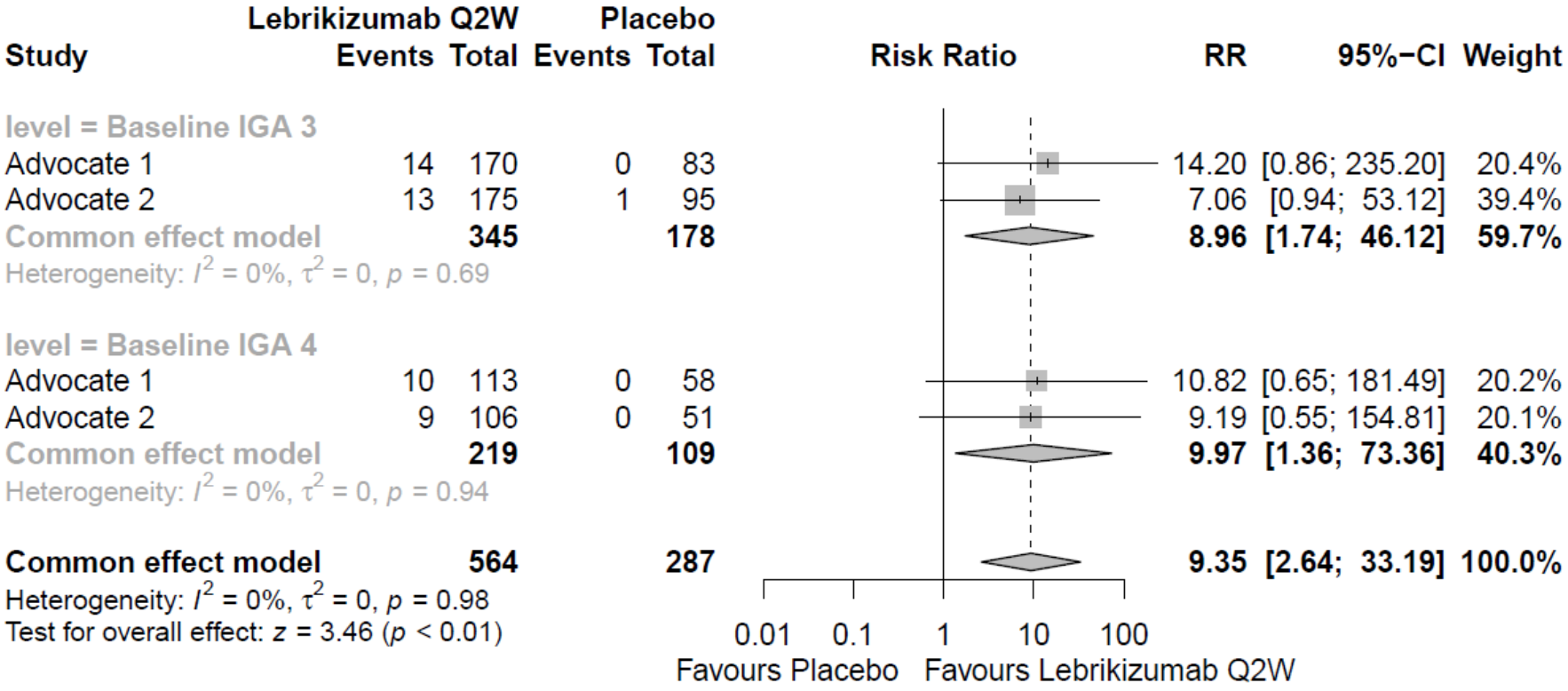
4.5.1.5.1 Altersgruppe

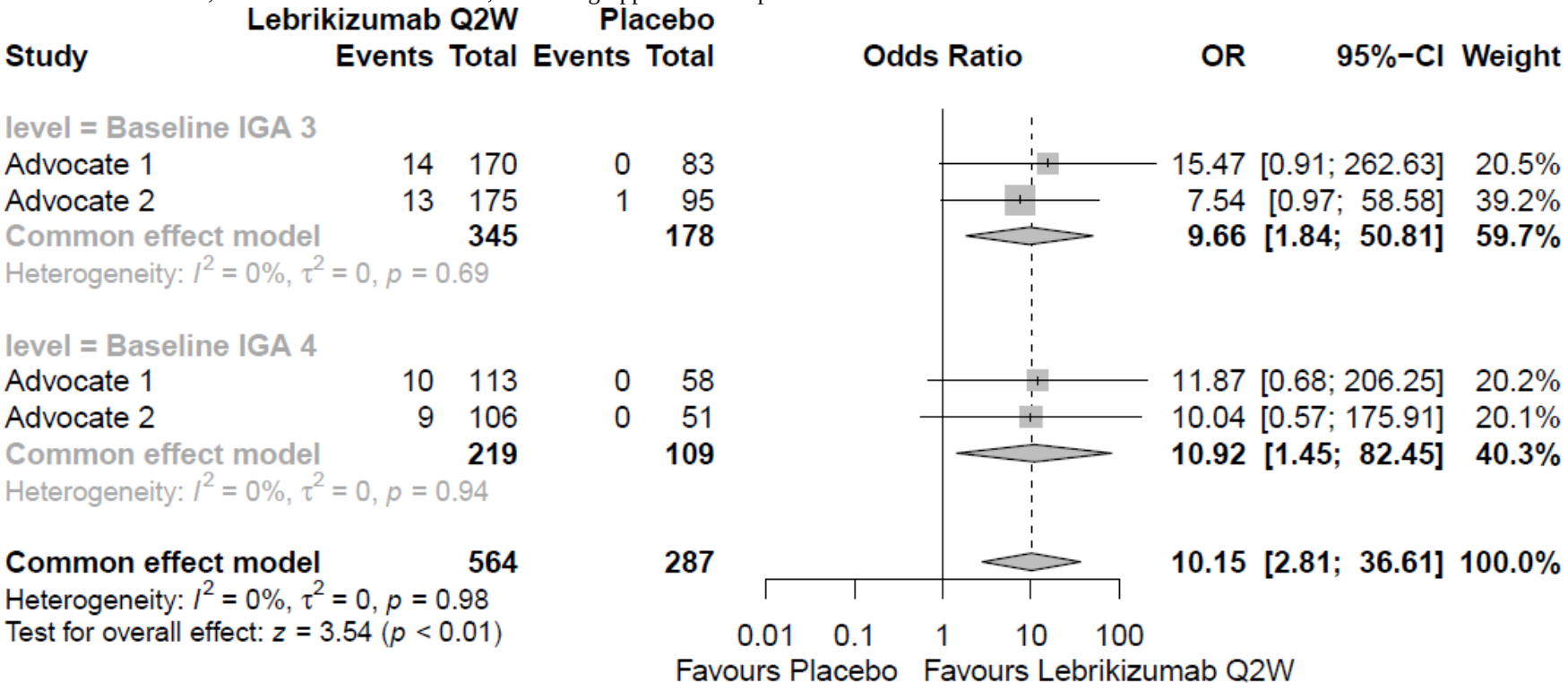


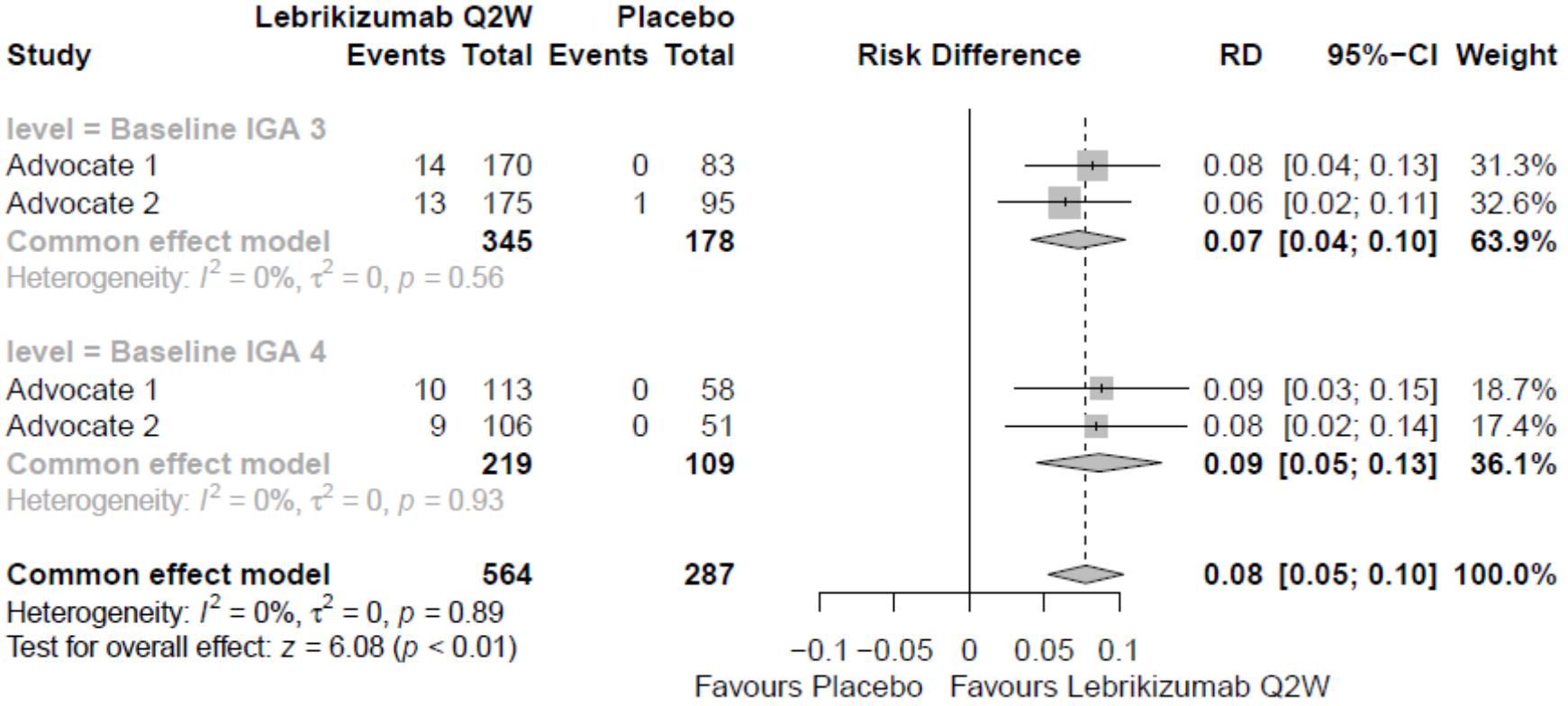

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 2 37 0 18 2.61 [0.12; 57.15] 18.4%
Advocate 2 1 30 0 17 1.78 [0.07; 46.12] 16.5%
Common effect model 67 35 2.18 [0.23; 20.43] 34.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.87
level = Adults >= 18
Advocate 1 22 246 0 123 24.76 [1.49; 411.60] 22.1%
Advocate 2 21 251 1 129 11.69 [1.55; 87.90] 43.0%
Common effect model 497 252 15.08 [2.93; 77.70] 65.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.67
Common effect model 564 287 7.68 [2.05; 28.82] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.56
Test for overall effect: z = 3.02 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 2 37 0 18 0.05 [−0.05; 0.16] 5.5%
Advocate 2 1 30 0 17 0.03 [−0.07; 0.14] 5.5%
Common effect model 67 35 0.04 [−0.03; 0.12] 11.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.79
level = Adults >= 18
Advocate 1 22 246 0 123 0.09 [0.05; 0.13] 44.4%
Advocate 2 21 251 1 129 0.08 [0.04; 0.11] 44.7%
Common effect model 497 252 0.08 [0.06; 0.11] 89.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.62
Common effect model 564 287 0.08 [0.05; 0.10] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.75
Test for overall effect: z = 6.14 (p < 0.01)
−0.15 −0.05 0 0.05 0.1 0.15
Favours Placebo
Favours Lebrikizumab Q2W

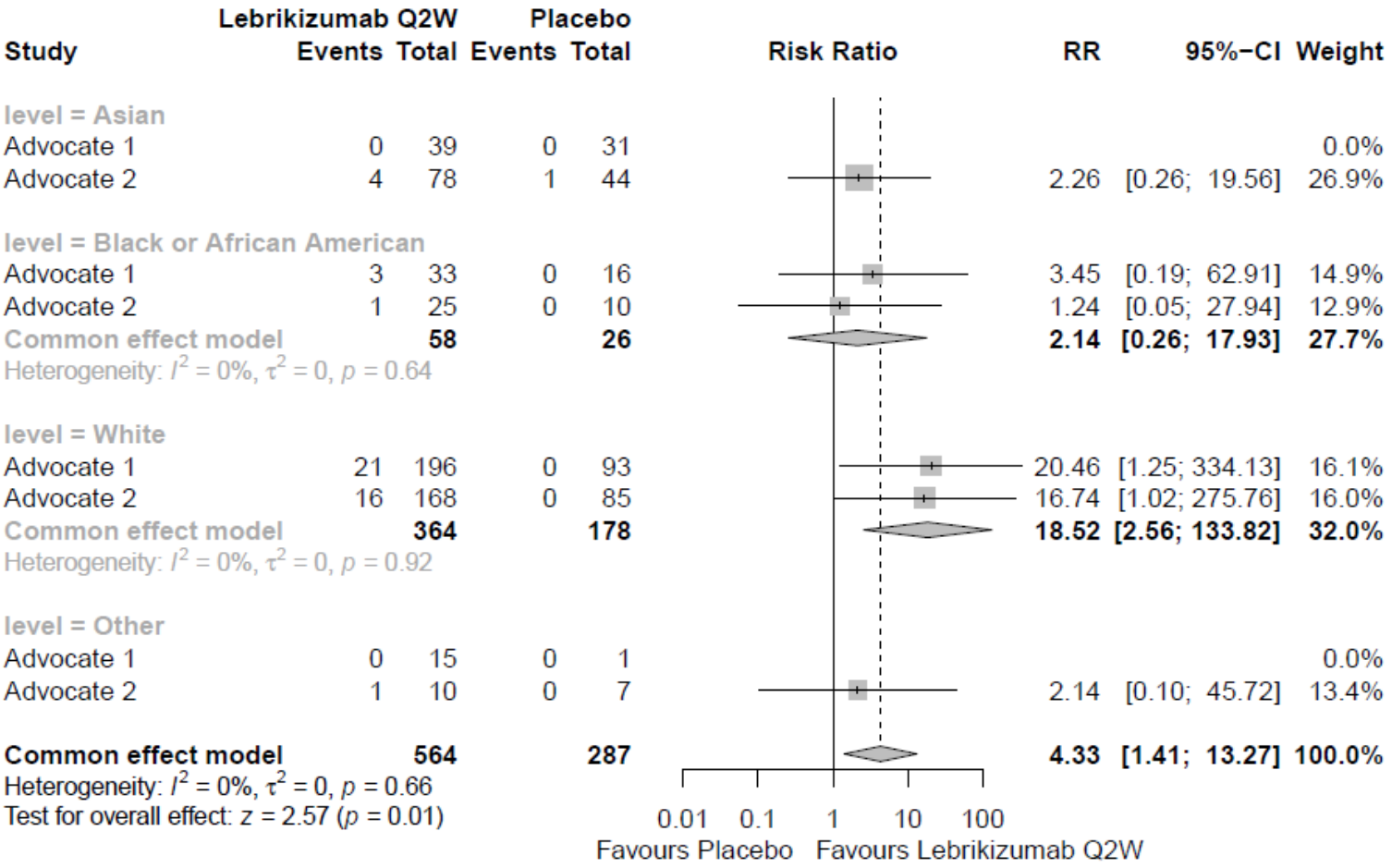
4.5.1.5.2 Krankheitsschwere

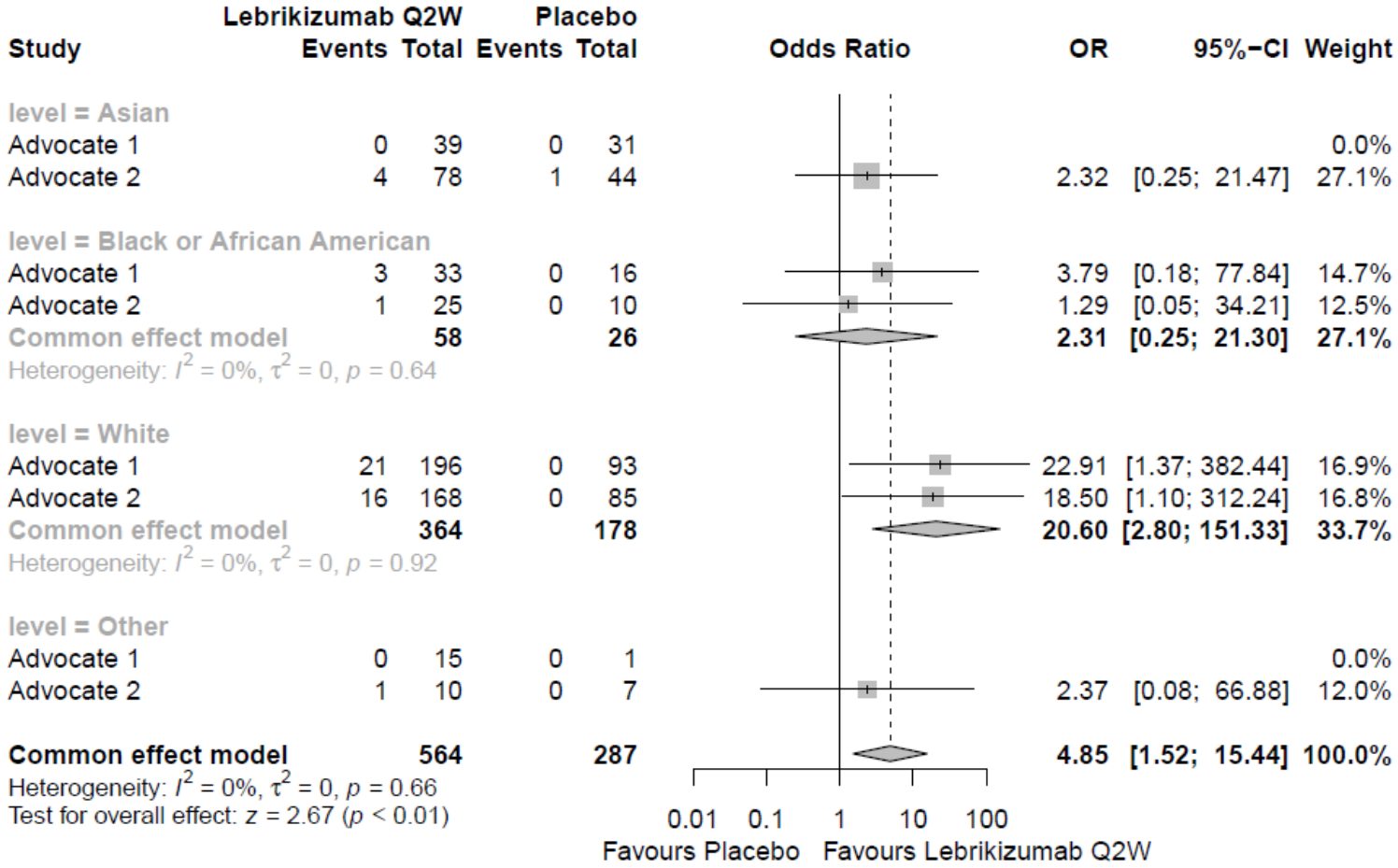


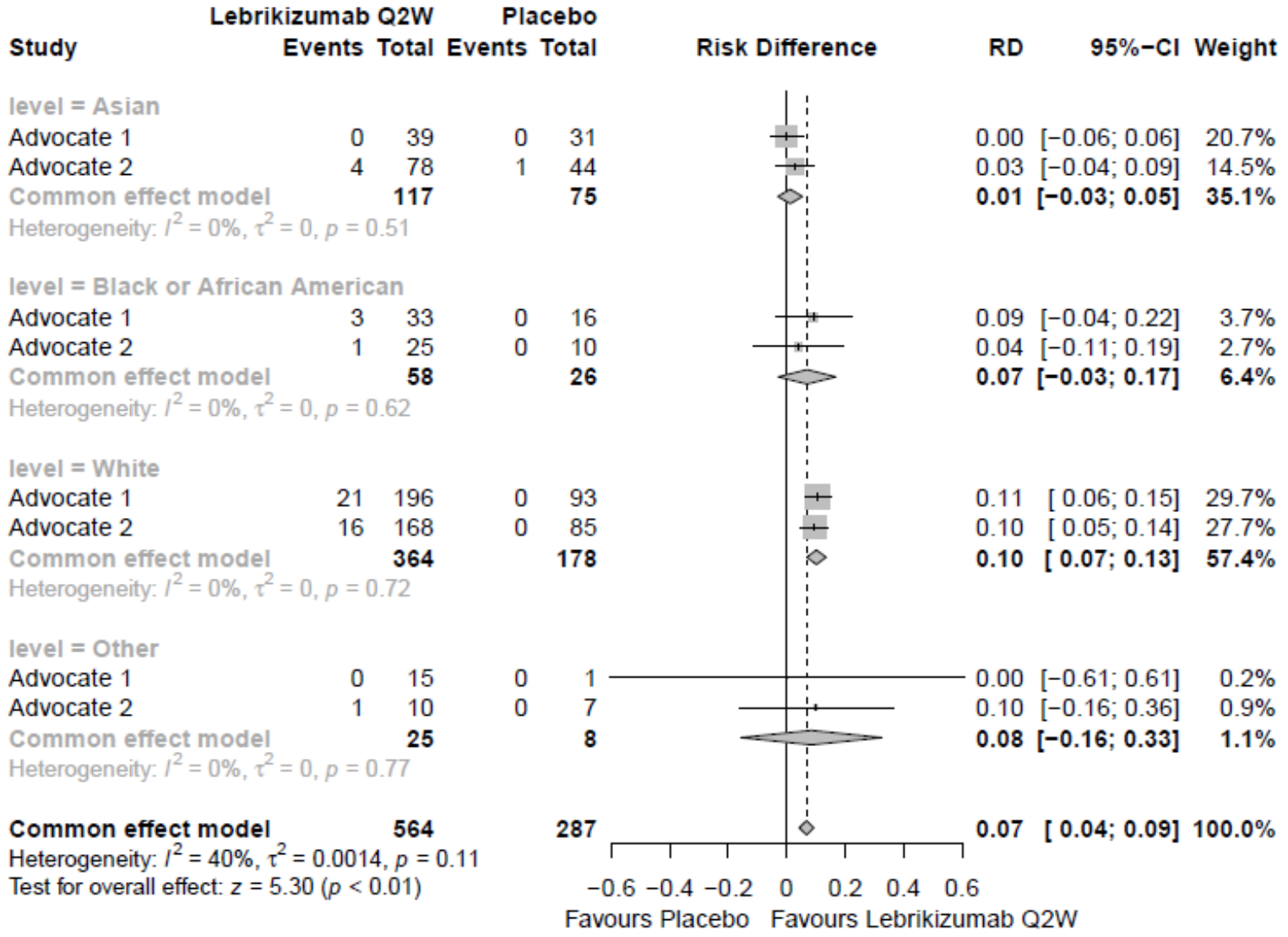

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Baseline IGA 3
Advocate 1 14 170 0 83 15.47 [0.91; 262.63] 20.5%
Advocate 2 13 175 1 95 7.54 [0.97; 58.58] 39.2%
Common effect model 345 178 9.66 [1.84; 50.81] 59.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.69
level = Baseline IGA 4
Advocate 1 10 113 0 58 11.87 [0.68; 206.25] 20.2%
Advocate 2 9 106 0 51 10.04 [0.57; 175.91] 20.1%
Common effect model 219 109 10.92 [1.45; 82.45] 40.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.94
Common effect model 564 287 10.15 [2.81; 36.61] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.98
Test for overall effect: z = 3.54 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Baseline IGA 3
Advocate 1 14 170 0 83 0.08 [0.04; 0.13] 31.3%
Advocate 2 13 175 1 95 0.06 [0.02; 0.11] 32.6%
Common effect model 345 178 0.07 [0.04; 0.10] 63.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.56
level = Baseline IGA 4
Advocate 1 10 113 0 58 0.09 [0.03; 0.15] 18.7%
Advocate 2 9 106 0 51 0.08 [0.02; 0.14] 17.4%
Common effect model 219 109 0.09 [0.05; 0.13] 36.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.93
Common effect model 564 287 0.08 [0.05; 0.10] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.89
Test for overall effect: z = 6.08 (p < 0.01)
−0.1 −0.05 0 0.05 0.1
Favours Placebo
Favours Lebrikizumab Q2W

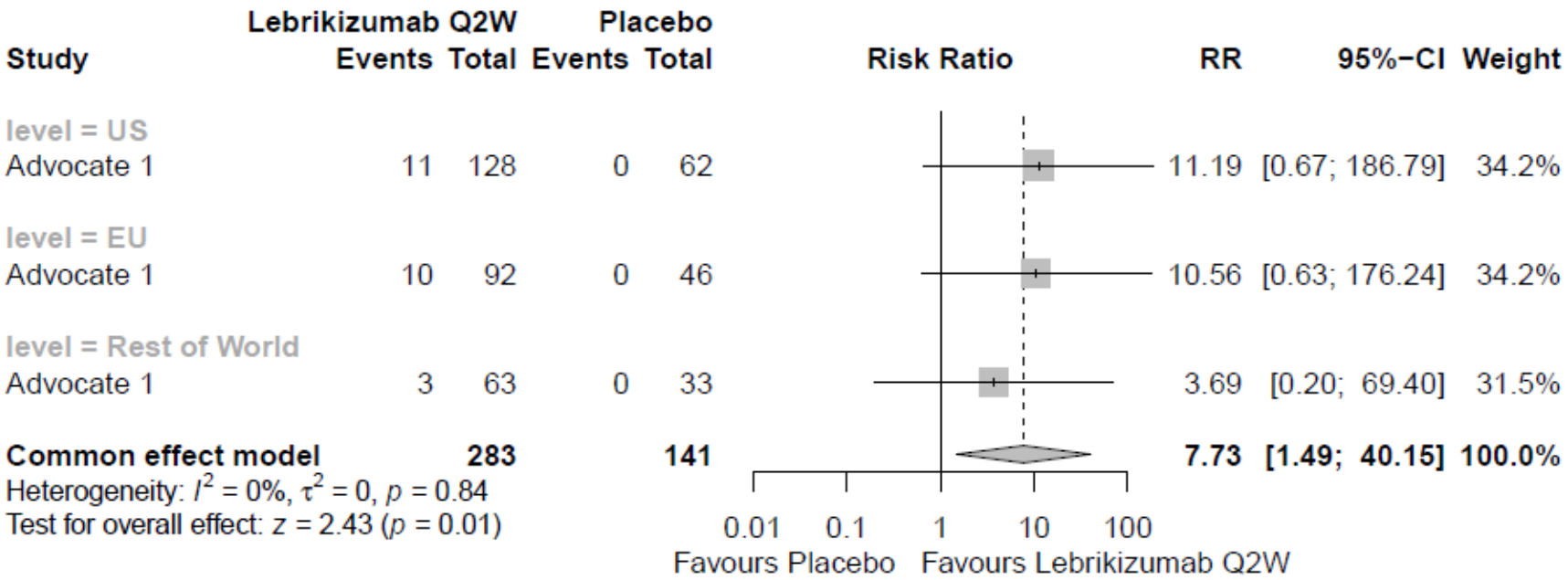
4.5.1.5.3 Ethnie

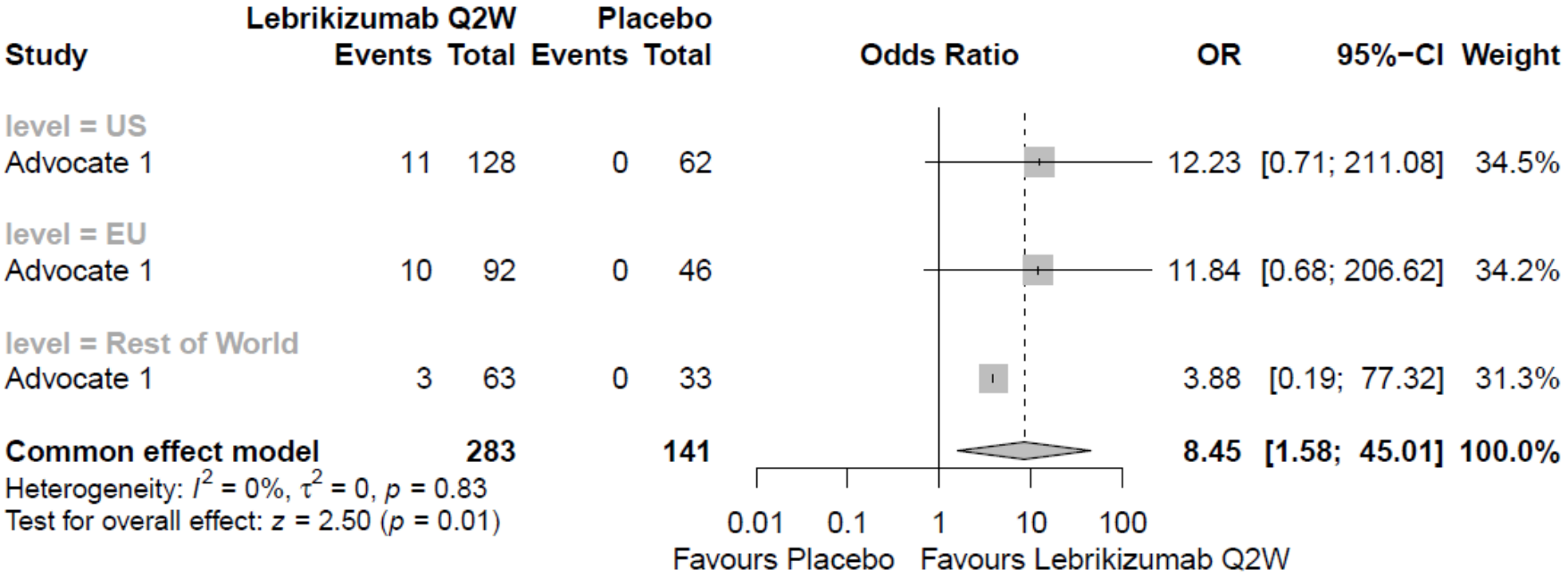


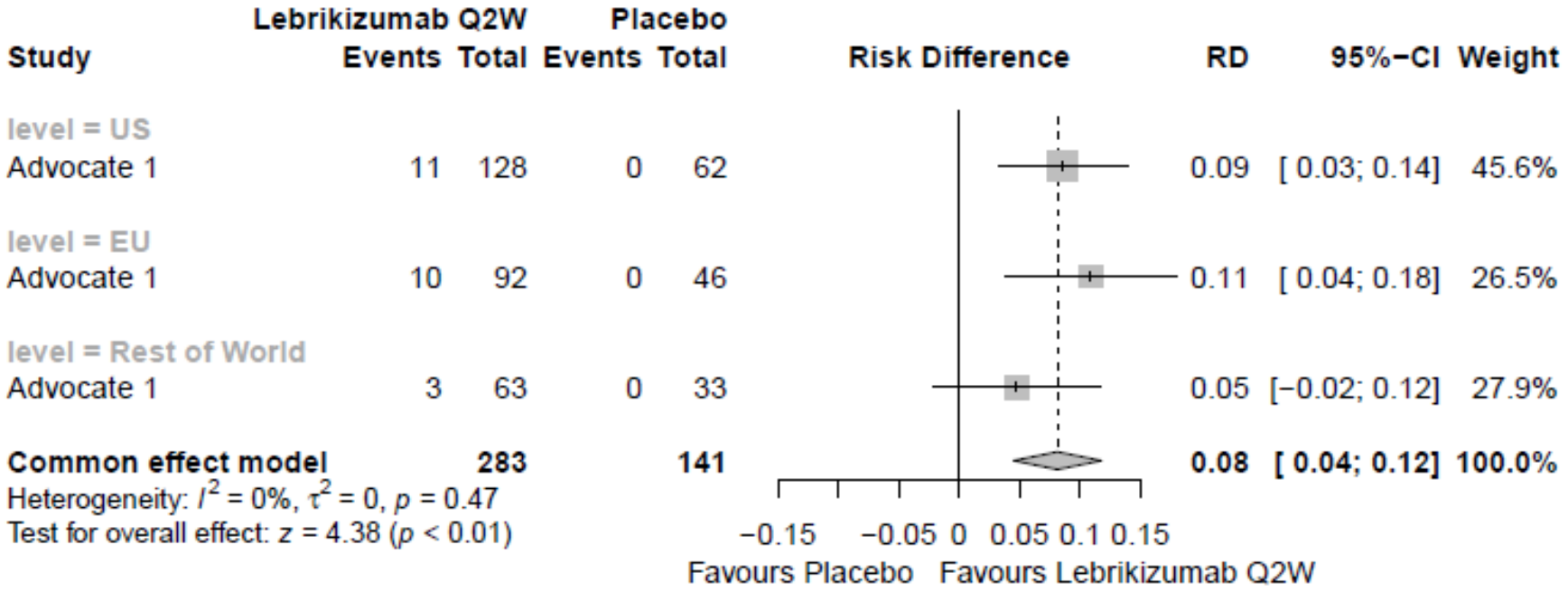

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Asian
Advocate 1 0 39 0 31 0.0%
Advocate 2 4 78 1 44 2.32 [0.25; 21.47] 27.1%
level = Black or African American
Advocate 1 3 33 0 16 3.79 [0.18; 77.84] 14.7%
Advocate 2 1 25 0 10 1.29 [0.05; 34.21] 12.5%
Common effect model 58 26 2.31 [0.25; 21.30] 27.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.64
level = White
Advocate 1 21 196 0 93 22.91 [1.37; 382.44] 16.9%
Advocate 2 16 168 0 85 18.50 [1.10; 312.24] 16.8%
Common effect model 364 178 20.60 [2.80; 151.33] 33.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.92
level = Other
Advocate 1 0 15 0 1 0.0%
Advocate 2 1 10 0 7 2.37 [0.08; 66.88] 12.0%
Common effect model 564 287 4.85 [1.52; 15.44] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.66
Test for overall effect: z = 2.67 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Asian
Advocate 1 0 39 0 31 0.00 [−0.06; 0.06] 20.7%
Advocate 2 4 78 1 44 0.03 [−0.04; 0.09] 14.5%
Common effect model 117 75 0.01 [−0.03; 0.05] 35.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.51
level = Black or African American
Advocate 1 3 33 0 16 0.09 [−0.04; 0.22] 3.7%
Advocate 2 1 25 0 10 0.04 [−0.11; 0.19] 2.7%
Common effect model 58 26 0.07 [−0.03; 0.17] 6.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.62
level = White
Advocate 1 21 196 0 93 0.11 [0.06; 0.15] 29.7%
Advocate 2 16 168 0 85 0.10 [0.05; 0.14] 27.7%
Common effect model 364 178 0.10 [0.07; 0.13] 57.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.72
level = Other
Advocate 1 0 15 0 1 0.00 [−0.61; 0.61] 0.2%
Advocate 2 1 10 0 7 0.10 [−0.16; 0.36] 0.9%
Common effect model 25 8 0.08 [−0.16; 0.33] 1.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.77
Common effect model 564 287 0.07 [0.04; 0.09] 100.0%
Heterogeneity: I^2 = 40%, τ^2 = 0.0014, p = 0.11
Test for overall effect: z = 5.30 (p < 0.01)
−0.6 −0.4 −0.2 0 0.2 0.4 0.6
Favours Placebo
Favours Lebrikizumab Q2W

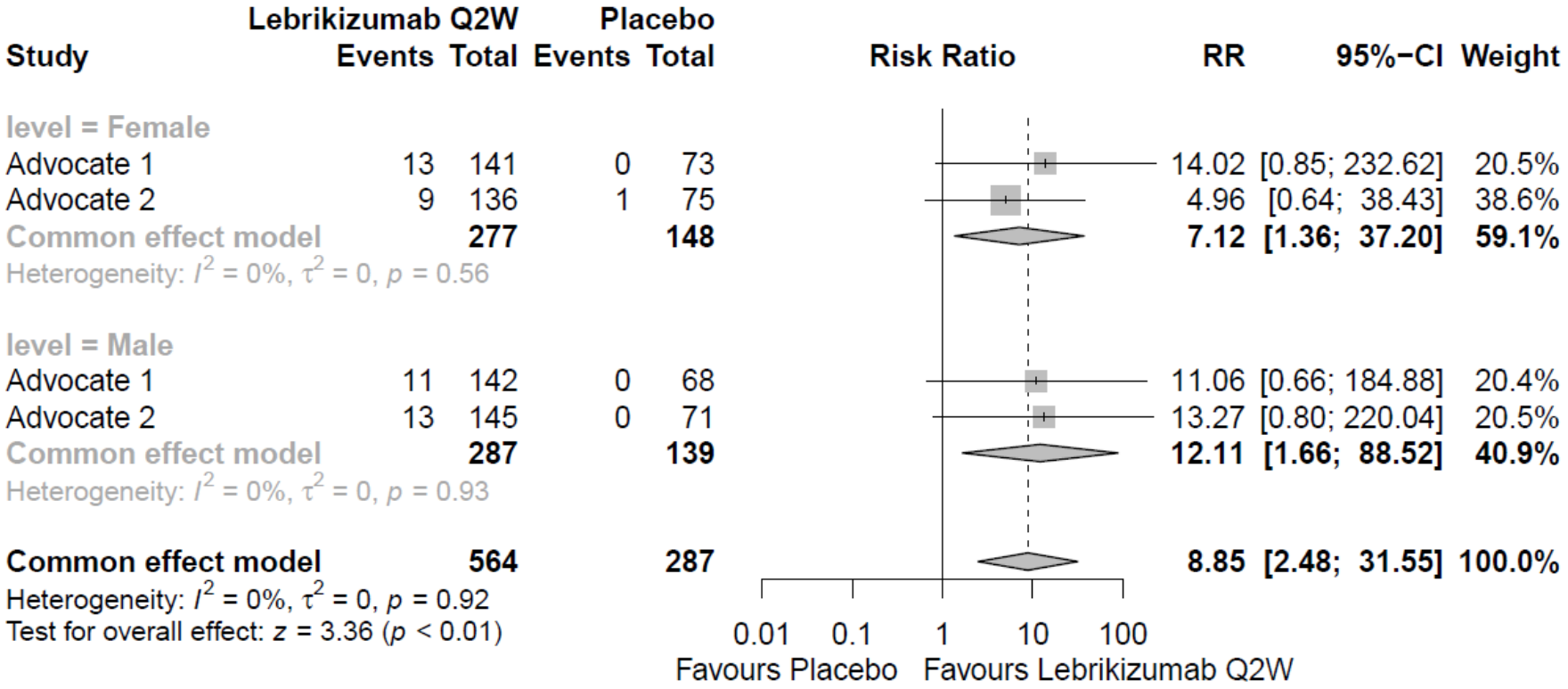
4.5.1.5.4 Region

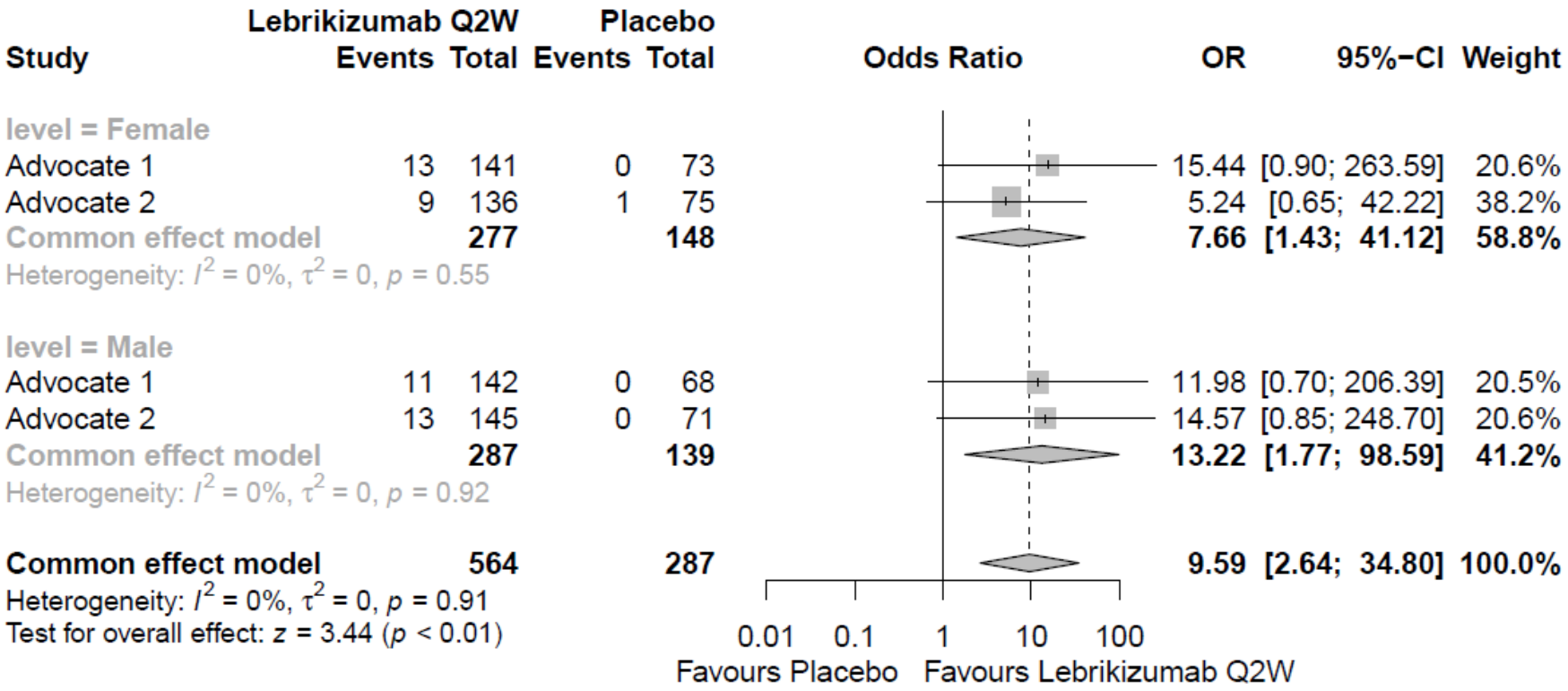


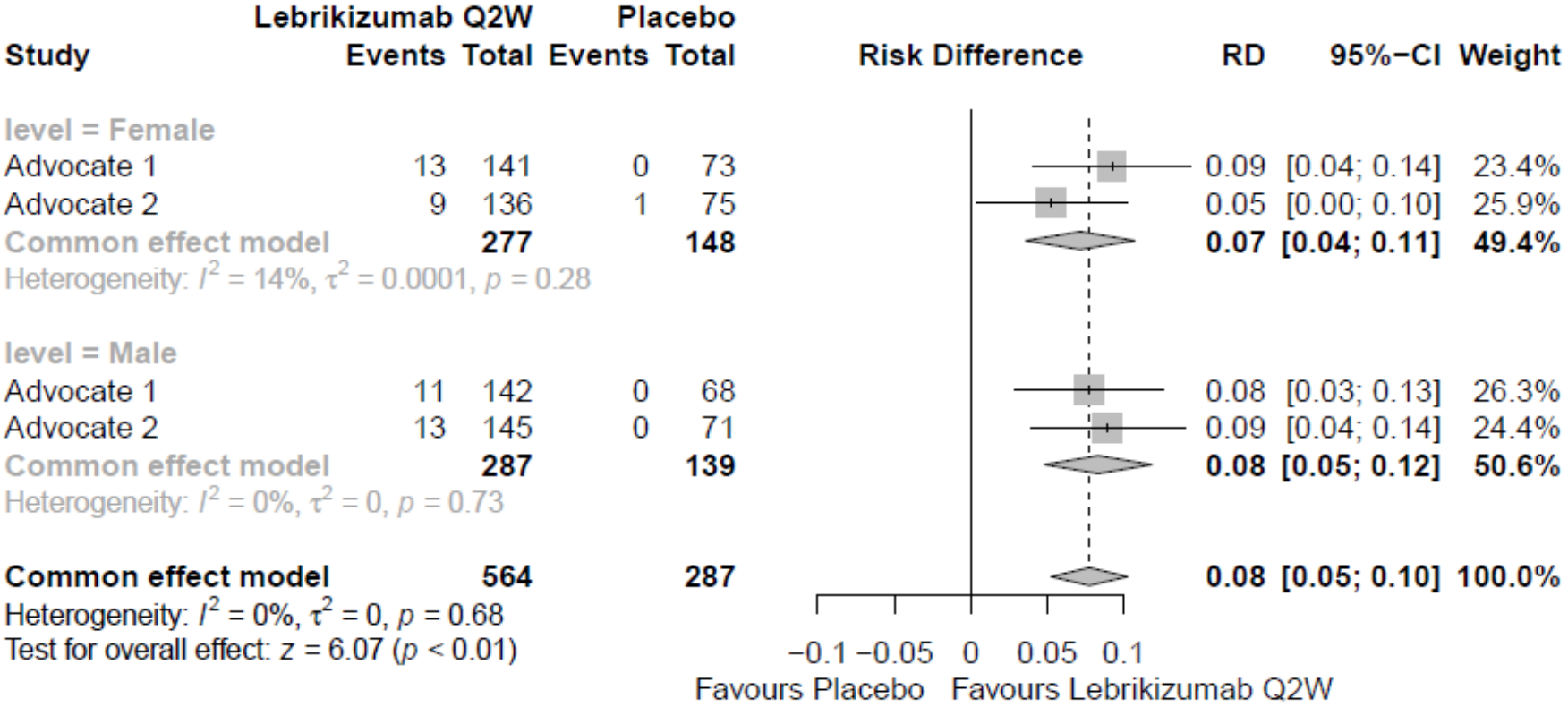

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = US
Advocate 1 11 128 0 62 12.23 [0.71; 211.08] 34.5%
level = EU
Advocate 1 10 92 0 46 11.84 [0.68; 206.62] 34.2%
level = Rest of World
Advocate 1 3 63 0 33 3.88 [0.19; 77.32] 31.3%
Common effect model 283 141 8.45 [1.58; 45.01] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.83
Test for overall effect: z = 2.50 (p = 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = US
Advocate 1 11 128 0 62 0.09 [0.03; 0.14] 45.6%
level = EU
Advocate 1 10 92 0 46 0.11 [0.04; 0.18] 26.5%
level = Rest of World
Advocate 1 3 63 0 33 0.05 [−0.02; 0.12] 27.9%
Common effect model 283 141 0.08 [0.04; 0.12] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.47
Test for overall effect: z = 4.38 (p < 0.01)
−0.15 −0.05 0 0.05 0.1 0.15
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.5.5 Geschlecht

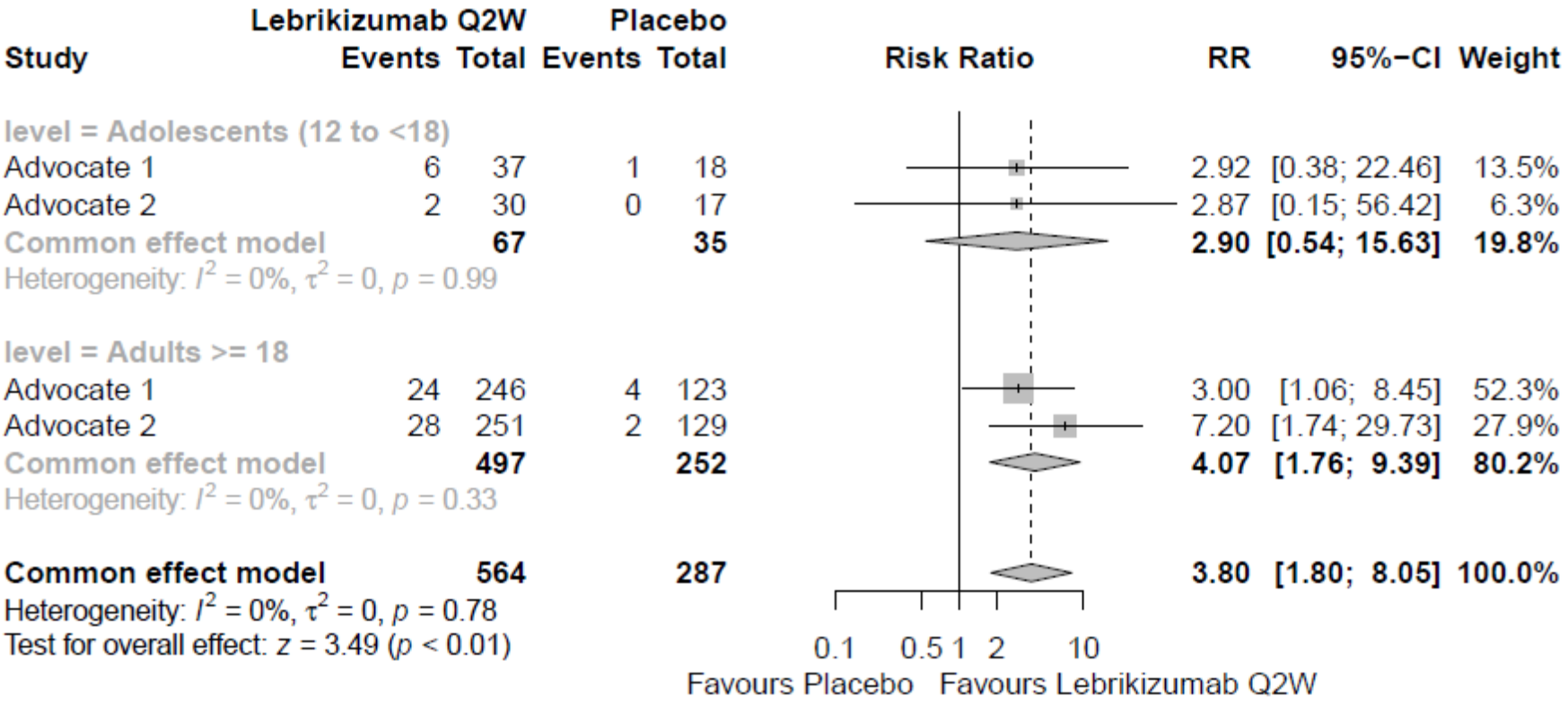


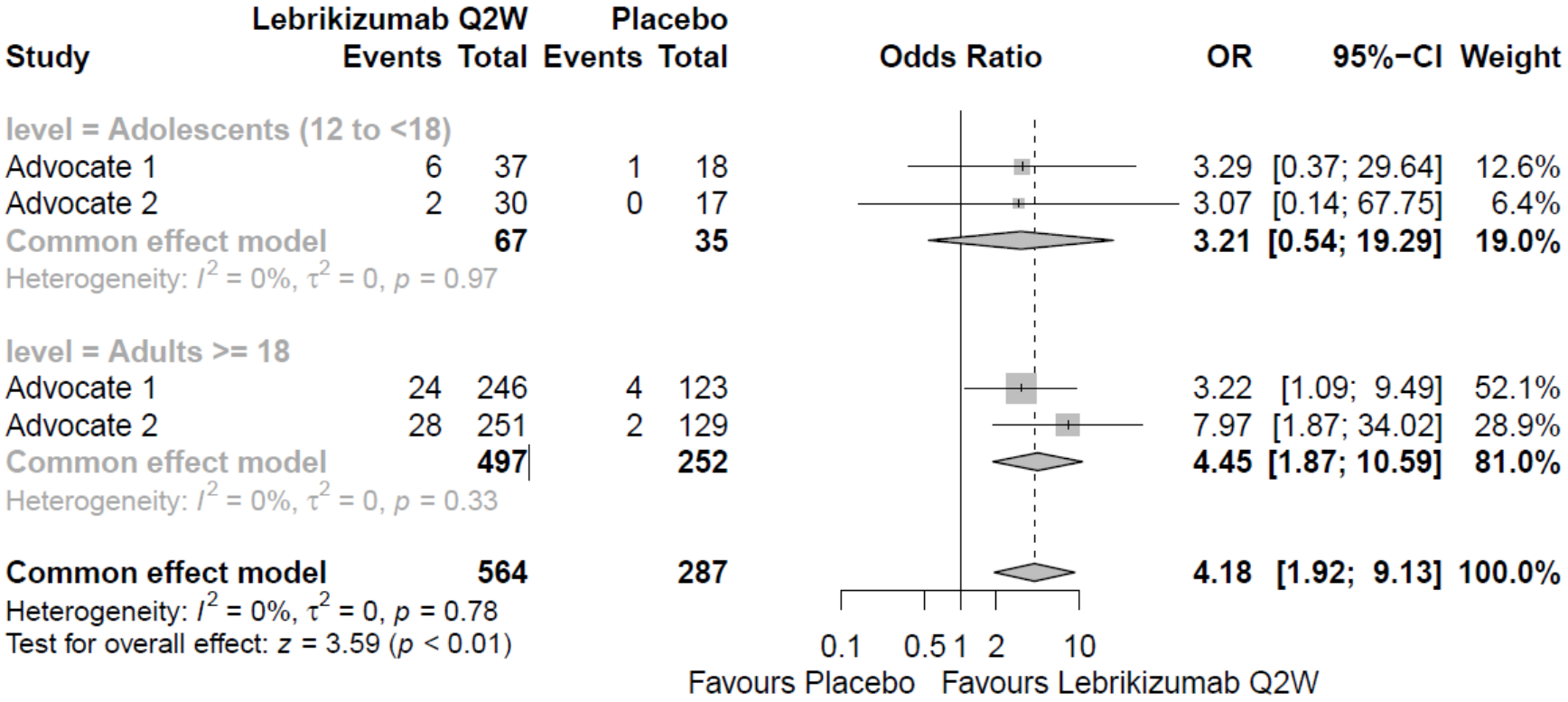

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Female
Advocate 1 13 141 0 73 15.44 [0.90; 263.59] 20.6%
Advocate 2 9 136 1 75 5.24 [0.65; 42.22] 38.2%
Common effect model 277 148 7.66 [1.43; 41.12] 58.8%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.55
level = Male
Advocate 1 11 142 0 68 11.98 [0.70; 206.39] 20.5%
Advocate 2 13 145 0 71 14.57 [0.85; 248.70] 20.6%
Common effect model 287 139 13.22 [1.77; 98.59] 41.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.92
Common effect model 564 287 9.59 [2.64; 34.80] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.91
Test for overall effect: z = 3.44 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W

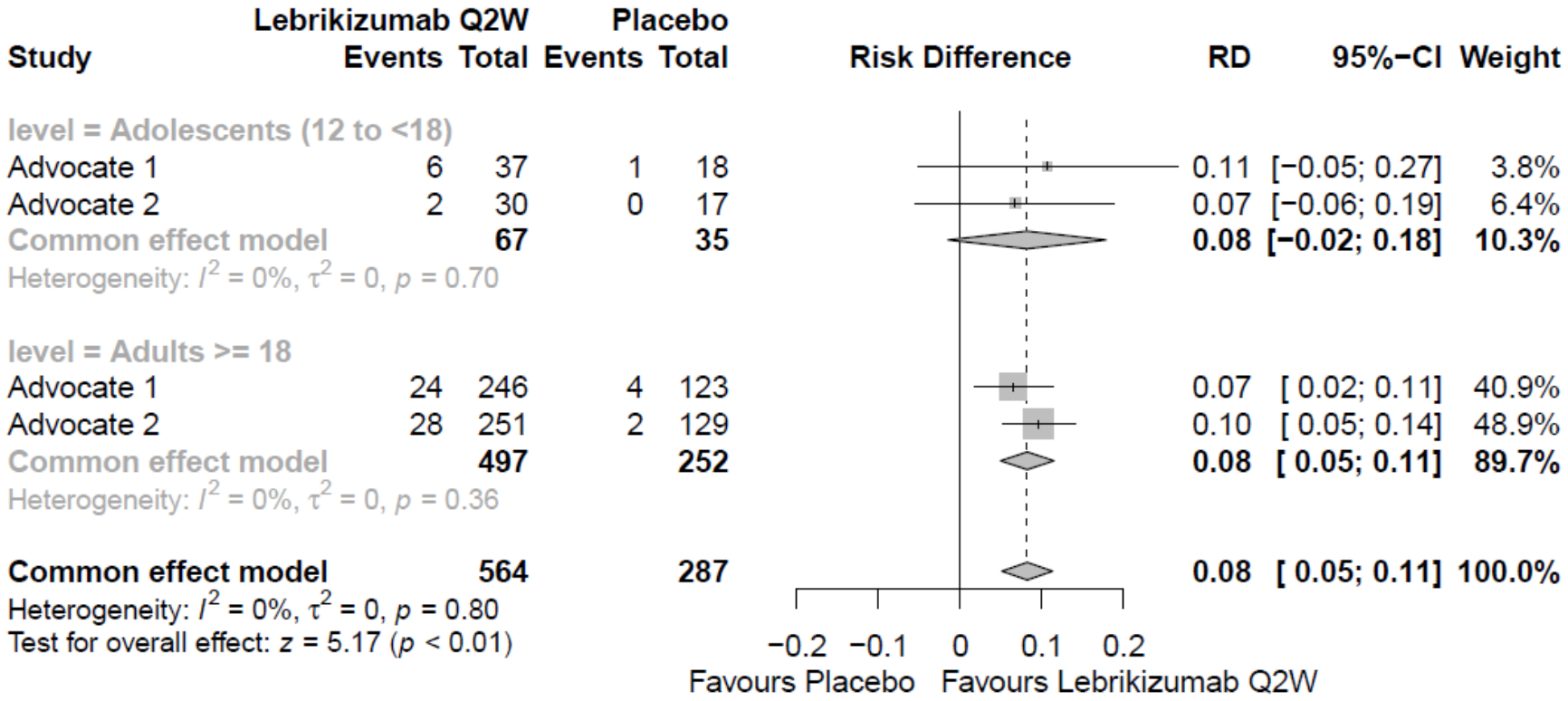

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Female
Advocate 1 13 141 0 73 0.09 [0.04; 0.14] 23.4%
Advocate 2 9 136 1 75 0.05 [0.00; 0.10] 25.9%
Common effect model 277 148 0.07 [0.04; 0.11] 49.4%
Heterogeneity: I^2 = 14%, τ^2 = 0.0001, p = 0.28
level = Male
Advocate 1 11 142 0 68 0.08 [0.03; 0.13] 26.3%
Advocate 2 13 145 0 71 0.09 [0.04; 0.14] 24.4%
Common effect model 287 139 0.08 [0.05; 0.12] 50.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.73
Common effect model 564 287 0.08 [0.05; 0.10] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.68
Test for overall effect: z = 6.07 (p < 0.01)
−0.1 −0.05 0 0.05 0.1
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.6 POEM 0-2

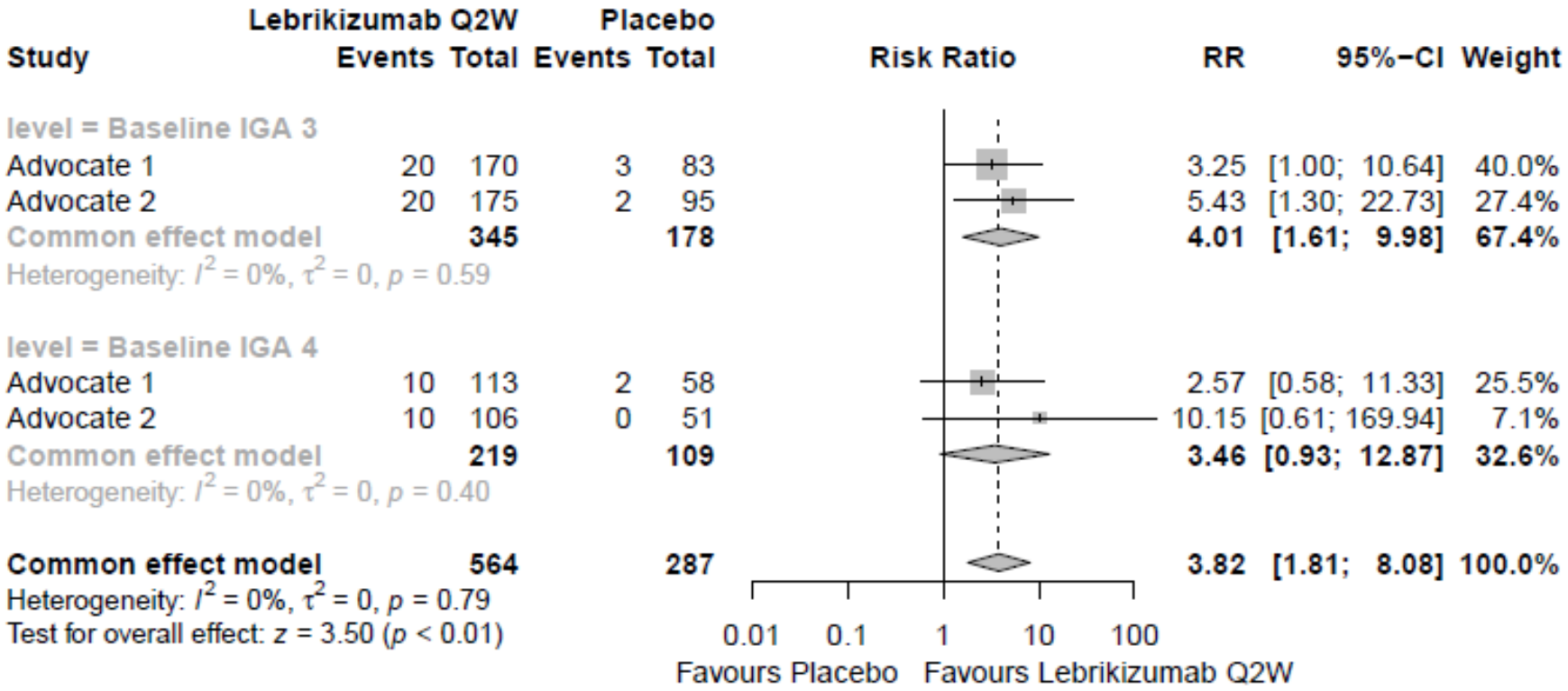
4.5.1.6.1 Altersgruppe

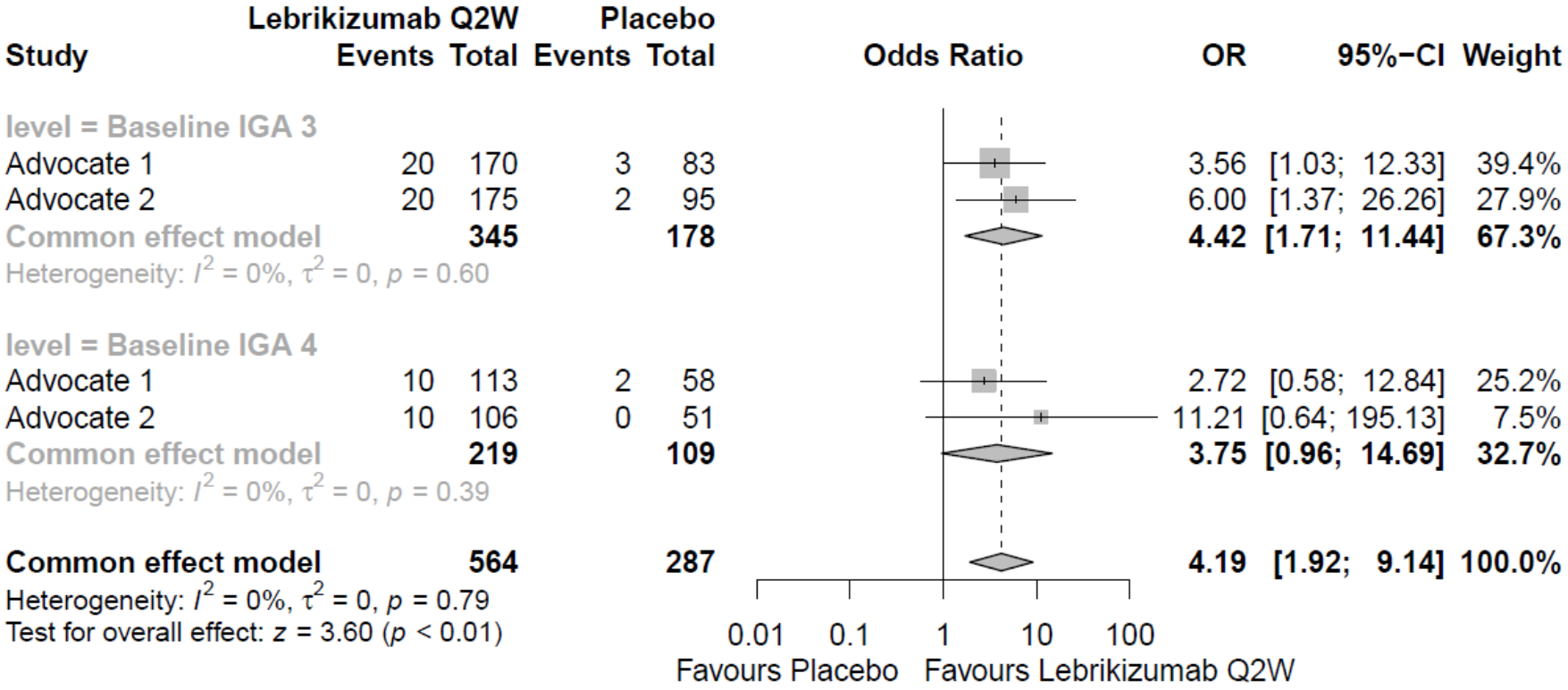


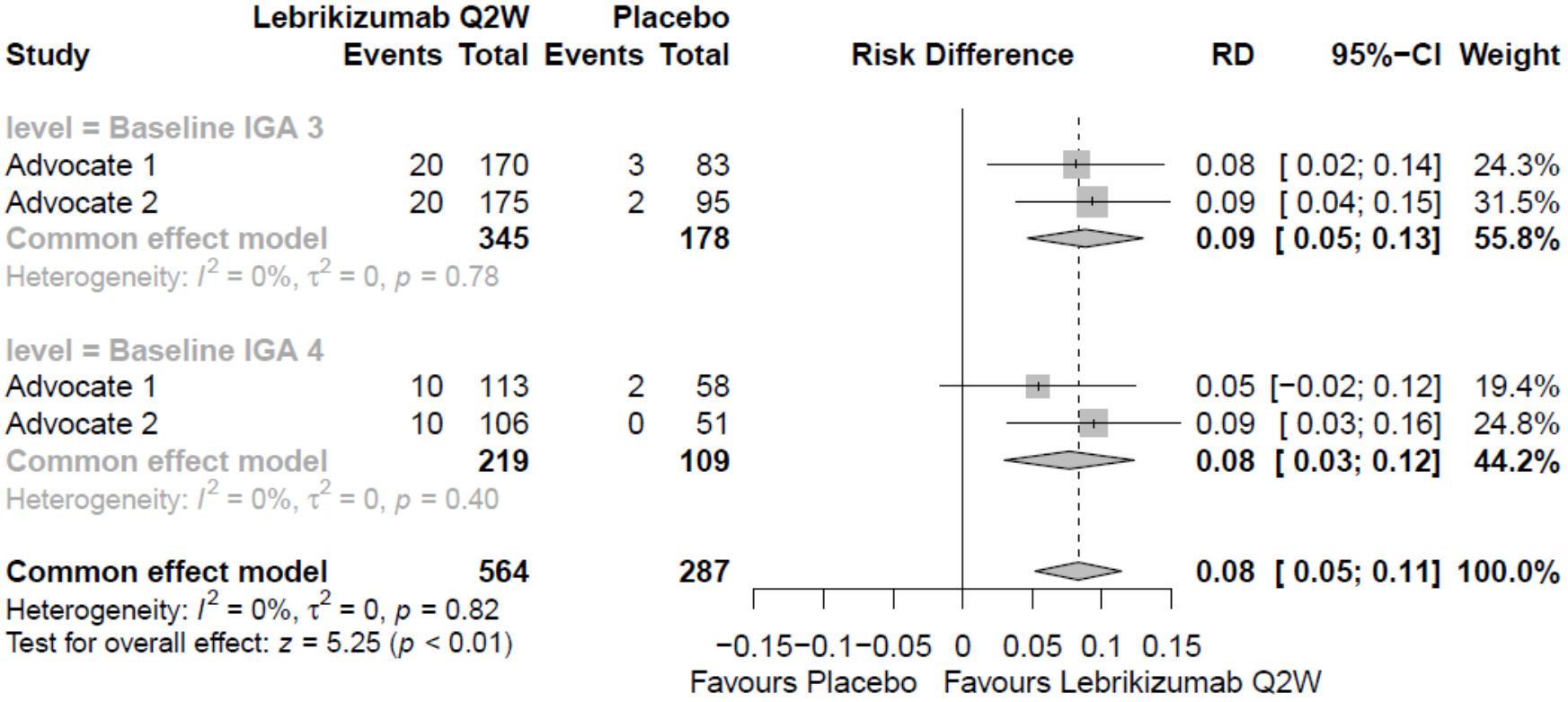

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 6 37 1 18 3.29 [0.37; 29.64] 12.6%
Advocate 2 2 30 0 17 3.07 [0.14; 67.75] 6.4%
Common effect model 67 35 3.21 [0.54; 19.29] 19.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.97
level = Adults >= 18
Advocate 1 24 246 4 123 3.22 [1.09; 9.49] 52.1%
Advocate 2 28 251 2 129 7.97 [1.87; 34.02] 28.9%
Common effect model 497 252 4.45 [1.87; 10.59] 81.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.33
Common effect model 564 287 4.18 [1.92; 9.13] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.78
Test for overall effect: z = 3.59 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 6 37 1 18 0.11 [−0.05; 0.27] 3.8%
Advocate 2 2 30 0 17 0.07 [−0.06; 0.19] 6.4%
Common effect model 67 35 0.08 [−0.02; 0.18] 10.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.70
level = Adults >= 18
Advocate 1 24 246 4 123 0.07 [0.02; 0.11] 40.9%
Advocate 2 28 251 2 129 0.10 [0.05; 0.14] 48.9%
Common effect model 497 252 0.08 [0.05; 0.11] 89.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.36
Common effect model 564 287 0.08 [0.05; 0.11] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.80
Test for overall effect: z = 5.17 (p < 0.01)
−0.2 −0.1 0 0.1 0.2
Favours Placebo
Favours Lebrikizumab Q2W

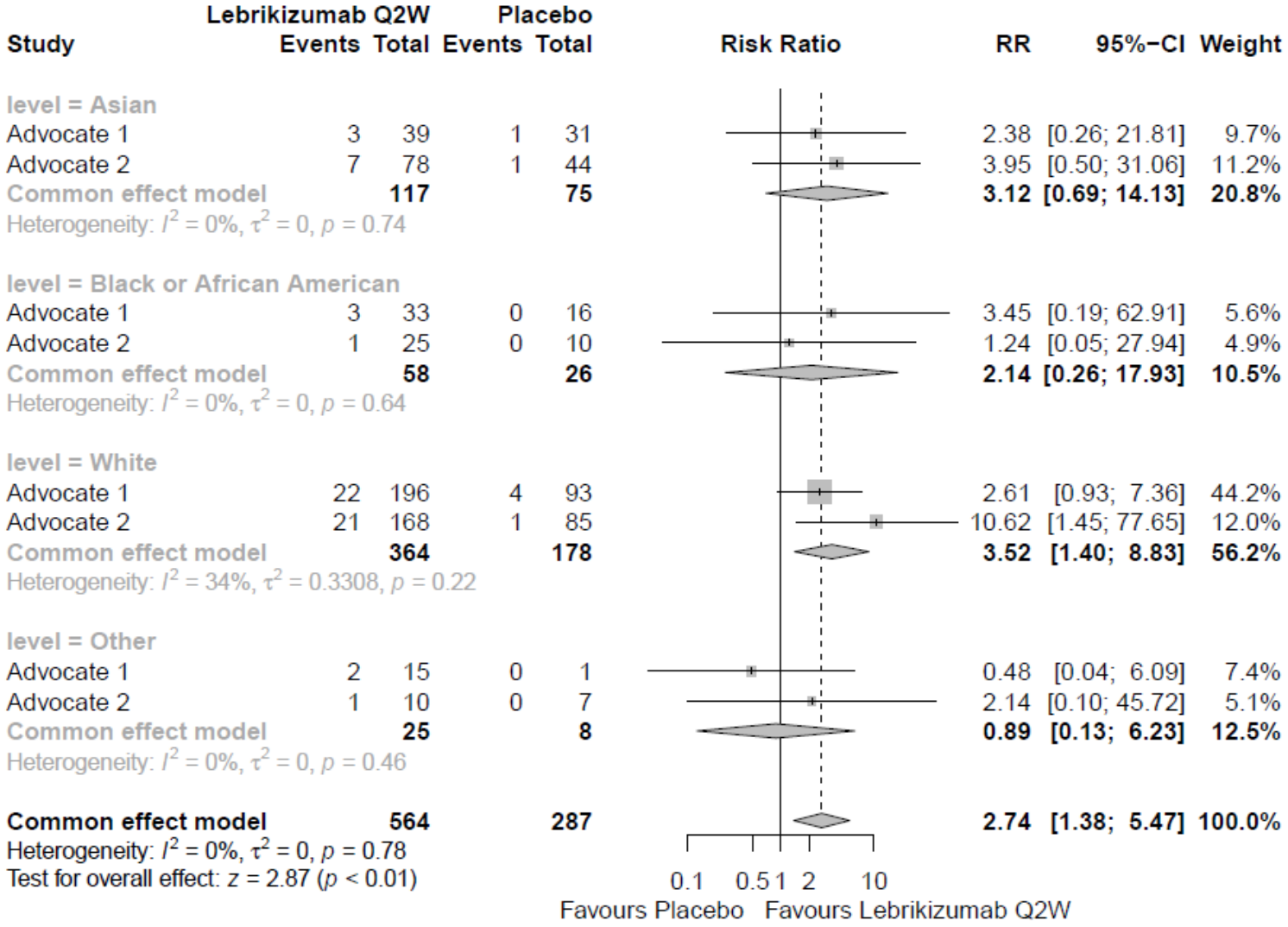
4.5.1.6.2 Krankheitsschwere

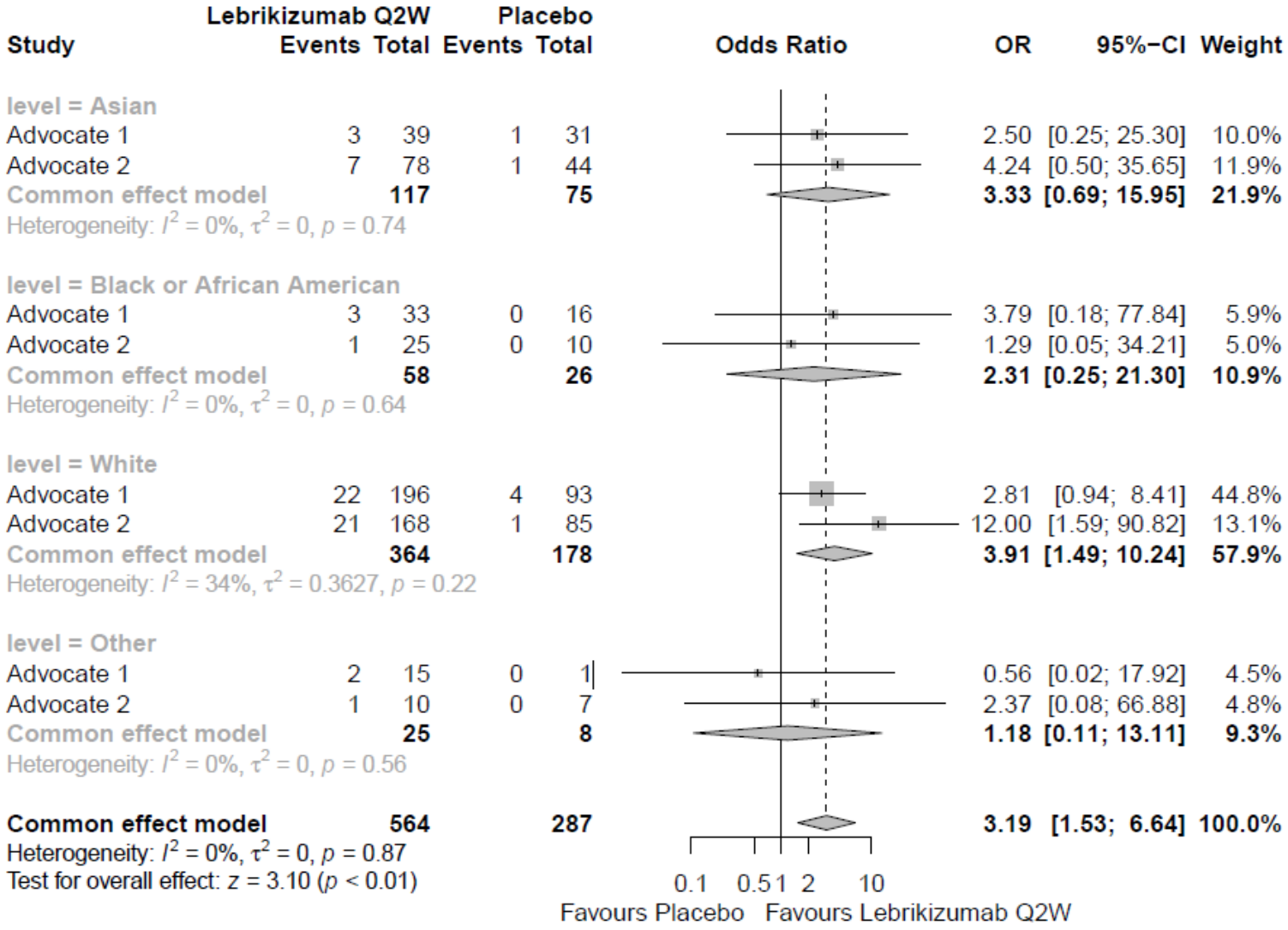


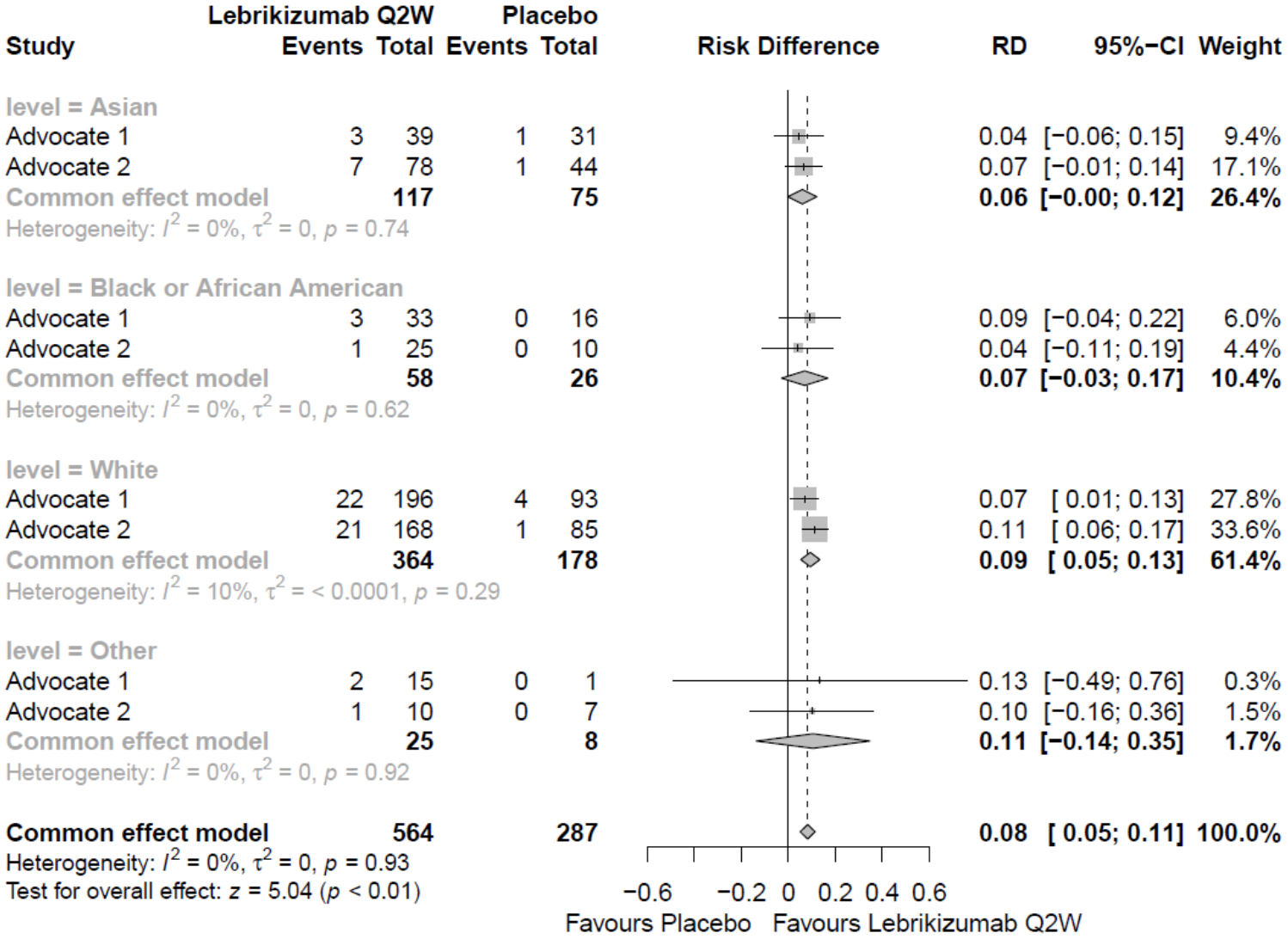

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Baseline IGA 3
Advocate 1 20 170 3 83 3.56 [1.03; 12.33] 39.4%
Advocate 2 20 175 2 95 6.00 [1.37; 26.26] 27.9%
Common effect model 345 178 4.42 [1.71; 11.44] 67.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.60
level = Baseline IGA 4
Advocate 1 10 113 2 58 2.72 [0.58; 12.84] 25.2%
Advocate 2 10 106 0 51 11.21 [0.64; 195.13] 7.5%
Common effect model 219 109 3.75 [0.96; 14.69] 32.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.39
Common effect model 564 287 4.19 [1.92; 9.14] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.79
Test for overall effect: z = 3.60 (p < 0.01)
0.01
0.1
1
10
100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Baseline IGA 3
Advocate 1 20 170 3 83 0.08 [0.02; 0.14] 24.3%
Advocate 2 20 175 2 95 0.09 [0.04; 0.15] 31.5%
Common effect model 345 178 0.09 [0.05; 0.13] 55.8%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.78
level = Baseline IGA 4
Advocate 1 10 113 2 58 0.05 [−0.02; 0.12] 19.4%
Advocate 2 10 106 0 51 0.09 [0.03; 0.16] 24.8%
Common effect model 219 109 0.08 [0.03; 0.12] 44.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.40
Common effect model 564 287 0.08 [0.05; 0.11] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.82
Test for overall effect: z = 5.25 (p < 0.01)
−0.15 −0.1 −0.05 0 0.05 0.1 0.15
Favours Placebo
Favours Lebrikizumab Q2W

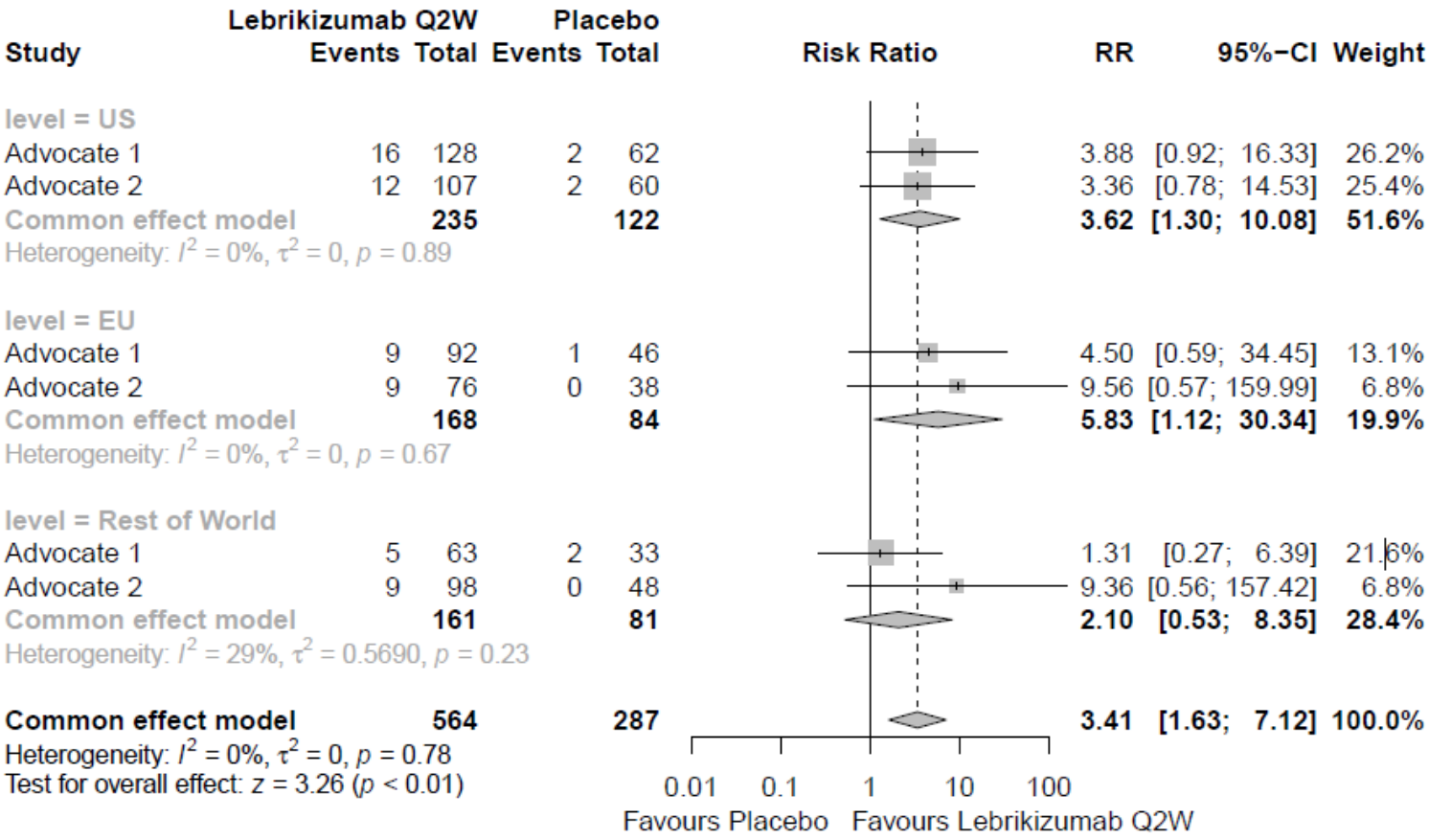
4.5.1.6.3 Ethnie

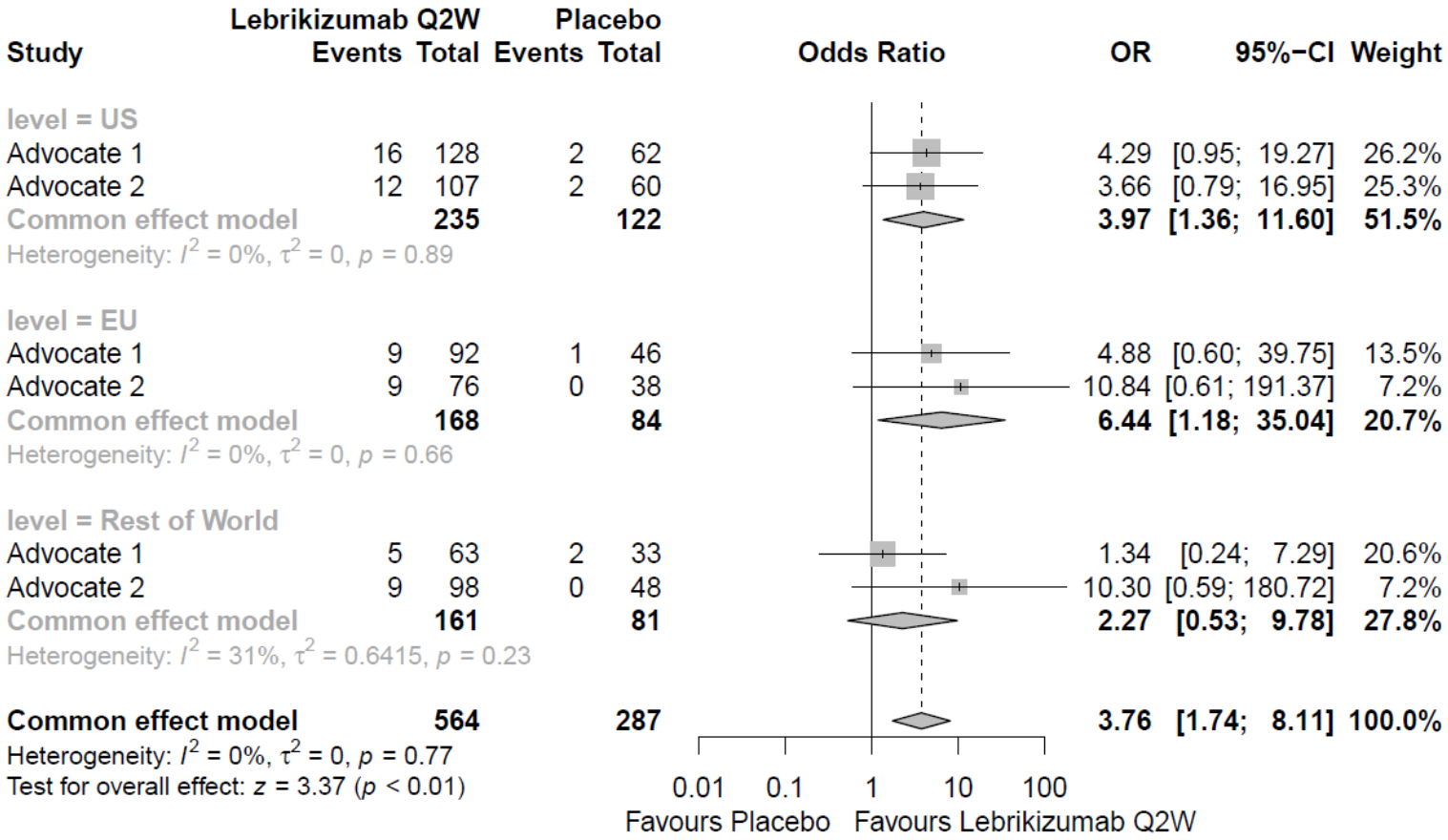


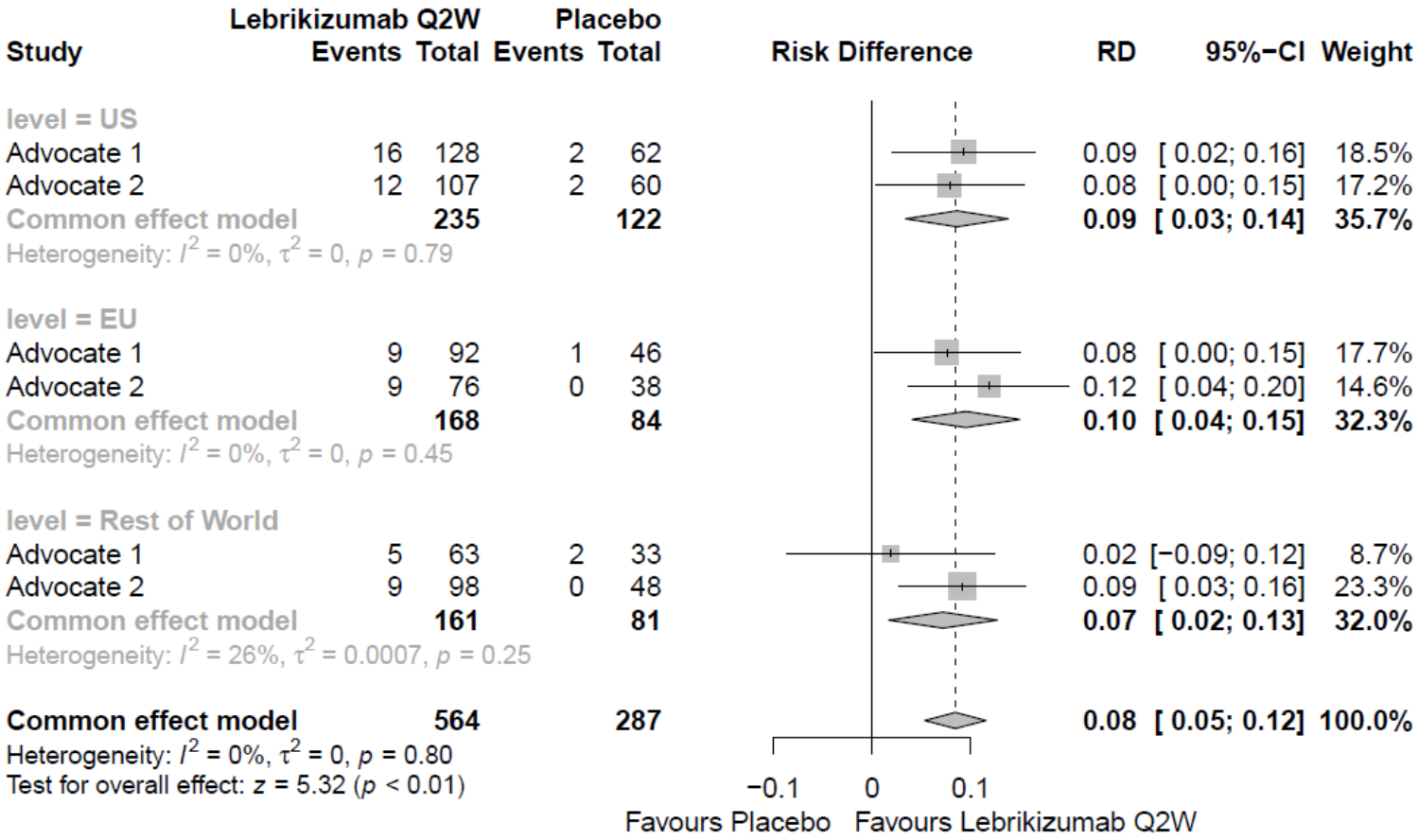

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Asian
Advocate 1 3 39 1 31 2.50 [0.25; 25.30] 10.0%
Advocate 2 7 78 1 44 4.24 [0.50; 35.65] 11.9%
Common effect model 117 75 3.33 [0.69; 15.95] 21.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.74
level = Black or African American
Advocate 1 3 33 0 16 3.79 [0.18; 77.84] 5.9%
Advocate 2 1 25 0 10 1.29 [0.05; 34.21] 5.0%
Common effect model 58 26 2.31 [0.25; 21.30] 10.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.64
level = White
Advocate 1 22 196 4 93 2.81 [0.94; 8.41] 44.8%
Advocate 2 21 168 1 85 12.00 [1.59; 90.82] 13.1%
Common effect model 364 178 3.91 [1.49; 10.24] 57.9%
Heterogeneity: I^2 = 34%, τ^2 = 0.3627, p = 0.22
level = Other
Advocate 1 2 15 0 1 0.56 [0.02; 17.92] 4.5%
Advocate 2 1 10 0 7 2.37 [0.08; 66.88] 4.8%
Common effect model 25 8 1.18 [0.11; 13.11] 9.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.56
Common effect model 564 287 3.19 [1.53; 6.64] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.87
Test for overall effect: z = 3.10 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Asian
Advocate 1 3 39 1 31 0.04 [−0.06; 0.15] 9.4%
Advocate 2 7 78 1 44 0.07 [−0.01; 0.14] 17.1%
Common effect model 117 75 0.06 [−0.00; 0.12] 26.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.74
level = Black or African American
Advocate 1 3 33 0 16 0.09 [−0.04; 0.22] 6.0%
Advocate 2 1 25 0 10 0.04 [−0.11; 0.19] 4.4%
Common effect model 58 26 0.07 [−0.03; 0.17] 10.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.62
level = White
Advocate 1 22 196 4 93 0.07 [0.01; 0.13] 27.8%
Advocate 2 21 168 1 85 0.11 [0.06; 0.17] 33.6%
Common effect model 364 178 0.09 [0.05; 0.13] 61.4%
Heterogeneity: I^2 = 10%, τ^2 = < 0.0001, p = 0.29
level = Other
Advocate 1 2 15 0 1 0.13 [−0.49; 0.76] 0.3%
Advocate 2 1 10 0 7 0.10 [−0.16; 0.36] 1.5%
Common effect model 25 8 0.11 [−0.14; 0.35] 1.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.92
Common effect model 564 287 0.08 [0.05; 0.11] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.93
Test for overall effect: z = 5.04 (p < 0.01)
−0.6 −0.2 0 0.2 0.4 0.6
Favours Placebo
Favours Lebrikizumab Q2W

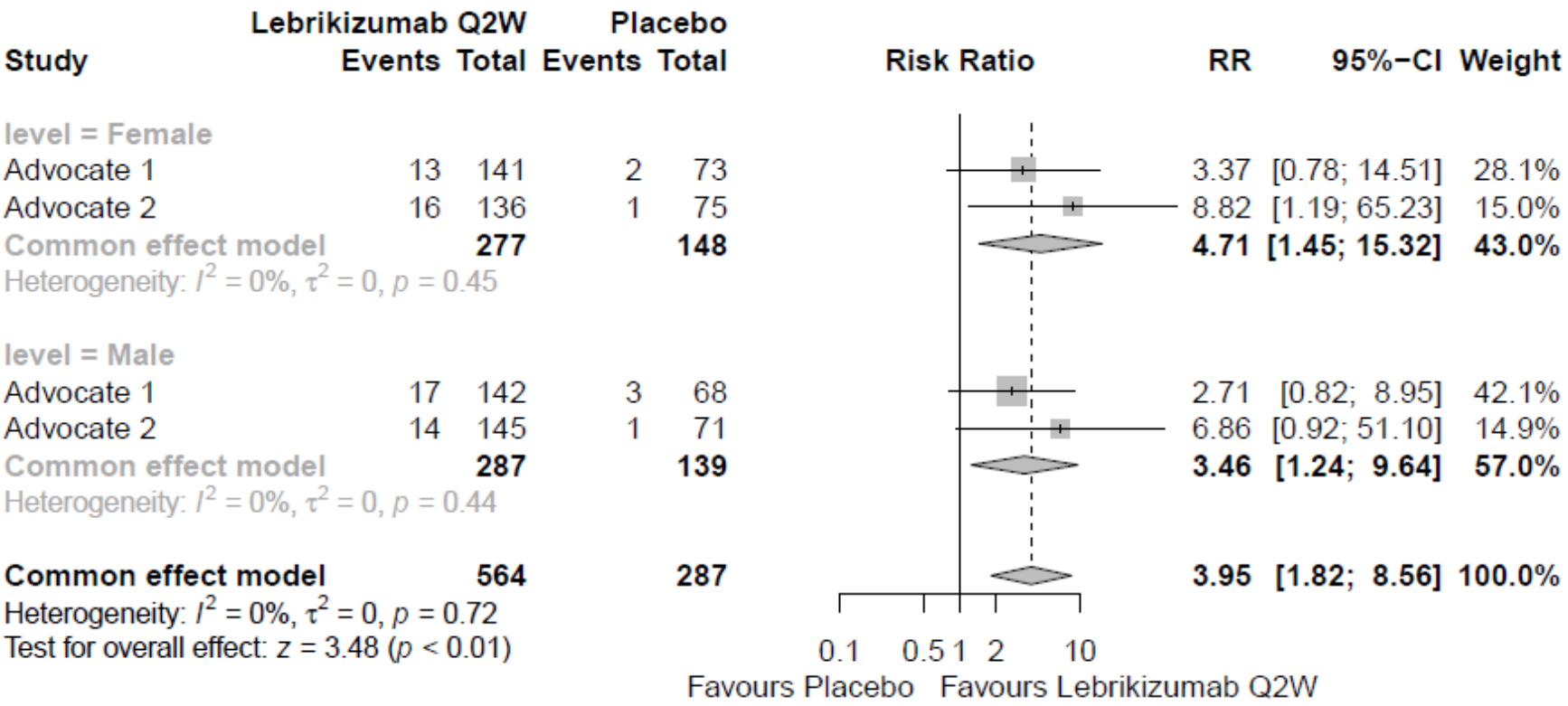
4.5.1.6.4 Region

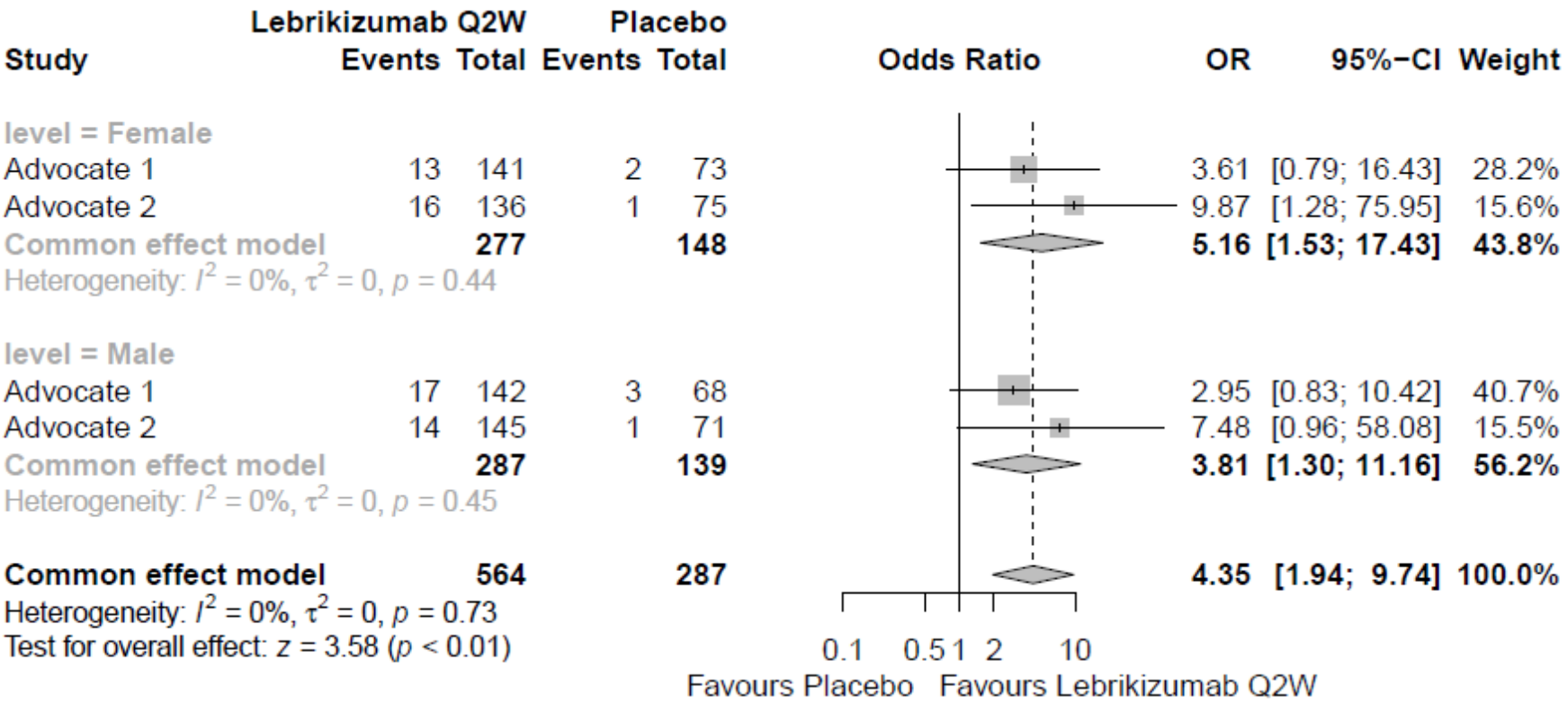


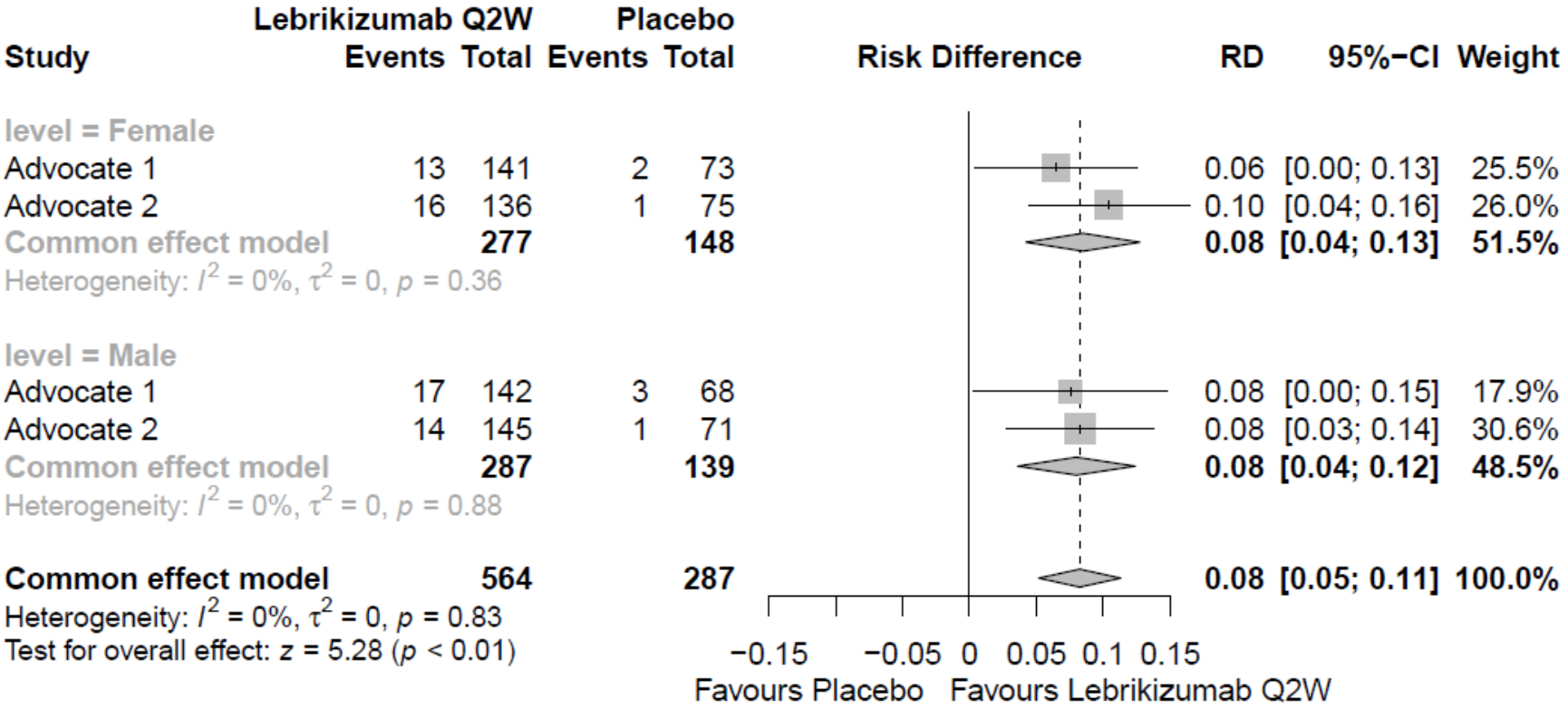

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = US
Advocate 1 16 128 2 62 4.29 [0.95; 19.27] 26.2%
Advocate 2 12 107 2 60 3.66 [0.79; 16.95] 25.3%
Common effect model 235 122 3.97 [1.36; 11.60] 51.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.89
level = EU
Advocate 1 9 92 1 46 4.88 [0.60; 39.75] 13.5%
Advocate 2 9 76 0 38 10.84 [0.61; 191.37] 7.2%
Common effect model 168 84 6.44 [1.18; 35.04] 20.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.66
level = Rest of World
Advocate 1 5 63 2 33 1.34 [0.24; 7.29] 20.6%
Advocate 2 9 98 0 48 10.30 [0.59; 180.72] 7.2%
Common effect model 161 81 2.27 [0.53; 9.78] 27.8%
Heterogeneity: I^2 = 31%, τ^2 = 0.6415, p = 0.23
Common effect model 564 287 3.76 [1.74; 8.11] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.77
Test for overall effect: z = 3.37 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = US
Advocate 1 16 128 2 62 0.09 [0.02; 0.16] 18.5%
Advocate 2 12 107 2 60 0.08 [0.00; 0.15] 17.2%
Common effect model 235 122 0.09 [0.03; 0.14] 35.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.79
level = EU
Advocate 1 9 92 1 46 0.08 [0.00; 0.15] 17.7%
Advocate 2 9 76 0 38 0.12 [0.04; 0.20] 14.6%
Common effect model 168 84 0.10 [0.04; 0.15] 32.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.45
level = Rest of World
Advocate 1 5 63 2 33 0.02 [−0.09; 0.12] 8.7%
Advocate 2 9 98 0 48 0.09 [0.03; 0.16] 23.3%
Common effect model 161 81 0.07 [0.02; 0.13] 32.0%
Heterogeneity: I^2 = 26%, τ^2 = 0.0007, p = 0.25
Common effect model 564 287 0.08 [0.05; 0.12] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.80
Test for overall effect: z = 5.32 (p < 0.01)
−0.1
0
0.1
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.6.5 Geschlecht

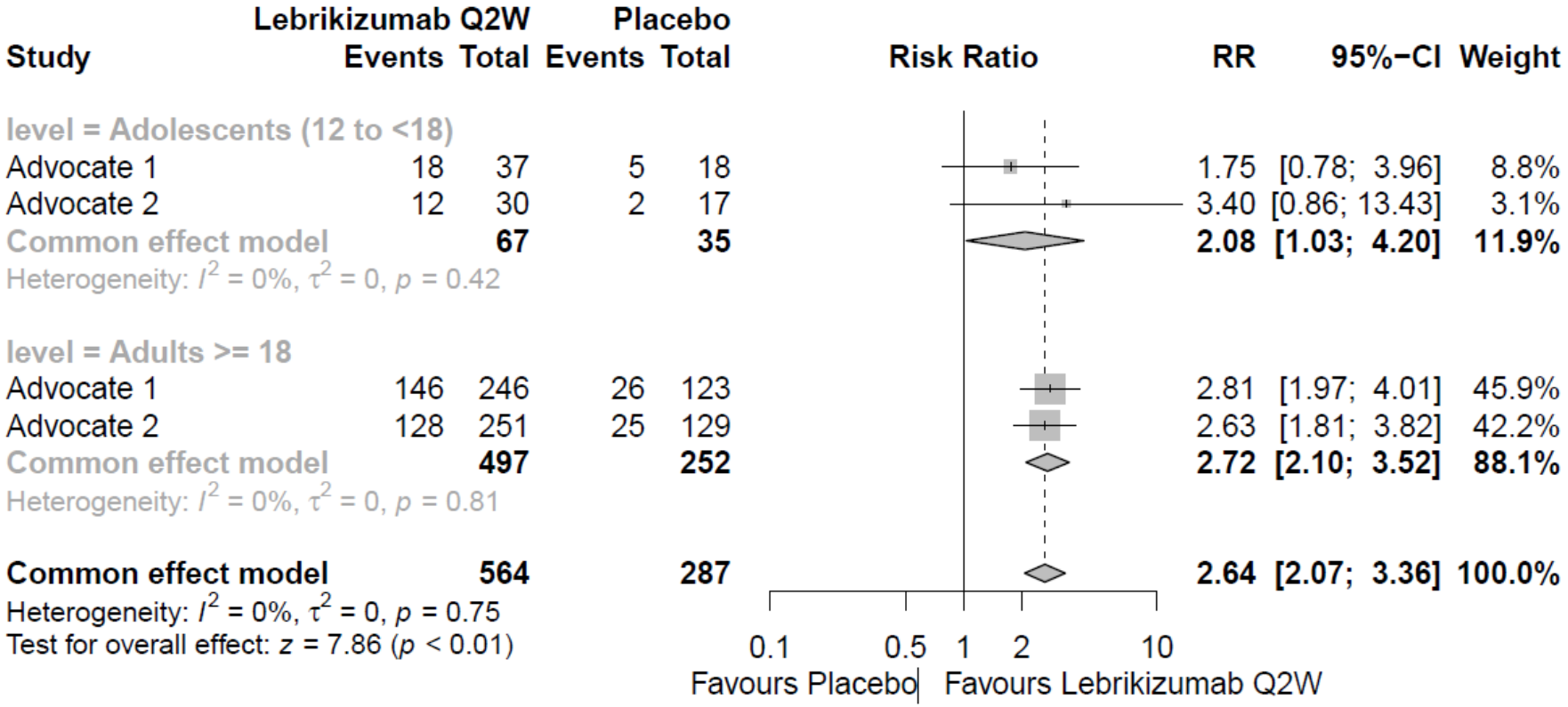


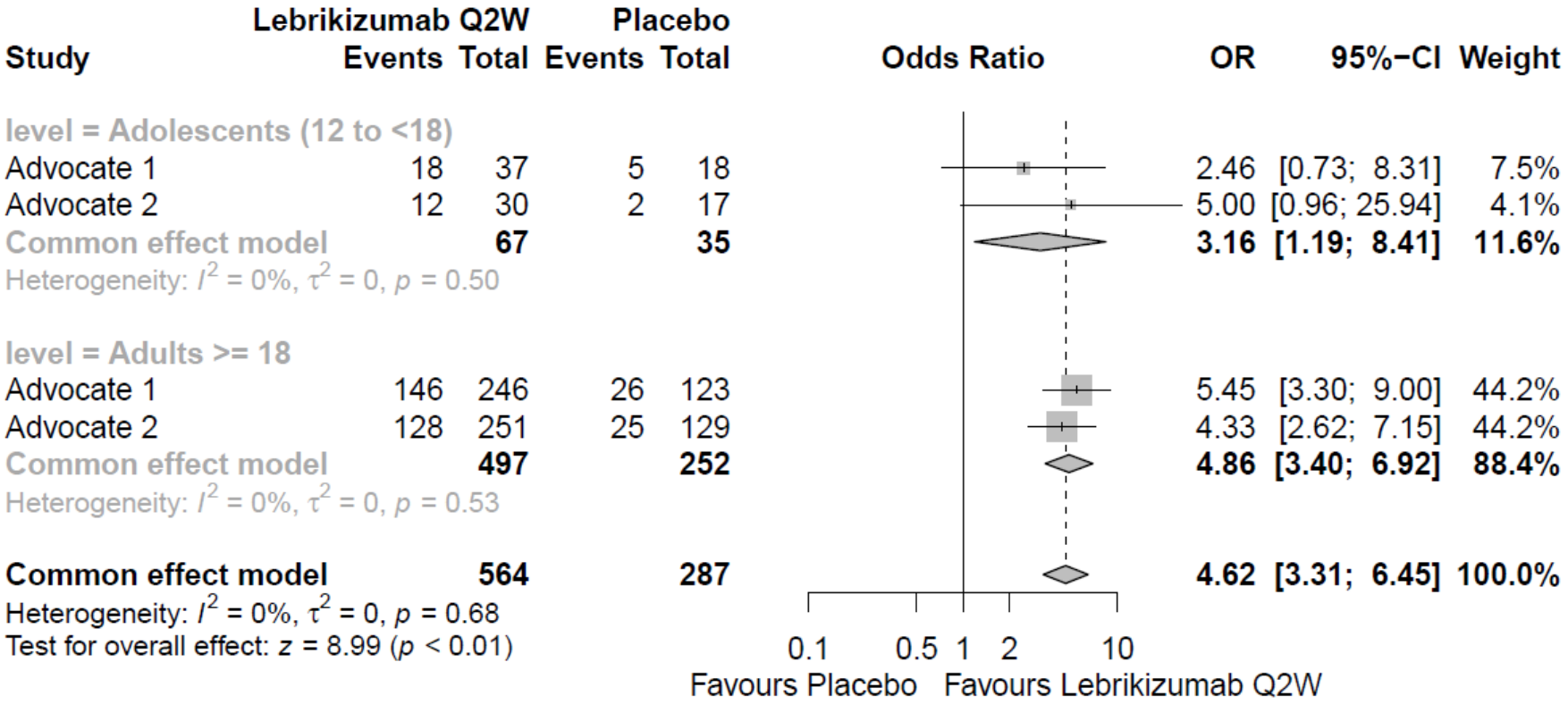

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Female
Advocate 1 13 141 2 73 3.61 [0.79; 16.43] 28.2%
Advocate 2 16 136 1 75 9.87 [1.28; 75.95] 15.6%
Common effect model 277 148 5.16 [1.53; 17.43] 43.8%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.44
level = Male
Advocate 1 17 142 3 68 2.95 [0.83; 10.42] 40.7%
Advocate 2 14 145 1 71 7.48 [0.96; 58.08] 15.5%
Common effect model 287 139 3.81 [1.30; 11.16] 56.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.45
Common effect model 564 287 4.35 [1.94; 9.74] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.73
Test for overall effect: z = 3.58 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo
Favours Lebrikizumab Q2W

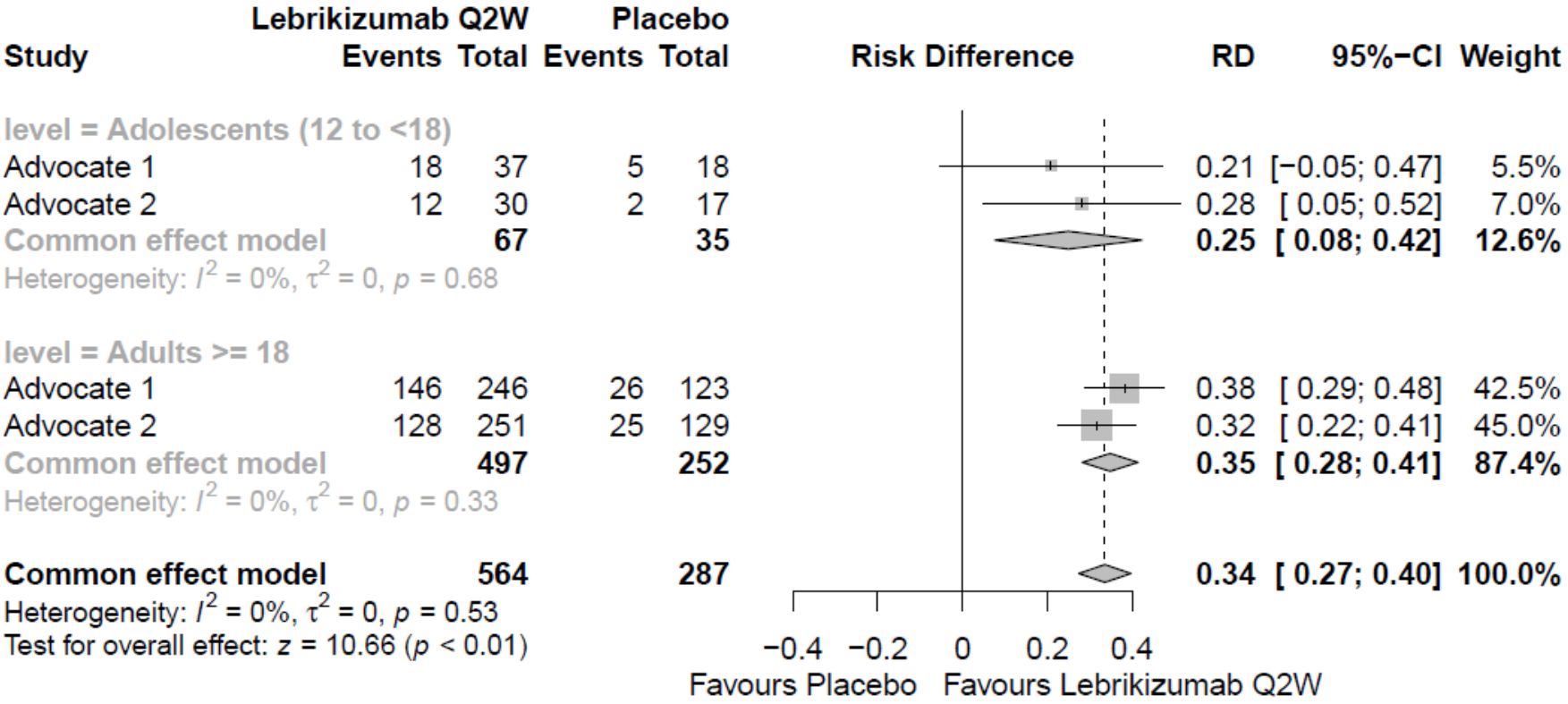

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Female
Advocate 1 13 141 2 73 0.06 [0.00; 0.13] 25.5%
Advocate 2 16 136 1 75 0.10 [0.04; 0.16] 26.0%
Common effect model 277 148 0.08 [0.04; 0.13] 51.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.36
level = Male
Advocate 1 17 142 3 68 0.08 [0.00; 0.15] 17.9%
Advocate 2 14 145 1 71 0.08 [0.03; 0.14] 30.6%
Common effect model 287 139 0.08 [0.04; 0.12] 48.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.88
Common effect model 564 287 0.08 [0.05; 0.11] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.83
Test for overall effect: z = 5.28 (p < 0.01)
−0.15 −0.05 0 0.05 0.1 0.15
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.7 POEM Reduktion um 5 Punkte

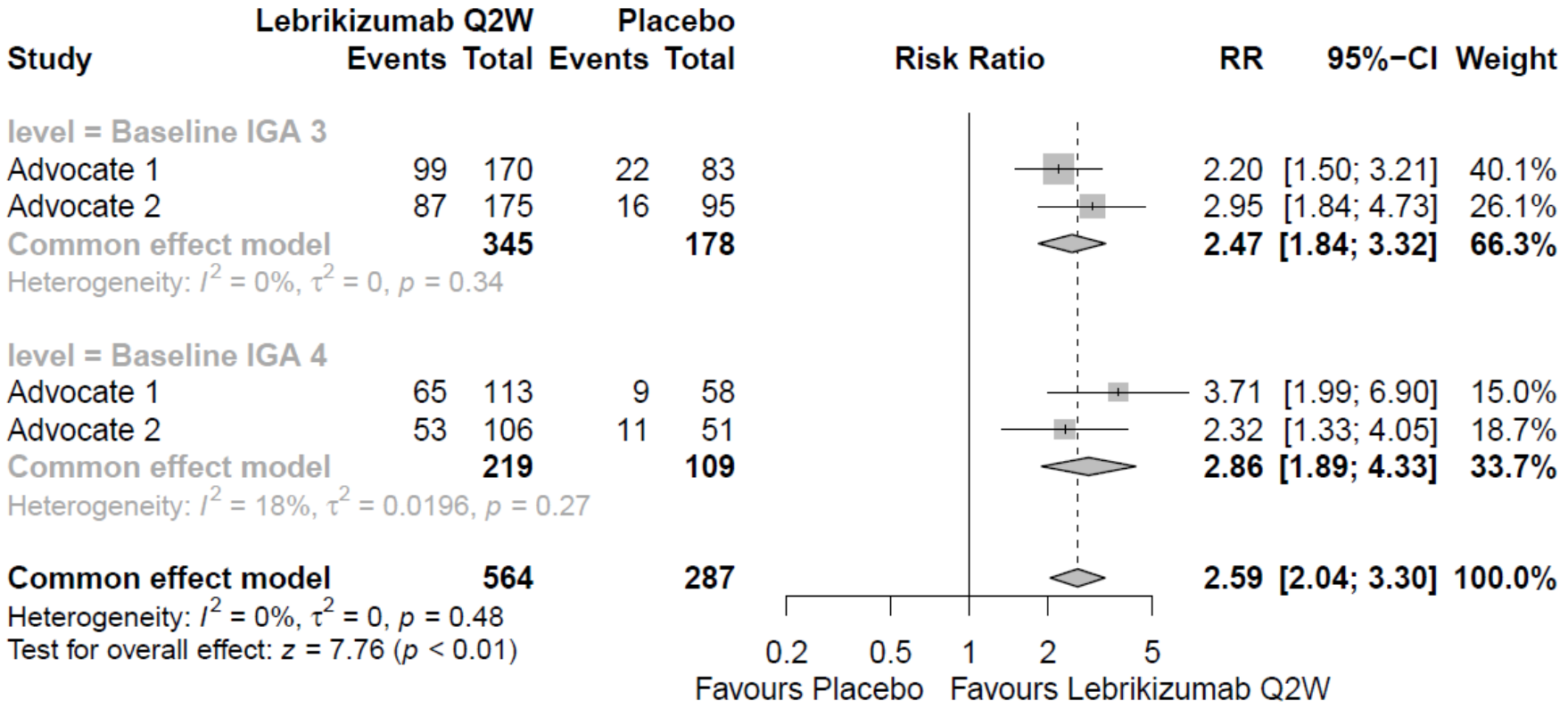
4.5.1.7.1 Altersgruppe

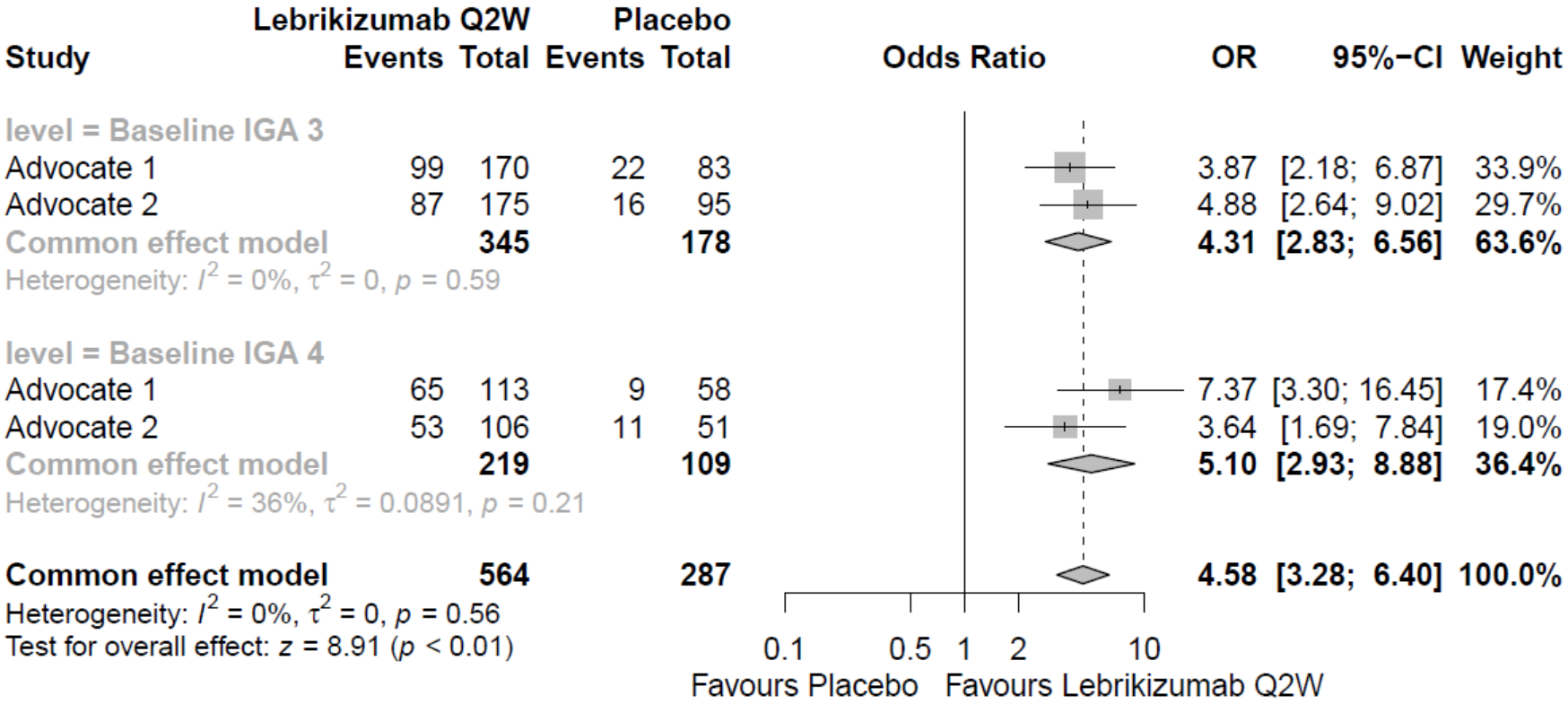


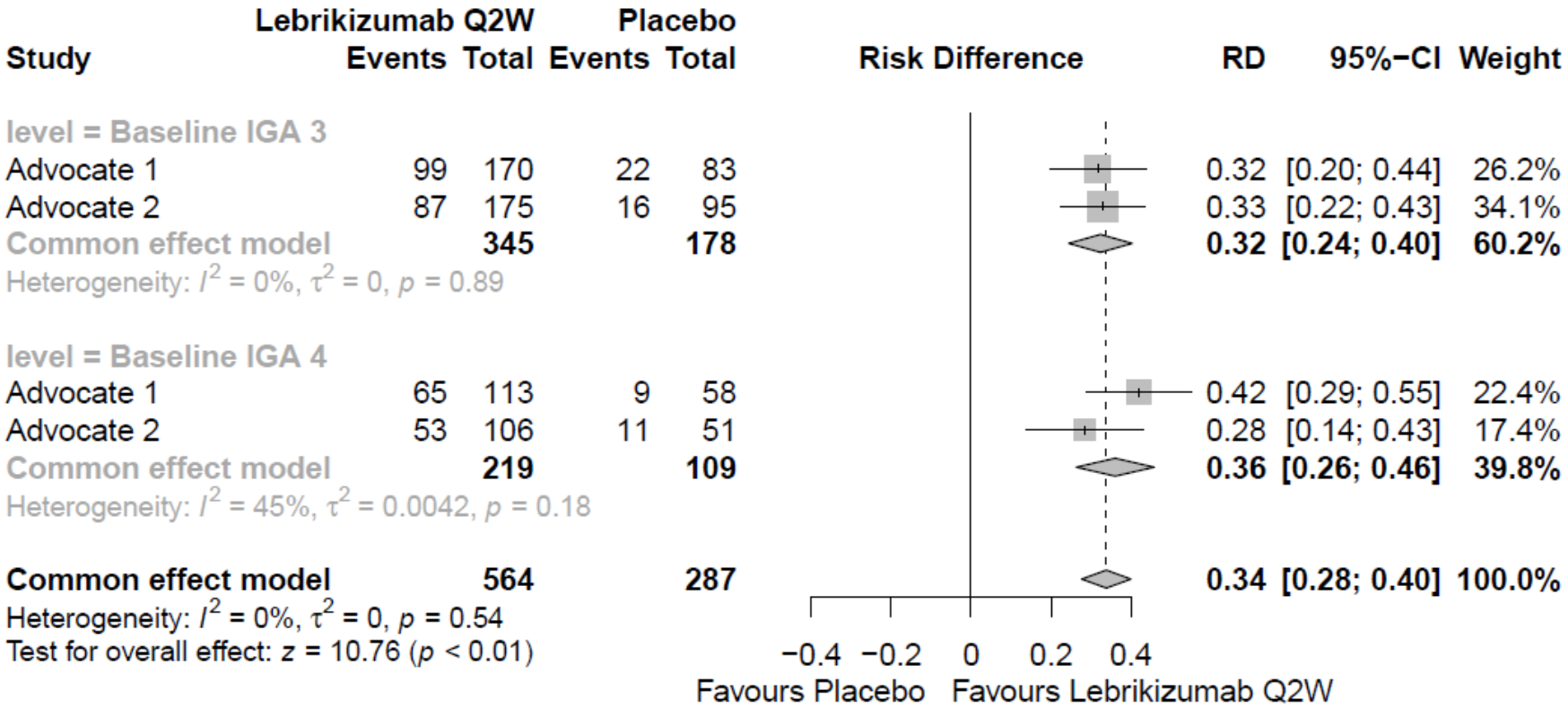

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 18 37 5 18 2.46 [0.73; 8.31] 7.5%
Advocate 2 12 30 2 17 5.00 [0.96; 25.94] 4.1%
Common effect model 67 35 3.16 [1.19; 8.41] 11.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.50
level = Adults >= 18
Advocate 1 146 246 26 123 5.45 [3.30; 9.00] 44.2%
Advocate 2 128 251 25 129 4.33 [2.62; 7.15] 44.2%
Common effect model 497 252 4.86 [3.40; 6.92] 88.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.53
Common effect model 564 287 4.62 [3.31; 6.45] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.68
Test for overall effect: z = 8.99 (p < 0.01)
0.1
0.5
1
2
10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 18 37 5 18 0.21 [−0.05; 0.47] 5.5%
Advocate 2 12 30 2 17 0.28 [0.05; 0.52] 7.0%
Common effect model 67 35 0.25 [0.08; 0.42] 12.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.68
level = Adults >= 18
Advocate 1 146 246 26 123 0.38 [0.29; 0.48] 42.5%
Advocate 2 128 251 25 129 0.32 [0.22; 0.41] 45.0%
Common effect model 497 252 0.35 [0.28; 0.41] 87.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.33
Common effect model 564 287 0.34 [0.27; 0.40] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.53
Test for overall effect: z = 10.66 (p < 0.01)
−0.4 −0.2 0 0.2 0.4
Favours Placebo
Favours Lebrikizumab Q2W

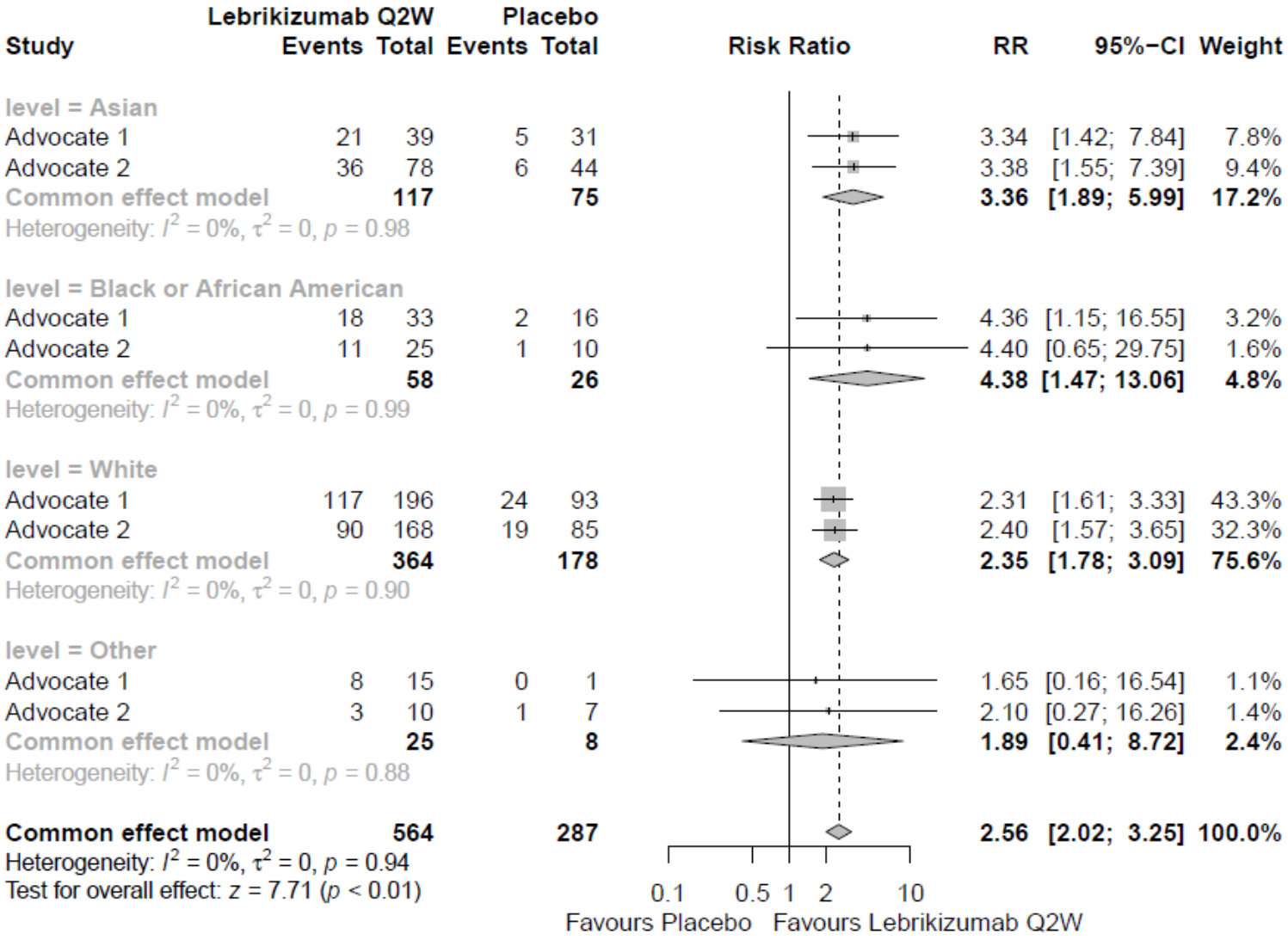
4.5.1.7.2 Krankheitsschwere

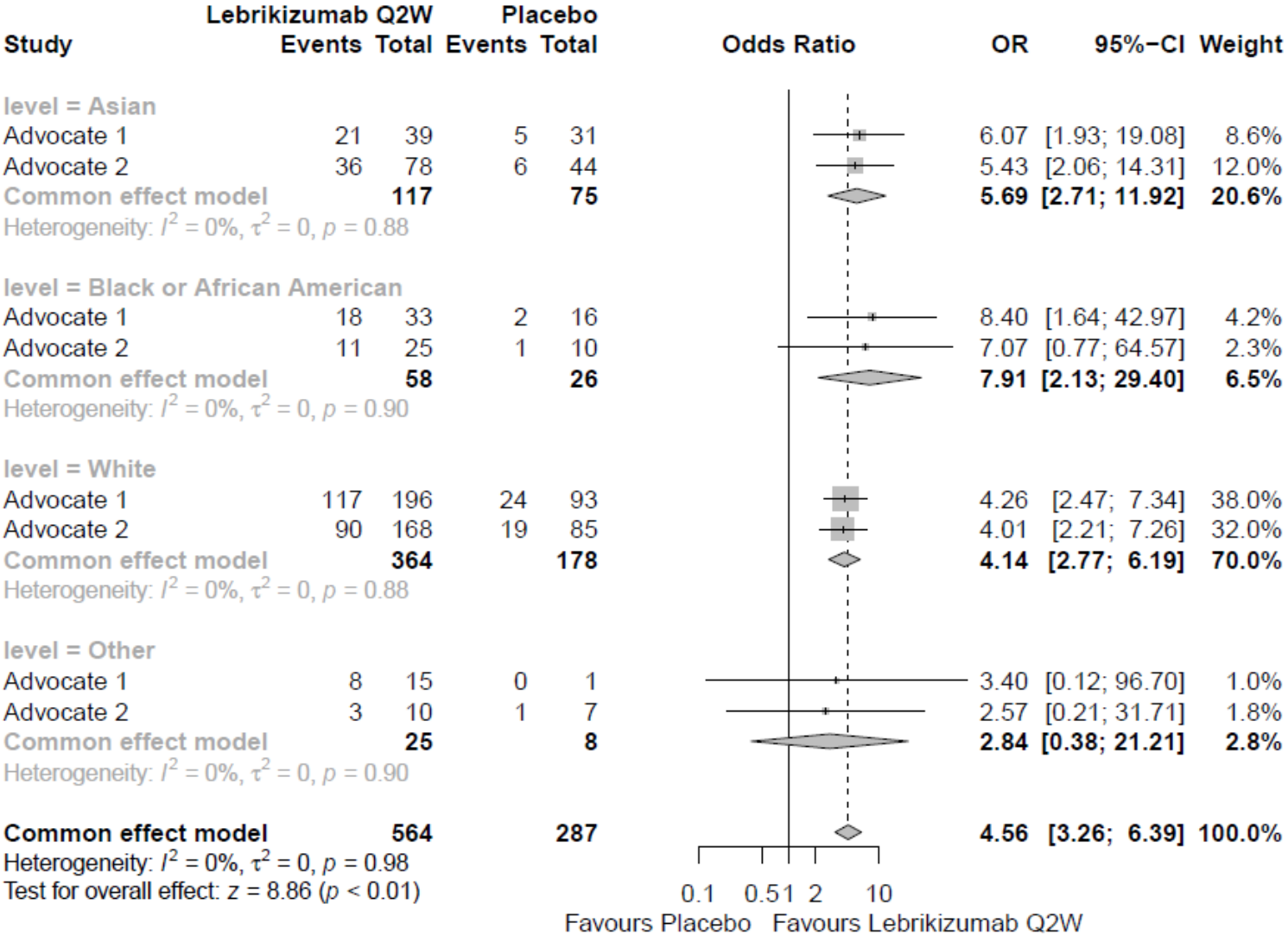


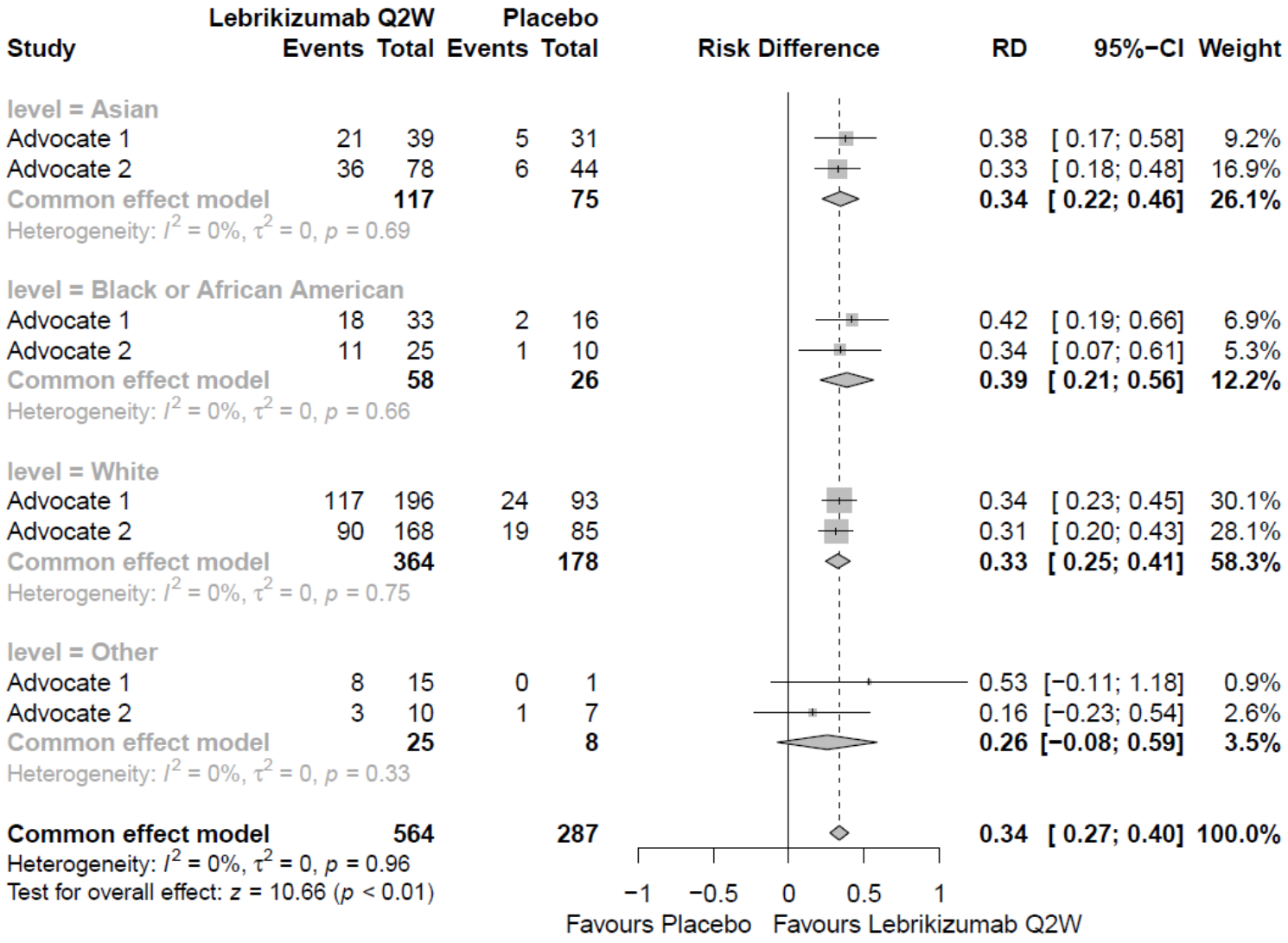

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Baseline IGA 3
Advocate 1 99 170 22 83 3.87 [2.18; 6.87] 33.9%
Advocate 2 87 175 16 95 4.88 [2.64; 9.02] 29.7%
Common effect model 345 178 4.31 [2.83; 6.56] 63.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.59
level = Baseline IGA 4
Advocate 1 65 113 9 58 7.37 [3.30; 16.45] 17.4%
Advocate 2 53 106 11 51 3.64 [1.69; 7.84] 19.0%
Common effect model 219 109 5.10 [2.93; 8.88] 36.4%
Heterogeneity: I^2 = 36%, τ^2 = 0.0891, p = 0.21
Common effect model 564 287 4.58 [3.28; 6.40] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.56
Test for overall effect: z = 8.91 (p < 0.01)
0.1
0.5
1
2
10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Baseline IGA 3
Advocate 1 99 170 22 83 0.32 [0.20; 0.44] 26.2%
Advocate 2 87 175 16 95 0.33 [0.22; 0.43] 34.1%
Common effect model 345 178 0.32 [0.24; 0.40] 60.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.89
level = Baseline IGA 4
Advocate 1 65 113 9 58 0.42 [0.29; 0.55] 22.4%
Advocate 2 53 106 11 51 0.28 [0.14; 0.43] 17.4%
Common effect model 219 109 0.36 [0.26; 0.46] 39.8%
Heterogeneity: I^2 = 45%, τ^2 = 0.0042, p = 0.18
Common effect model 564 287 0.34 [0.28; 0.40] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.54
Test for overall effect: z = 10.76 (p < 0.01)
−0.4 −0.2 0 0.2 0.4
Favours Placebo
Favours Lebrikizumab Q2W

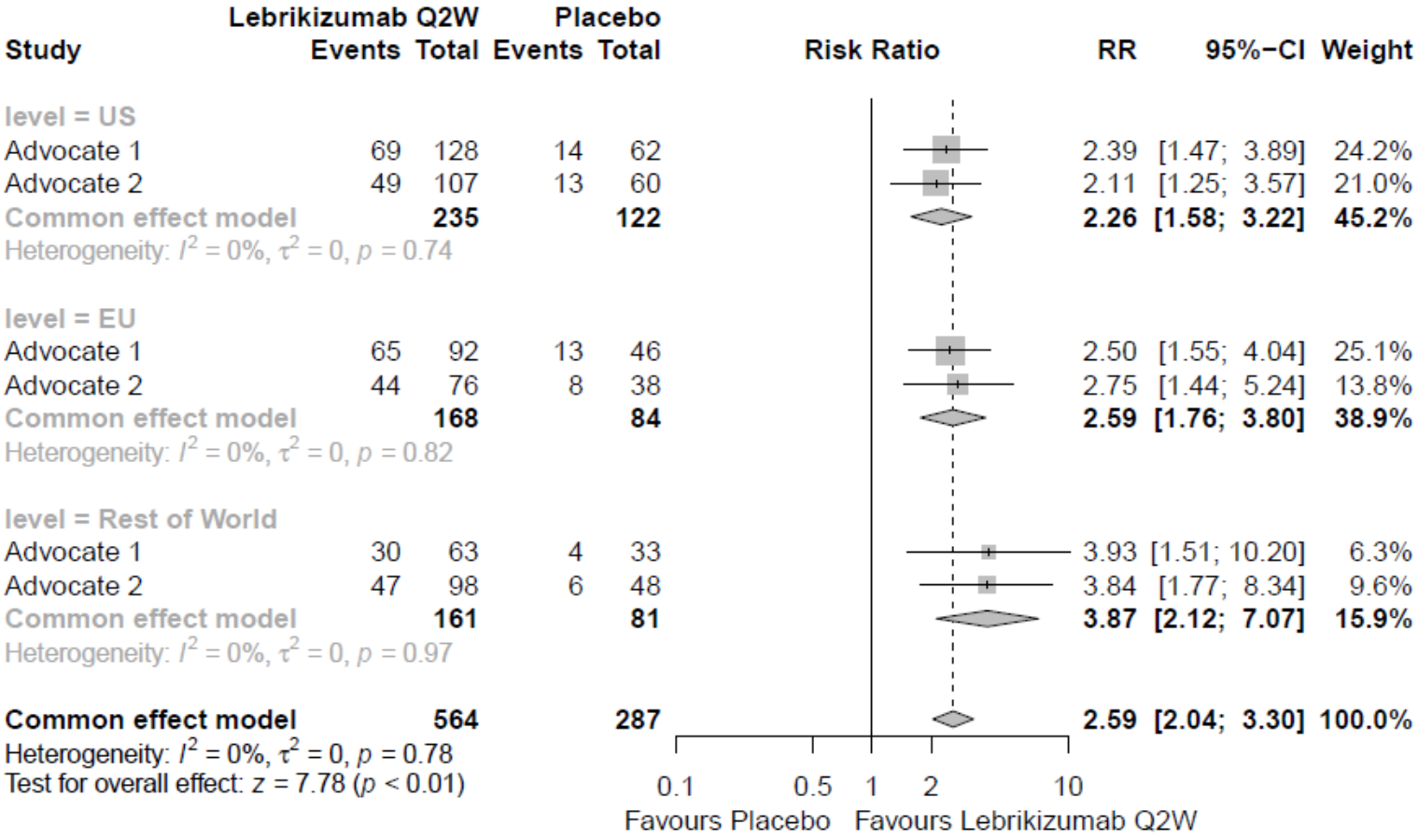
4.5.1.7.3 Ethnie

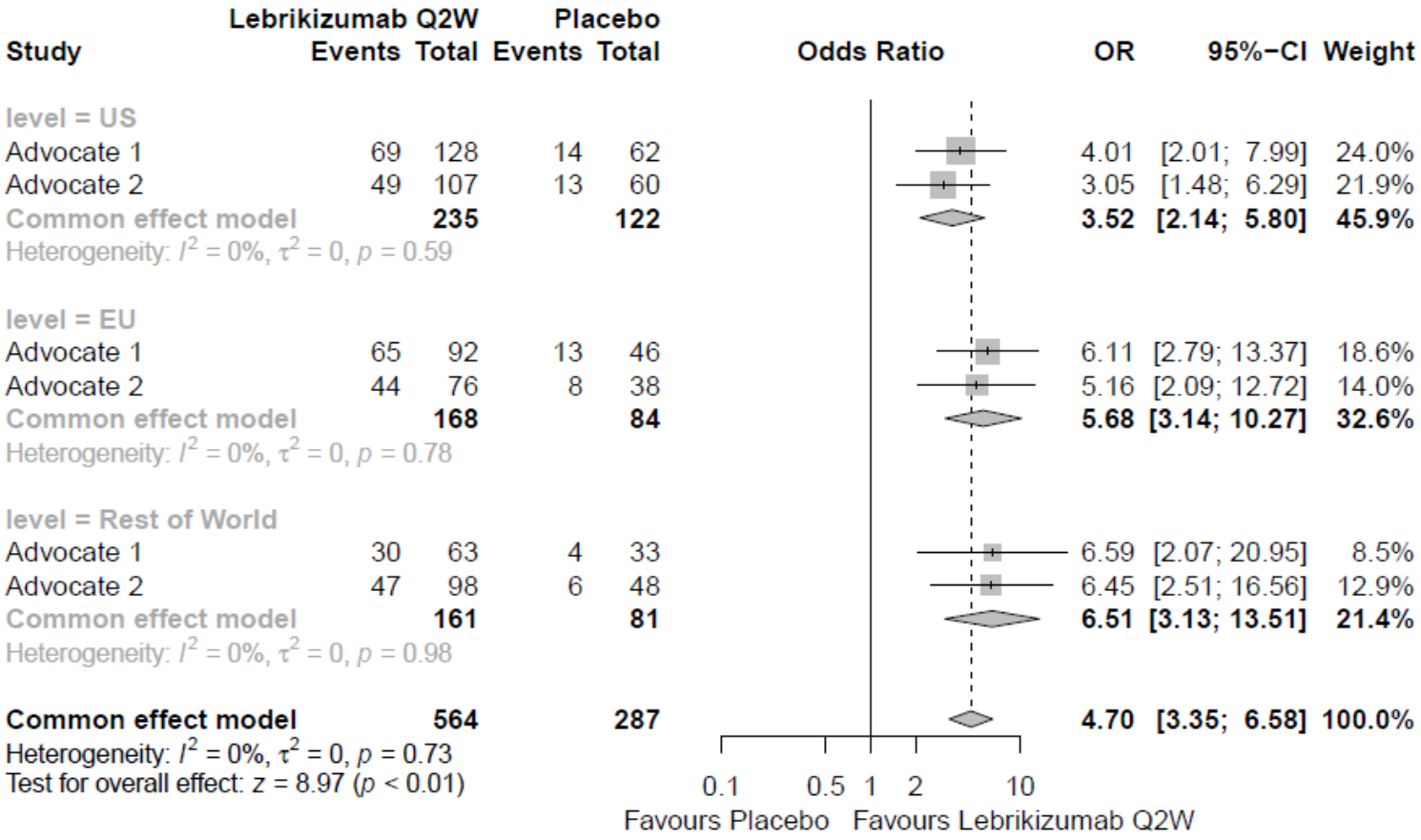


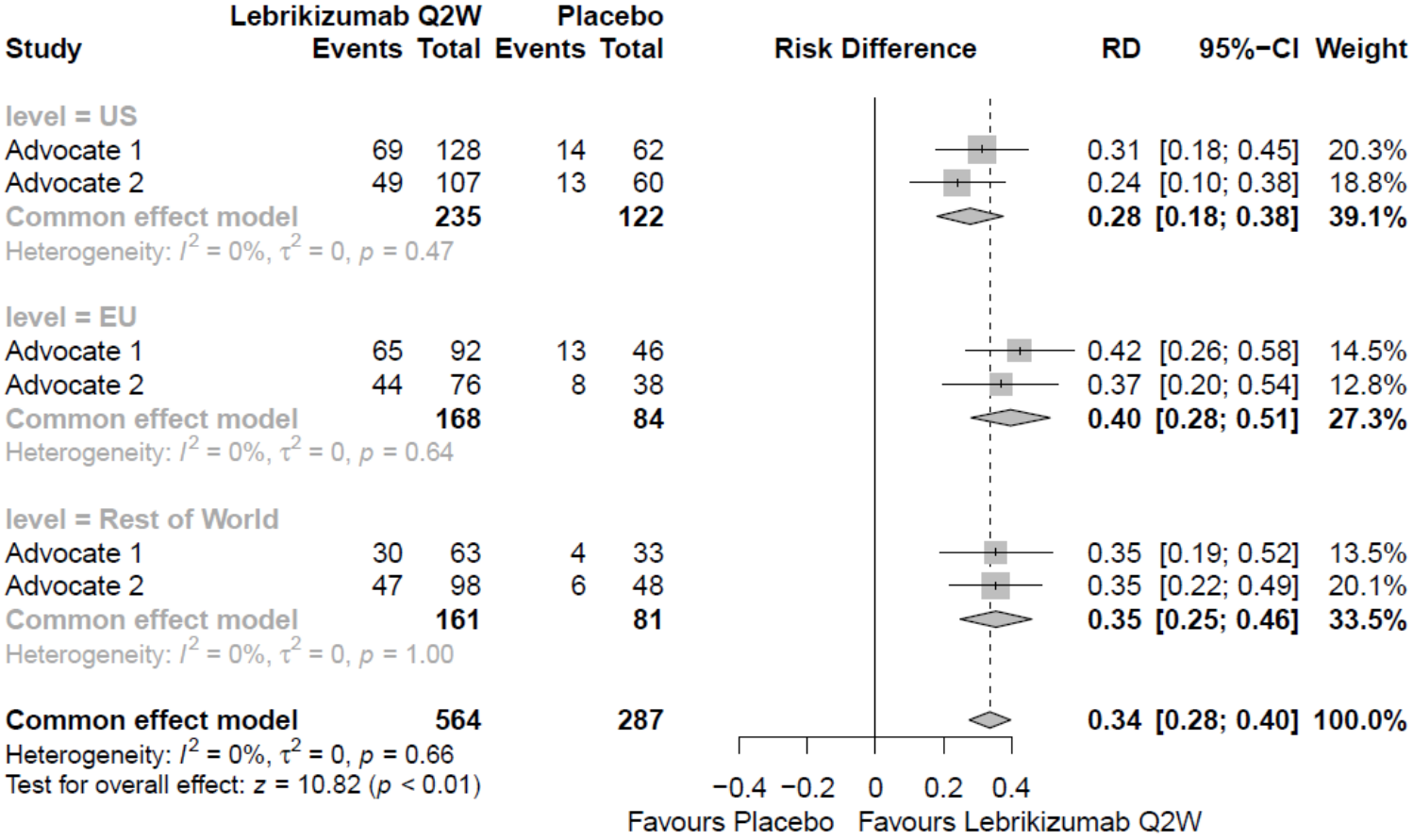

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Asian
Advocate 1 21 39 5 31 6.07 [1.93; 19.08] 8.6%
Advocate 2 36 78 6 44 5.43 [2.06; 14.31] 12.0%
Common effect model 117 75 5.69 [2.71; 11.92] 20.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.88
level = Black or African American
Advocate 1 18 33 2 16 8.40 [1.64; 42.97] 4.2%
Advocate 2 11 25 1 10 7.07 [0.77; 64.57] 2.3%
Common effect model 58 26 7.91 [2.13; 29.40] 6.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.90
level = White
Advocate 1 117 196 24 93 4.26 [2.47; 7.34] 38.0%
Advocate 2 90 168 19 85 4.01 [2.21; 7.26] 32.0%
Common effect model 364 178 4.14 [2.77; 6.19] 70.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.88
level = Other
Advocate 1 8 15 0 1 3.40 [0.12; 96.70] 1.0%
Advocate 2 3 10 1 7 2.57 [0.21; 31.71] 1.8%
Common effect model 25 8 2.84 [0.38; 21.21] 2.8%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.90
Common effect model 564 287 4.56 [3.26; 6.39] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.98
Test for overall effect: z = 8.86 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Asian
Advocate 1 21 39 5 31 0.38 [0.17; 0.58] 9.2%
Advocate 2 36 78 6 44 0.33 [0.18; 0.48] 16.9%
Common effect model 117 75 0.34 [0.22; 0.46] 26.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.69
level = Black or African American
Advocate 1 18 33 2 16 0.42 [0.19; 0.66] 6.9%
Advocate 2 11 25 1 10 0.34 [0.07; 0.61] 5.3%
Common effect model 58 26 0.39 [0.21; 0.56] 12.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.66
level = White
Advocate 1 117 196 24 93 0.34 [0.23; 0.45] 30.1%
Advocate 2 90 168 19 85 0.31 [0.20; 0.43] 28.1%
Common effect model 364 178 0.33 [0.25; 0.41] 58.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.75
level = Other
Advocate 1 8 15 0 1 0.53 [−0.11; 1.18] 0.9%
Advocate 2 3 10 1 7 0.16 [−0.23; 0.54] 2.6%
Common effect model 25 8 0.26 [−0.08; 0.59] 3.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.33
Common effect model 564 287 0.34 [0.27; 0.40] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.96
Test for overall effect: z = 10.66 (p < 0.01)
−1 −0.5 0 0.5 1
Favours Placebo
Favours Lebrikizumab Q2W

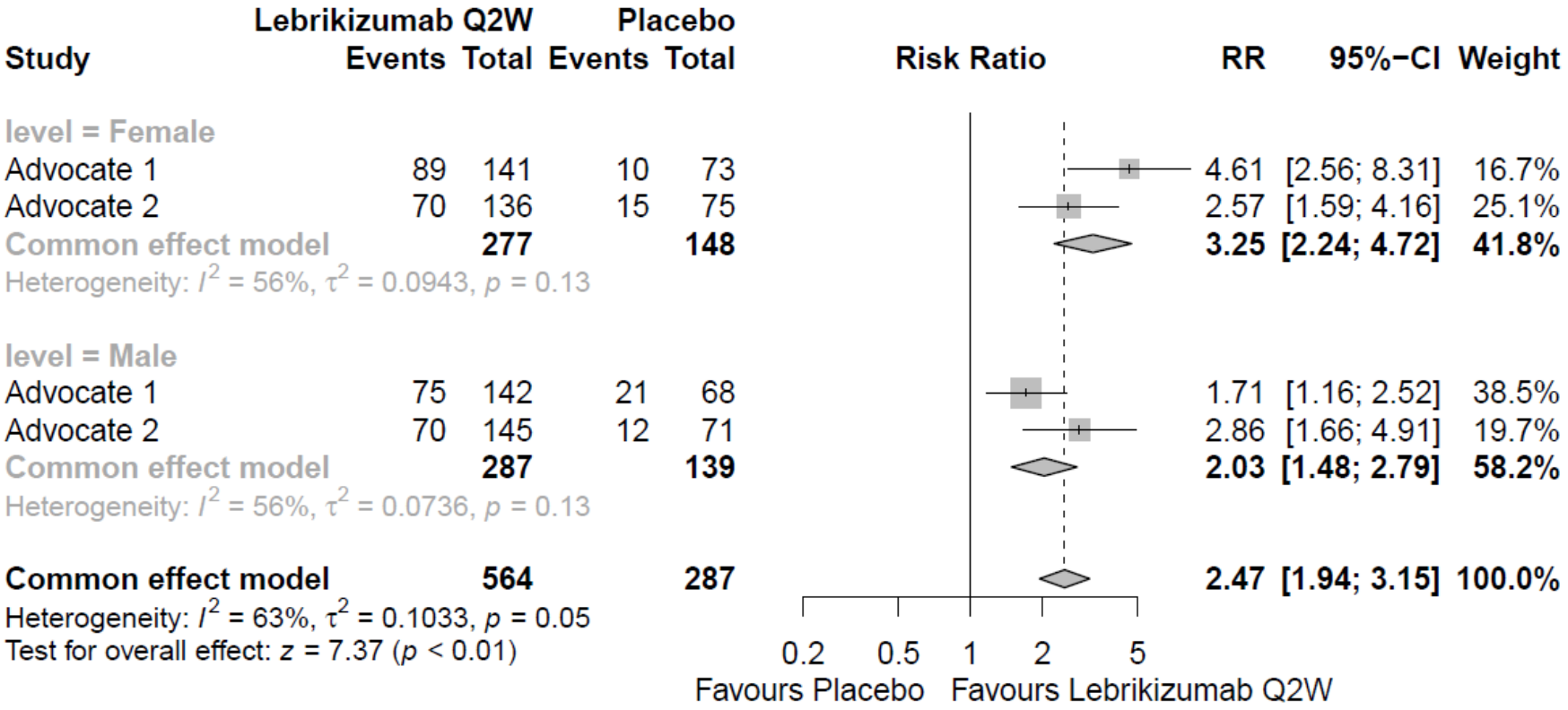
4.5.1.7.4 Region

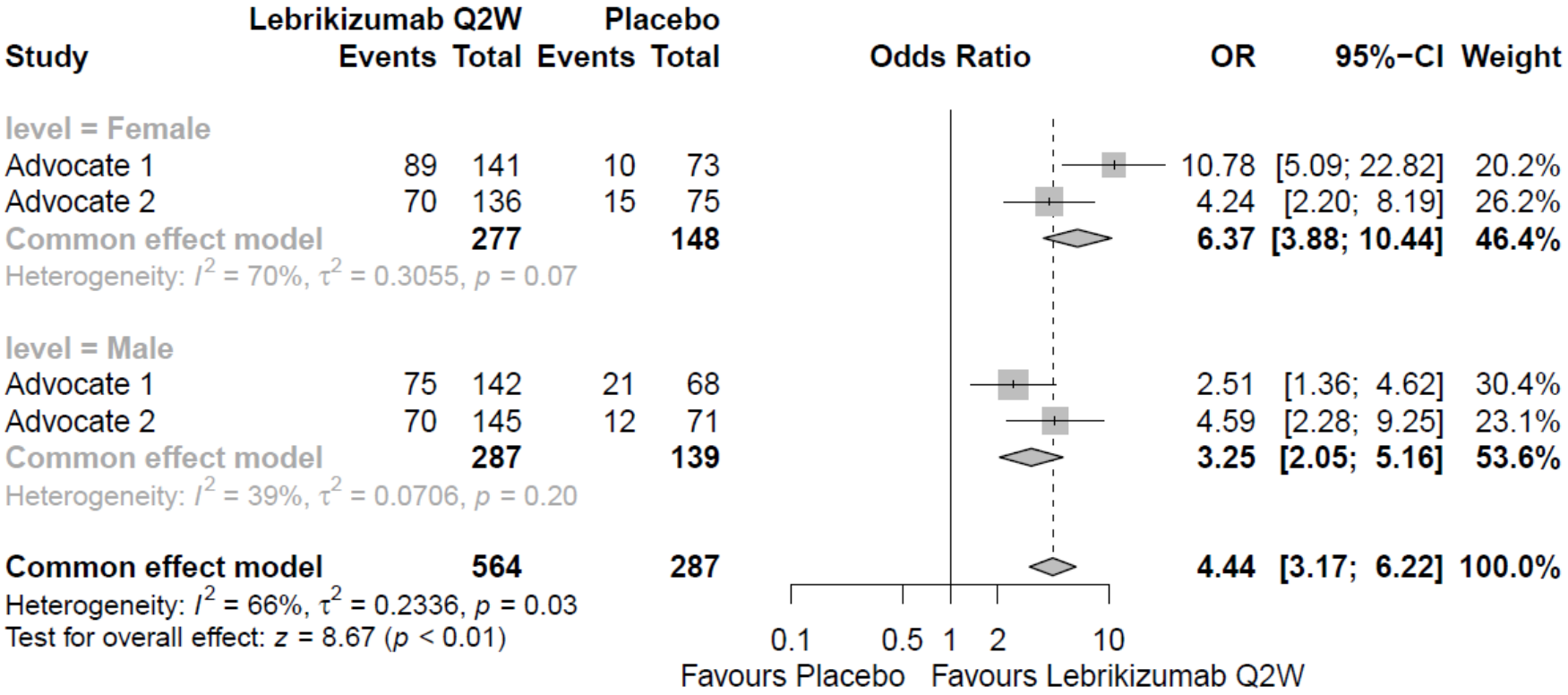


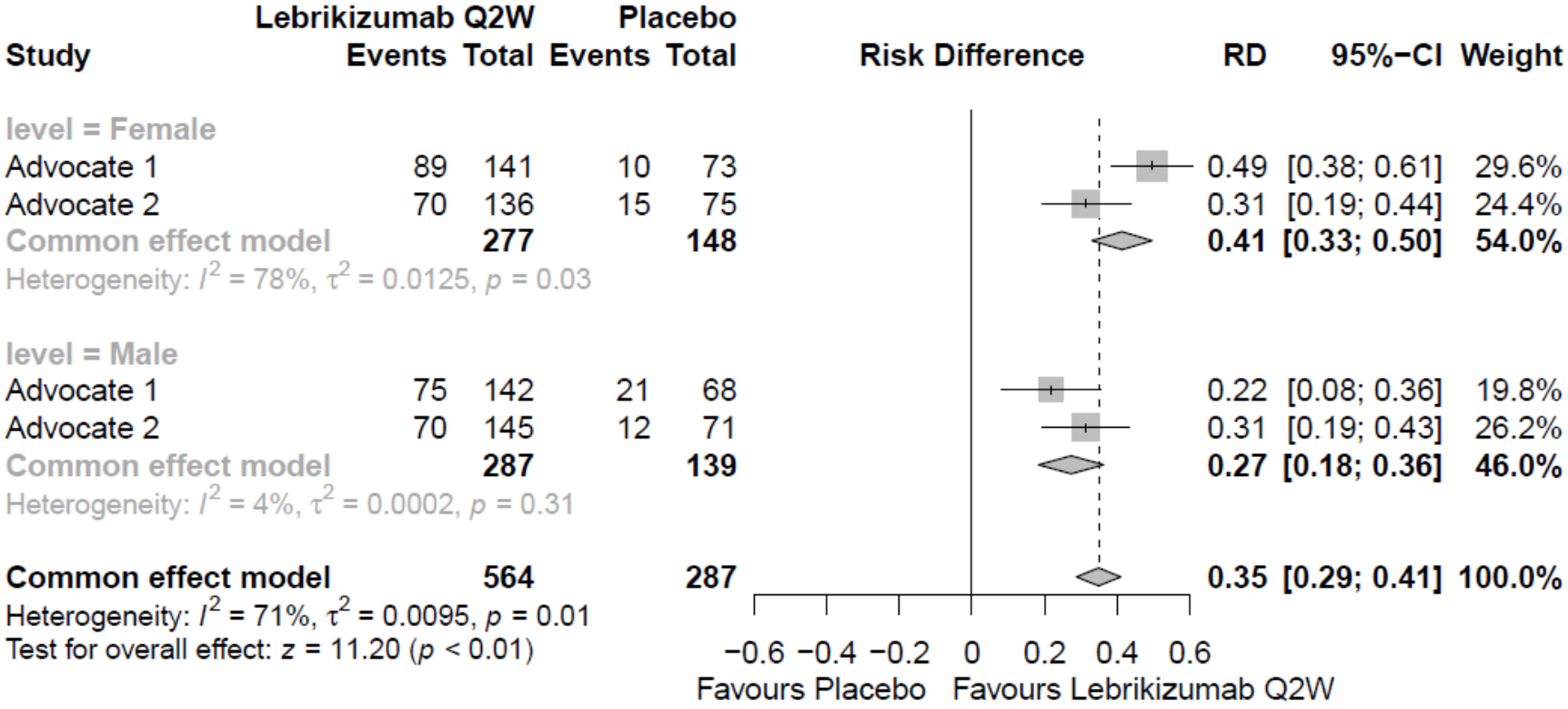

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = US
Advocate 1 69 128 14 62 4.01 [2.01; 7.99] 24.0%
Advocate 2 49 107 13 60 3.05 [1.48; 6.29] 21.9%
Common effect model 235 122 3.52 [2.14; 5.80] 45.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.59
level = EU
Advocate 1 65 92 13 46 6.11 [2.79; 13.37] 18.6%
Advocate 2 44 76 8 38 5.16 [2.09; 12.72] 14.0%
Common effect model 168 84 5.68 [3.14; 10.27] 32.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.78
level = Rest of World
Advocate 1 30 63 4 33 6.59 [2.07; 20.95] 8.5%
Advocate 2 47 98 6 48 6.45 [2.51; 16.56] 12.9%
Common effect model 161 81 6.51 [3.13; 13.51] 21.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.98
Common effect model 564 287 4.70 [3.35; 6.58] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.73
Test for overall effect: z = 8.97 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = US
Advocate 1 69 128 14 62 0.31 [0.18; 0.45] 20.3%
Advocate 2 49 107 13 60 0.24 [0.10; 0.38] 18.8%
Common effect model 235 122 0.28 [0.18; 0.38] 39.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.47
level = EU
Advocate 1 65 92 13 46 0.42 [0.26; 0.58] 14.5%
Advocate 2 44 76 8 38 0.37 [0.20; 0.54] 12.8%
Common effect model 168 84 0.40 [0.28; 0.51] 27.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.64
level = Rest of World
Advocate 1 30 63 4 33 0.35 [0.19; 0.52] 13.5%
Advocate 2 47 98 6 48 0.35 [0.22; 0.49] 20.1%
Common effect model 161 81 0.35 [0.25; 0.46] 33.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 1.00
Common effect model 564 287 0.34 [0.28; 0.40] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.66
Test for overall effect: z = 10.82 (p < 0.01)
−0.4 −0.2 0 0.2 0.4
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.7.5 Geschlecht

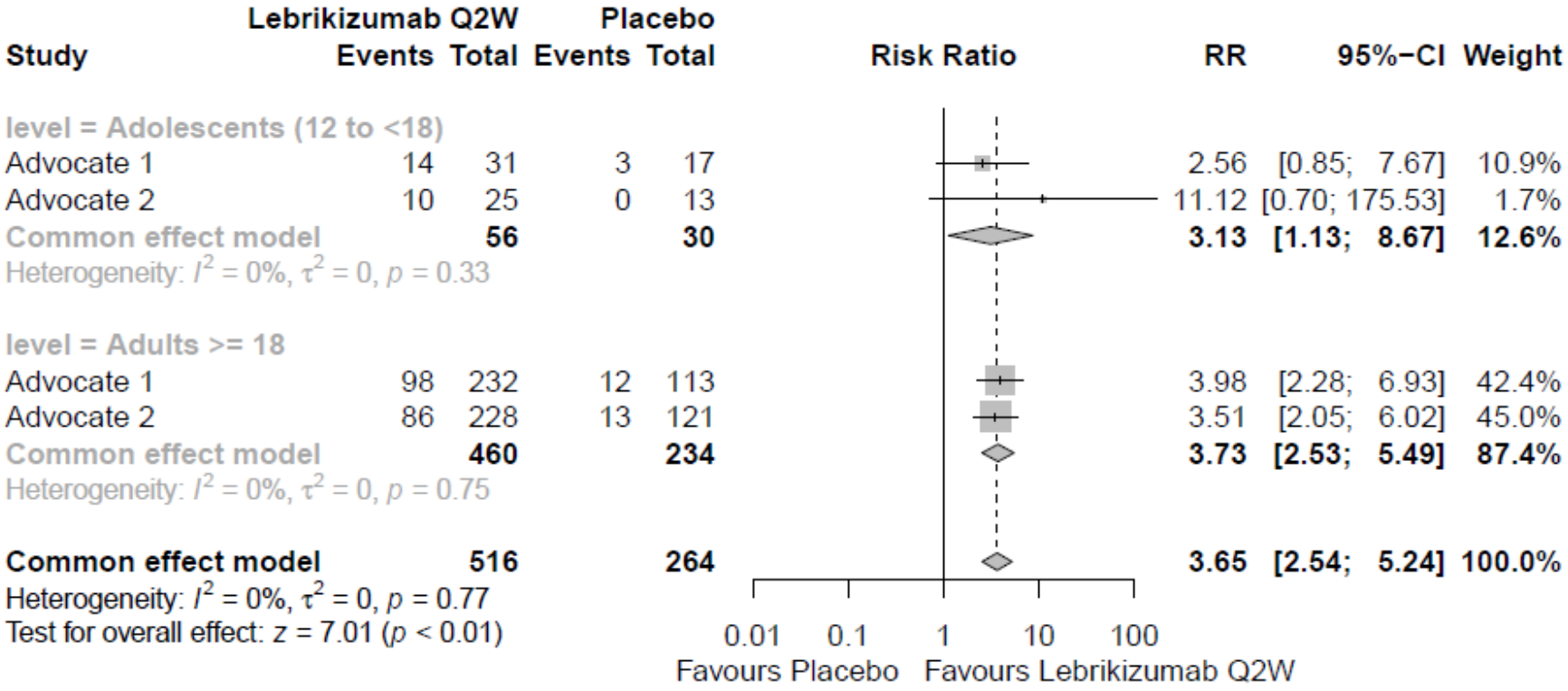


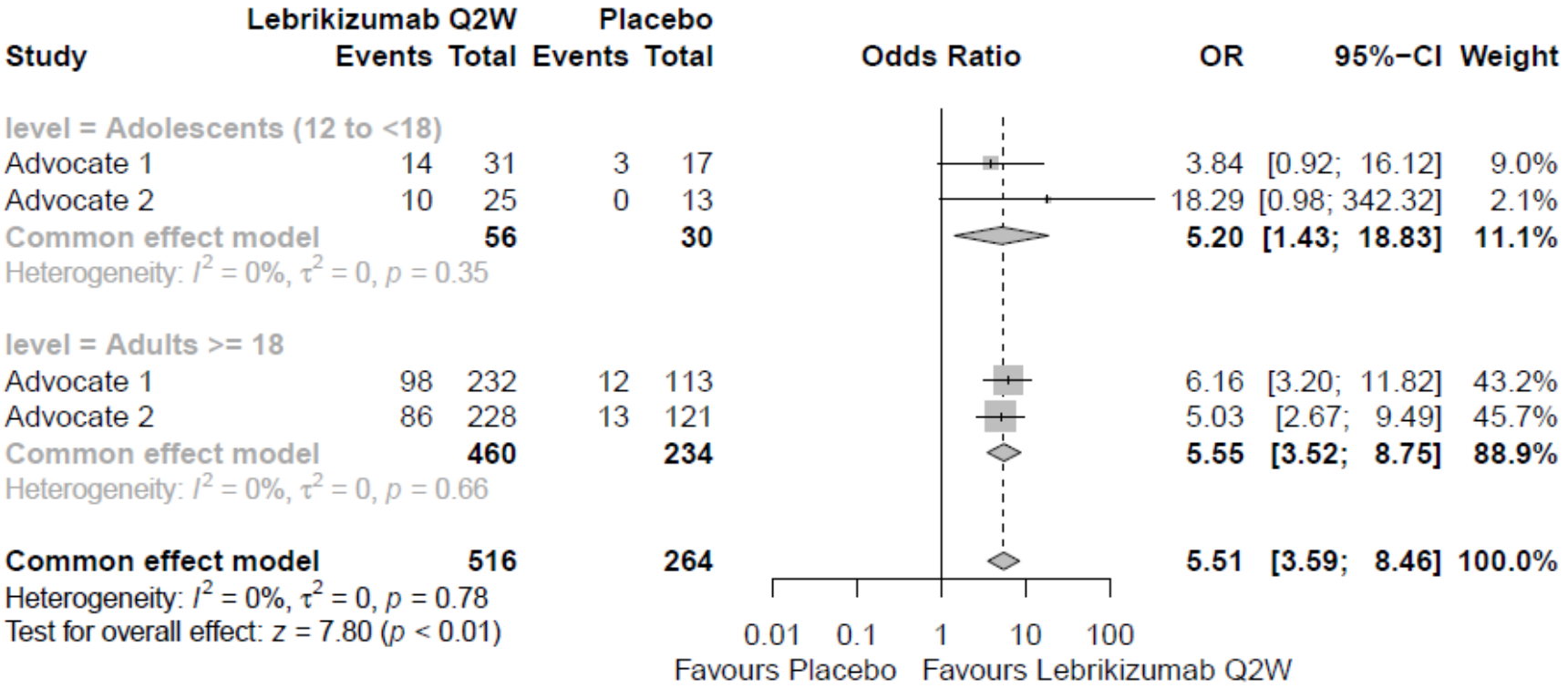

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Female
Advocate 1 89 141 10 73 10.78 [5.09; 22.82] 20.2%
Advocate 2 70 136 15 75 4.24 [2.20; 8.19] 26.2%
Common effect model 277 148 6.37 [3.88; 10.44] 46.4%
Heterogeneity: I^2 = 70%, τ^2 = 0.3055, p = 0.07
level = Male
Advocate 1 75 142 21 68 2.51 [1.36; 4.62] 30.4%
Advocate 2 70 145 12 71 4.59 [2.28; 9.25] 23.1%
Common effect model 287 139 3.25 [2.05; 5.16] 53.6%
Heterogeneity: I^2 = 39%, τ^2 = 0.0706, p = 0.20
Common effect model 564 287 4.44 [3.17; 6.22] 100.0%
Heterogeneity: I^2 = 66%, τ^2 = 0.2336, p = 0.03
Test for overall effect: z = 8.67 (p < 0.01)
0.1
0.5
1
2
10
Favours Placebo
Favours Lebrikizumab Q2W

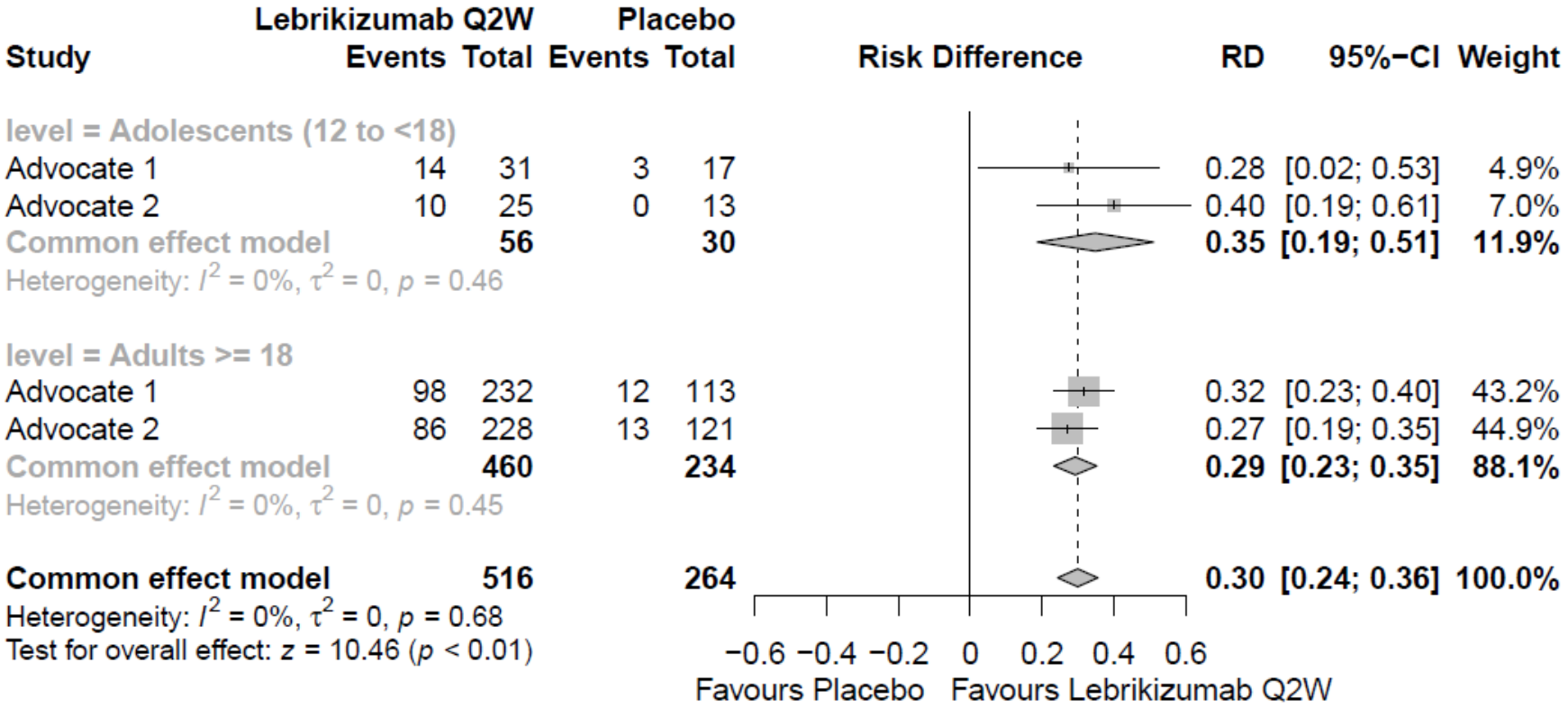

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Female
Advocate 1 89 141 10 73 0.49 [0.38; 0.61] 29.6%
Advocate 2 70 136 15 75 0.31 [0.19; 0.44] 24.4%
Common effect model 277 148 0.41 [0.33; 0.50] 54.0%
Heterogeneity: I^2 = 78%, τ^2 = 0.0125, p = 0.03
level = Male
Advocate 1 75 142 21 68 0.22 [0.08; 0.36] 19.8%
Advocate 2 70 145 12 71 0.31 [0.19; 0.43] 26.2%
Common effect model 287 139 0.27 [0.18; 0.36] 46.0%
Heterogeneity: I^2 = 4%, τ^2 = 0.0002, p = 0.31
Common effect model 564 287 0.35 [0.29; 0.41] 100.0%
Heterogeneity: I^2 = 71%, τ^2 = 0.0095, p = 0.01
Test for overall effect: z = 11.20 (p < 0.01)
−0.6 −0.4 −0.2 0 0.2 0.4 0.6
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.8 Pruritus NRS Reduktion um 4 Punkte (Baseline 4)

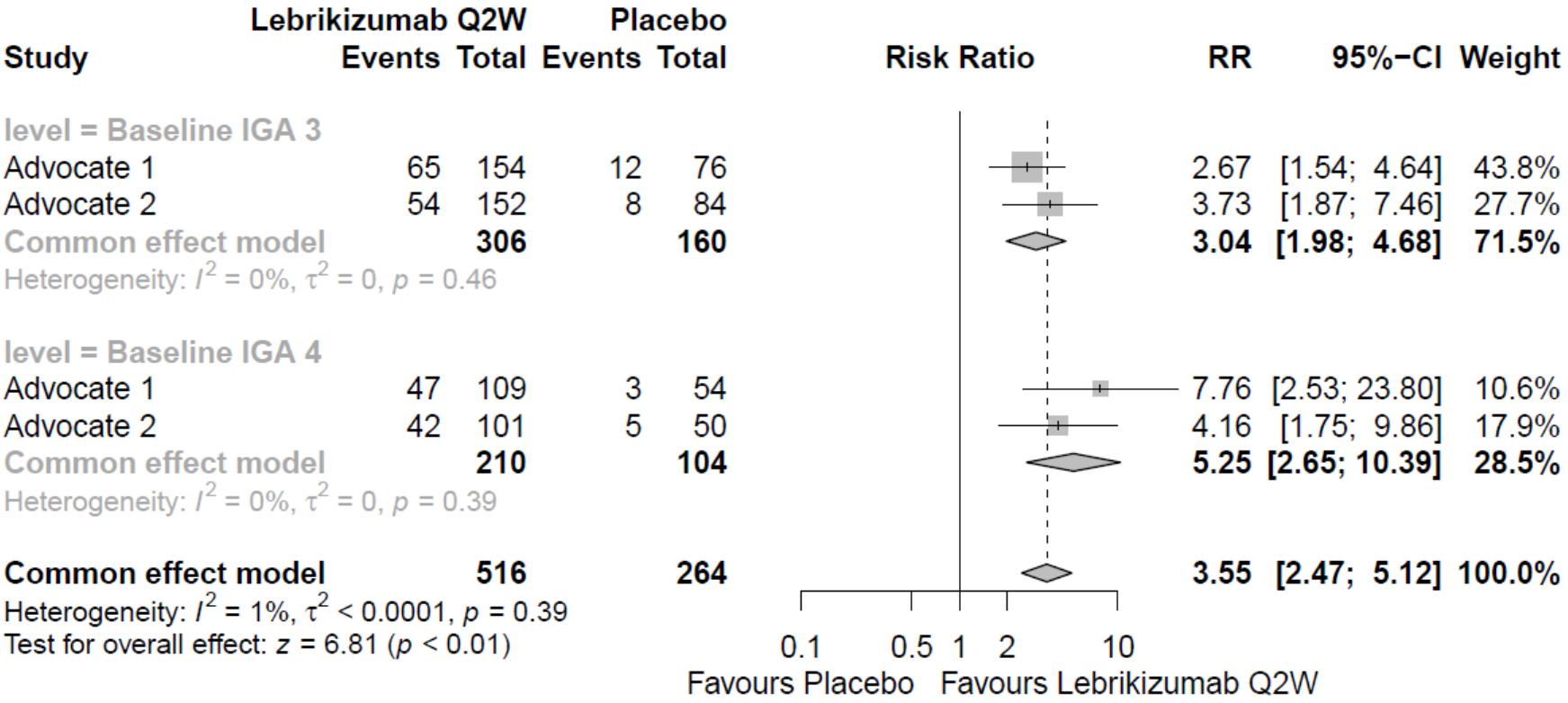
4.5.1.8.1 Altersgruppe

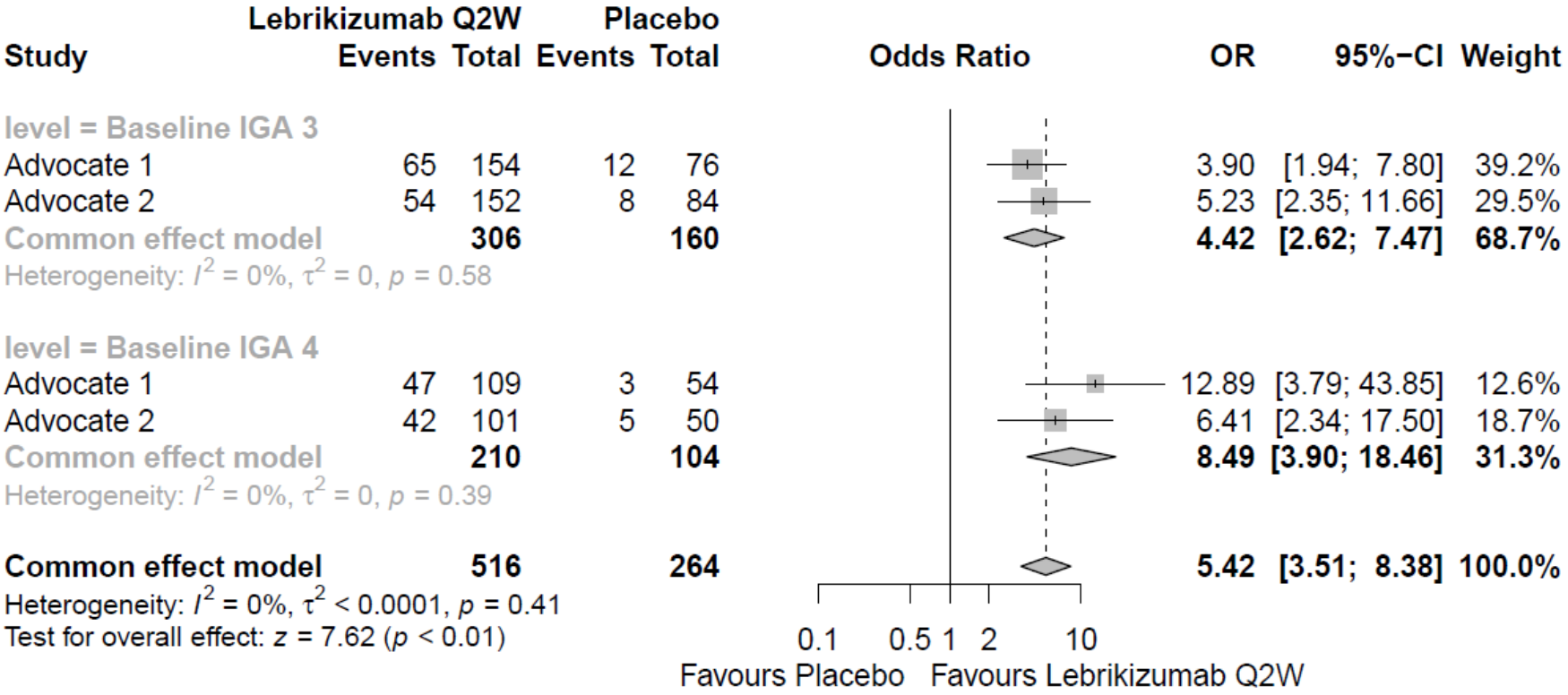


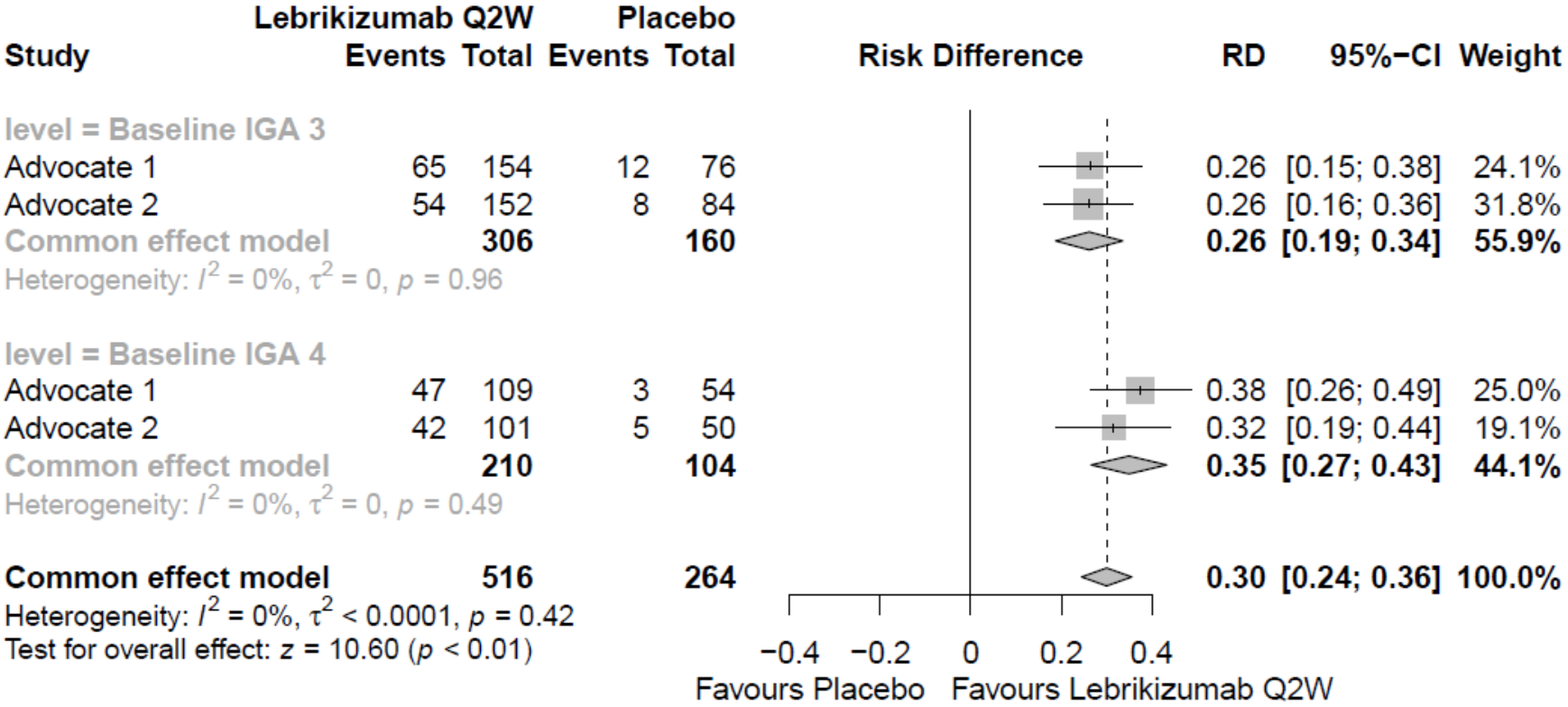

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 14 31 3 17 3.84 [0.92; 16.12] 9.0%
Advocate 2 10 25 0 13 18.29 [0.98; 342.32] 2.1%
Common effect model 56 30 5.20 [1.43; 18.83] 11.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.35
level = Adults >= 18
Advocate 1 98 232 12 113 6.16 [3.20; 11.82] 43.2%
Advocate 2 86 228 13 121 5.03 [2.67; 9.49] 45.7%
Common effect model 460 234 5.55 [3.52; 8.75] 88.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.66
Common effect model 516 264 5.51 [3.59; 8.46] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.78
Test for overall effect: z = 7.80 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 14 31 3 17 0.28 [0.02; 0.53] 4.9%
Advocate 2 10 25 0 13 0.40 [0.19; 0.61] 7.0%
Common effect model 56 30 0.35 [0.19; 0.51] 11.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.46
level = Adults >= 18
Advocate 1 98 232 12 113 0.32 [0.23; 0.40] 43.2%
Advocate 2 86 228 13 121 0.27 [0.19; 0.35] 44.9%
Common effect model 460 234 0.29 [0.23; 0.35] 88.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.45
Common effect model 516 264 0.30 [0.24; 0.36] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.68
Test for overall effect: z = 10.46 (p < 0.01)
−0.6 −0.4 −0.2 0 0.2 0.4 0.6
Favours Placebo
Favours Lebrikizumab Q2W

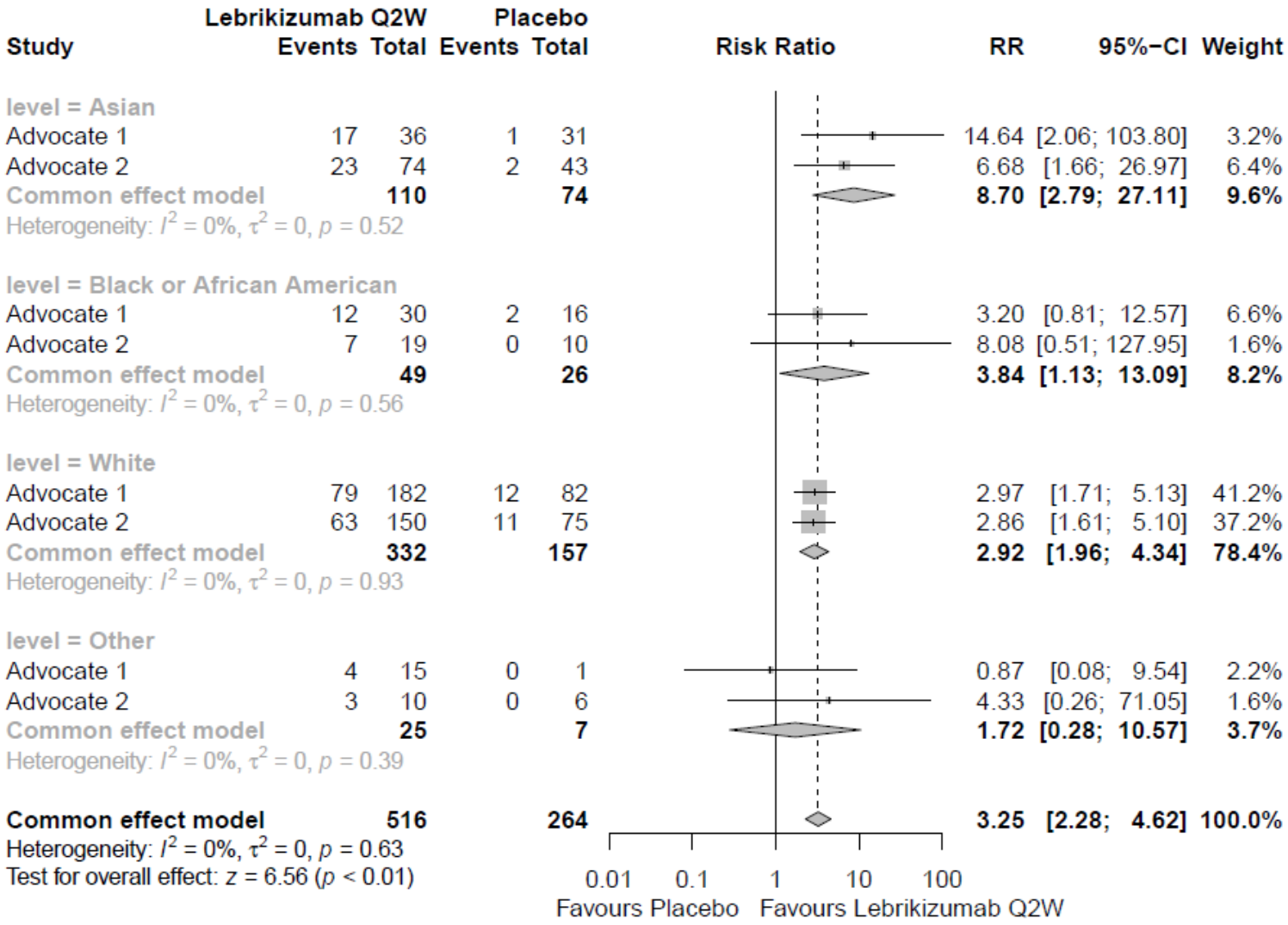
4.5.1.8.2 Krankheitsschwere

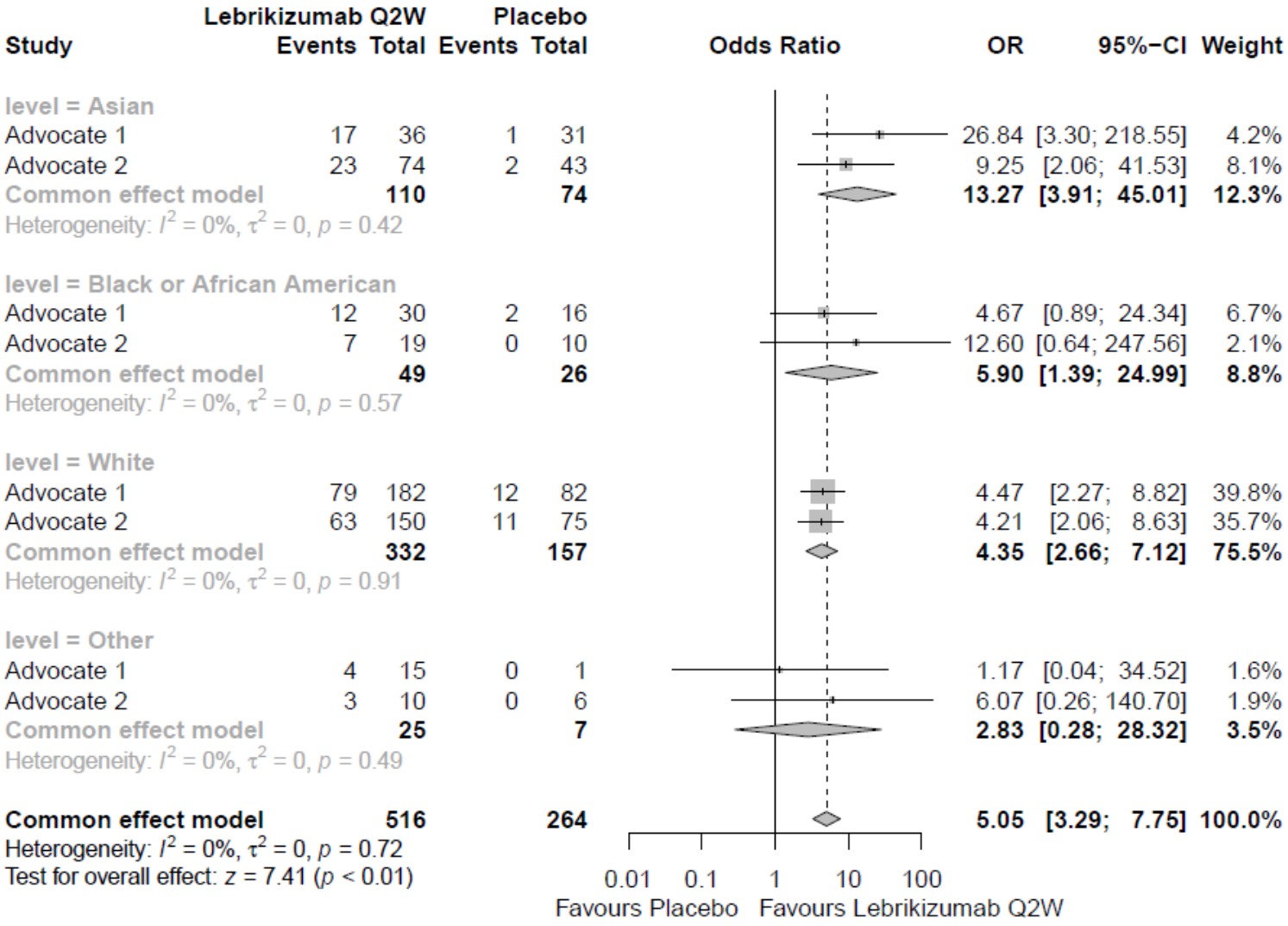


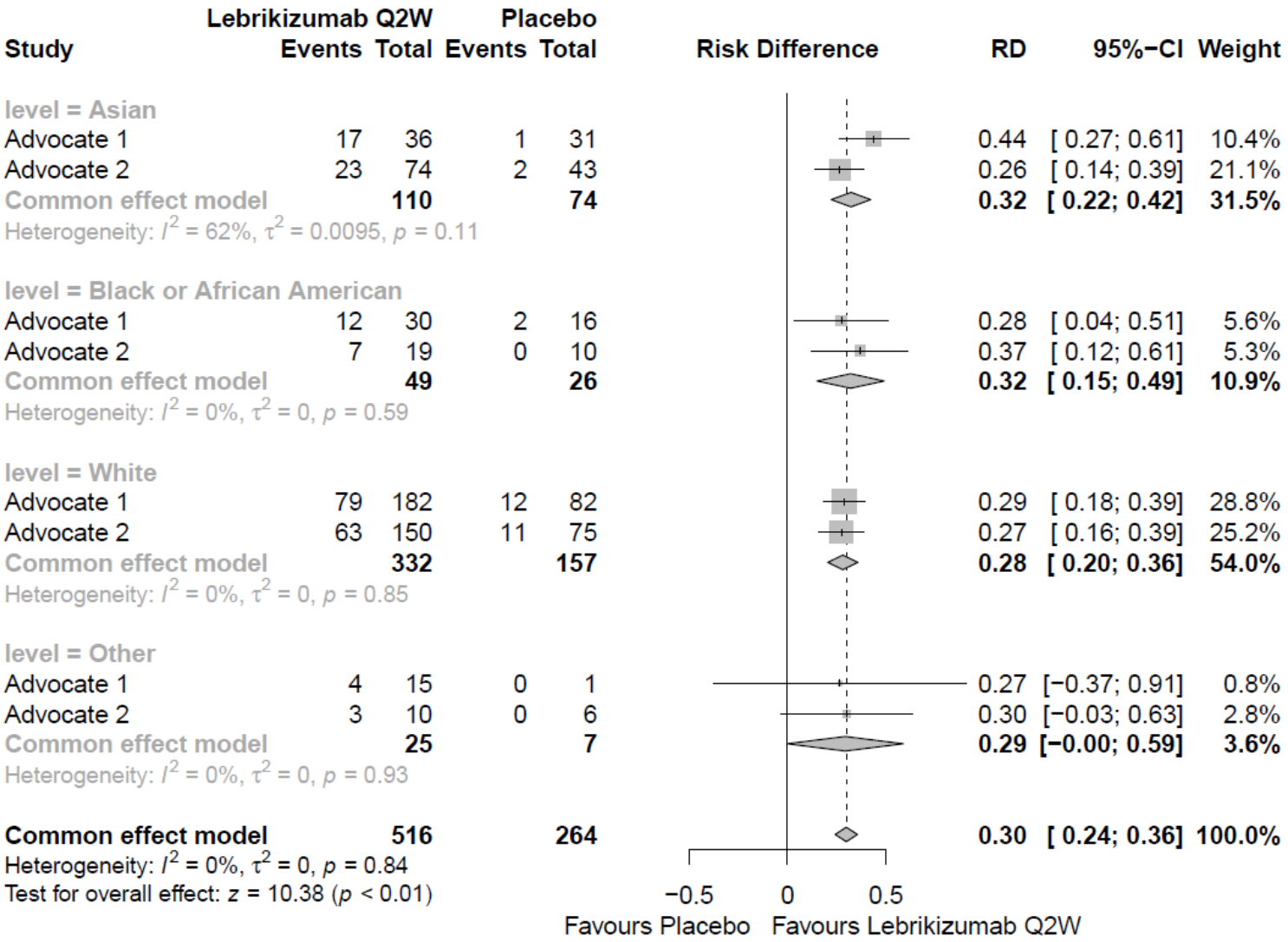

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Baseline IGA 3
Advocate 1 65 154 12 76 3.90 [1.94; 7.80] 39.2%
Advocate 2 54 152 8 84 5.23 [2.35; 11.66] 29.5%
Common effect model 306 160 4.42 [2.62; 7.47] 68.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.58
level = Baseline IGA 4
Advocate 1 47 109 3 54 12.89 [3.79; 43.85] 12.6%
Advocate 2 42 101 5 50 6.41 [2.34; 17.50] 18.7%
Common effect model 210 104 8.49 [3.90; 18.46] 31.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.39
Common effect model 516 264 5.42 [3.51; 8.38] 100.0%
Heterogeneity: I^2 = 0%, τ^2 < 0.0001, p = 0.41
Test for overall effect: z = 7.62 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Baseline IGA 3
Advocate 1 65 154 12 76 0.26 [0.15; 0.38] 24.1%
Advocate 2 54 152 8 84 0.26 [0.16; 0.36] 31.8%
Common effect model 306 160 0.26 [0.19; 0.34] 55.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.96
level = Baseline IGA 4
Advocate 1 47 109 3 54 0.38 [0.26; 0.49] 25.0%
Advocate 2 42 101 5 50 0.32 [0.19; 0.44] 19.1%
Common effect model 210 104 0.35 [0.27; 0.43] 44.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.49
Common effect model 516 264 0.30 [0.24; 0.36] 100.0%
Heterogeneity: I^2 = 0%, τ^2 < 0.0001, p = 0.42
Test for overall effect: z = 10.60 (p < 0.01)
−0.4 −0.2 0 0.2 0.4
Favours Placebo
Favours Lebrikizumab Q2W

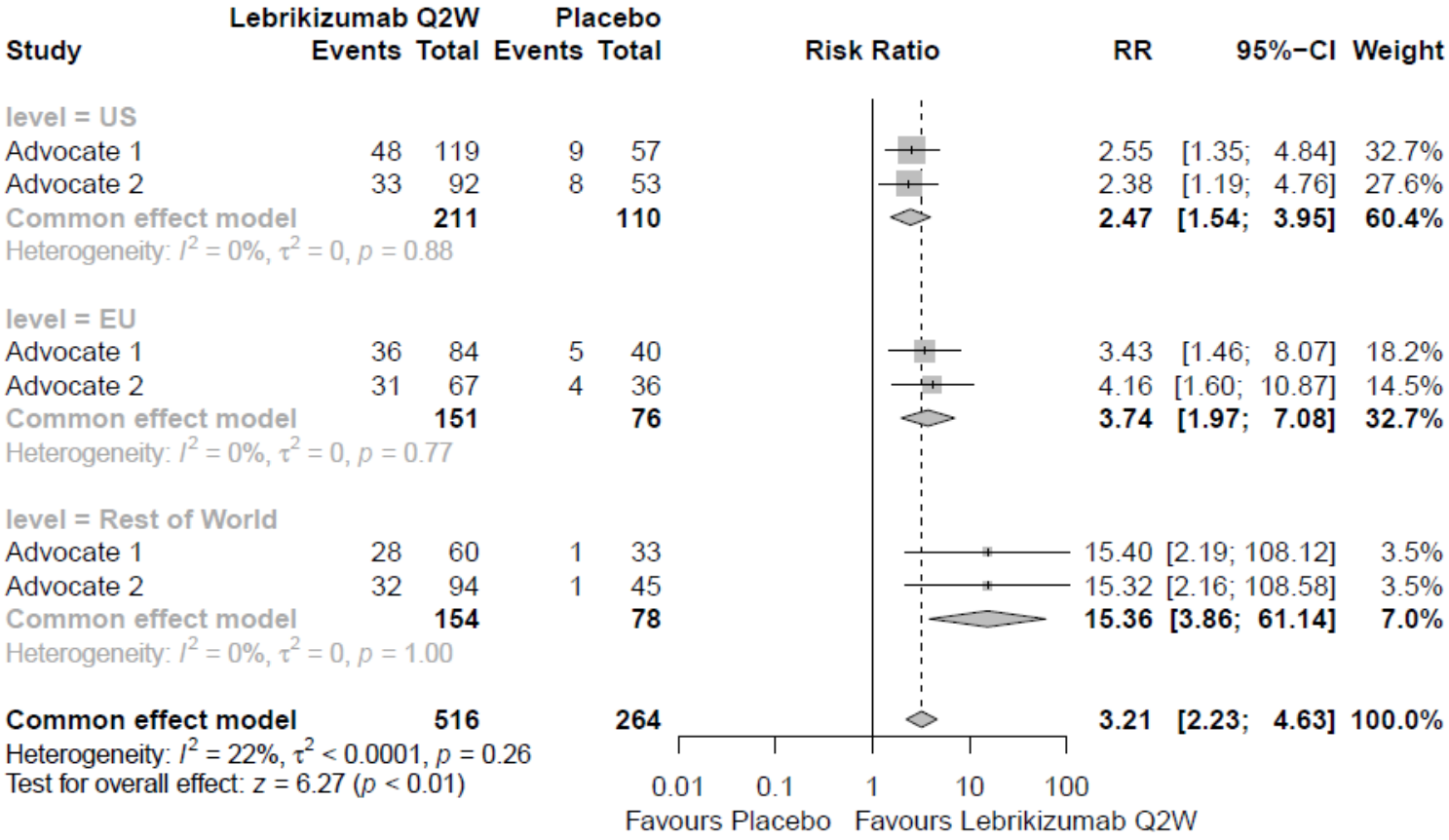
4.5.1.8.3 Ethnie

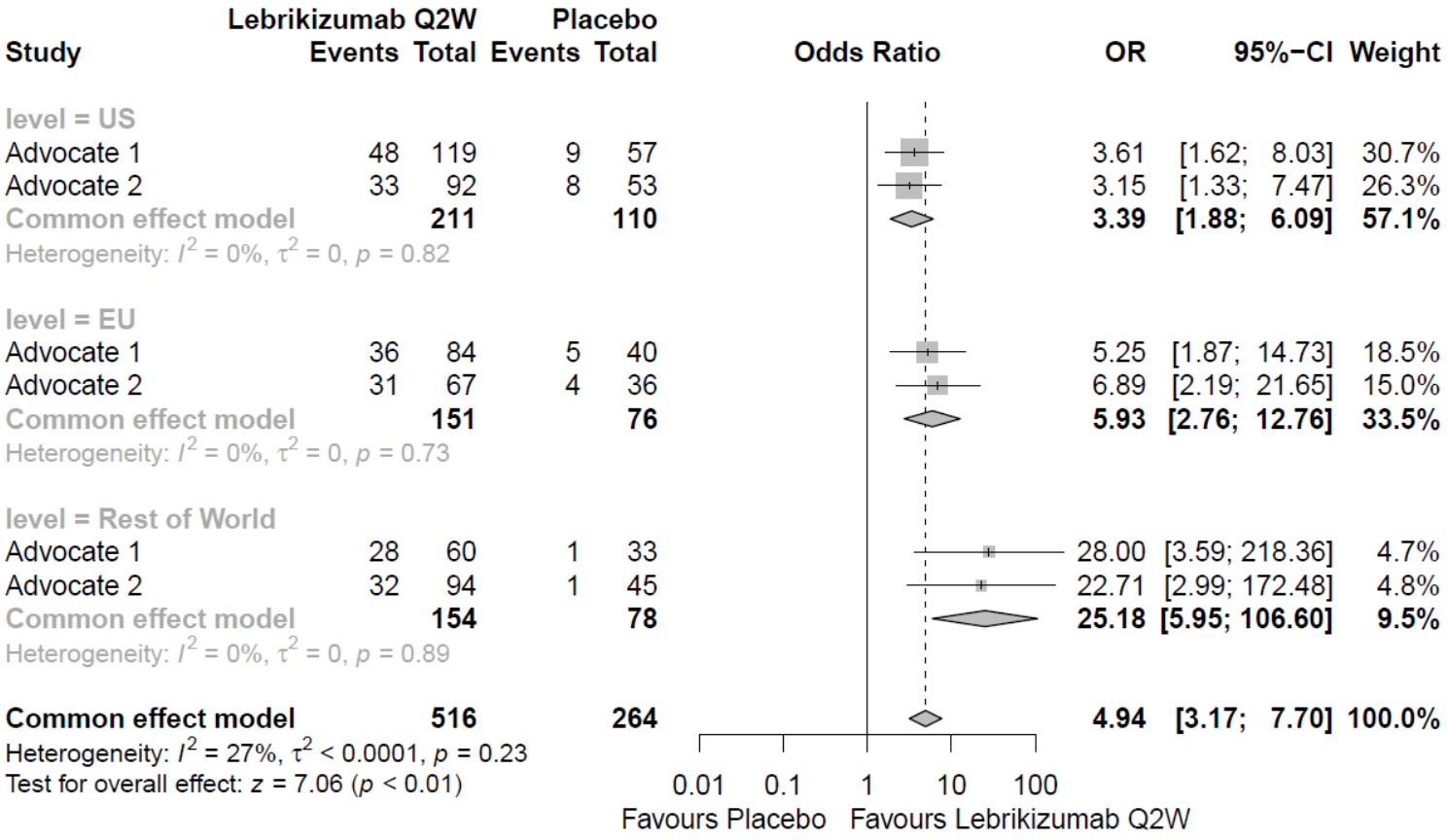


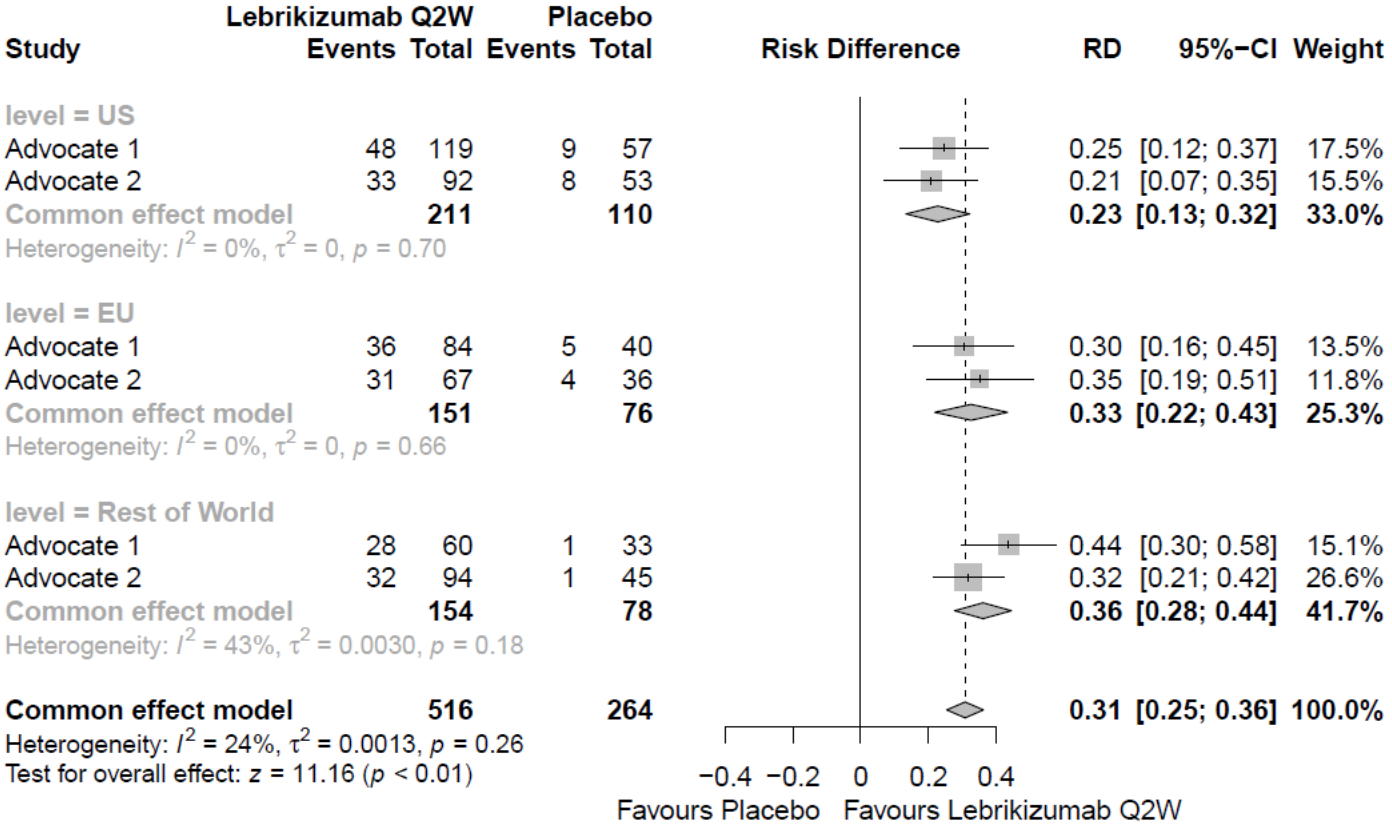

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Asian
Advocate 1 17 36 1 31 26.84 [3.30; 218.55] 4.2%
Advocate 2 23 74 2 43 9.25 [2.06; 41.53] 8.1%
Common effect model 110 74 13.27 [3.91; 45.01] 12.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.42
level = Black or African American
Advocate 1 12 30 2 16 4.67 [0.89; 24.34] 6.7%
Advocate 2 7 19 0 10 12.60 [0.64; 247.56] 2.1%
Common effect model 49 26 5.90 [1.39; 24.99] 8.8%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.57
level = White
Advocate 1 79 182 12 82 4.47 [2.27; 8.82] 39.8%
Advocate 2 63 150 11 75 4.21 [2.06; 8.63] 35.7%
Common effect model 332 157 4.35 [2.66; 7.12] 75.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.91
level = Other
Advocate 1 4 15 0 1 1.17 [0.04; 34.52] 1.6%
Advocate 2 3 10 0 6 6.07 [0.26; 140.70] 1.9%
Common effect model 25 7 2.83 [0.28; 28.32] 3.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.49
Common effect model 516 264 5.05 [3.29; 7.75] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.72
Test for overall effect: z = 7.41 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Asian
Advocate 1 17 36 1 31 0.44 [0.27; 0.61] 10.4%
Advocate 2 23 74 2 43 0.26 [0.14; 0.39] 21.1%
Common effect model 110 74 0.32 [0.22; 0.42] 31.5%
Heterogeneity: I^2 = 62%, τ^2 = 0.0095, p = 0.11
level = Black or African American
Advocate 1 12 30 2 16 0.28 [0.04; 0.51] 5.6%
Advocate 2 7 19 0 10 0.37 [0.12; 0.61] 5.3%
Common effect model 49 26 0.32 [0.15; 0.49] 10.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.59
level = White
Advocate 1 79 182 12 82 0.29 [0.18; 0.39] 28.8%
Advocate 2 63 150 11 75 0.27 [0.16; 0.39] 25.2%
Common effect model 332 157 0.28 [0.20; 0.36] 54.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.85
level = Other
Advocate 1 4 15 0 1 0.27 [−0.37; 0.91] 0.8%
Advocate 2 3 10 0 6 0.30 [−0.03; 0.63] 2.8%
Common effect model 25 7 0.29 [−0.00; 0.59] 3.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.93
Common effect model 516 264 0.30 [0.24; 0.36] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.84
Test for overall effect: z = 10.38 (p < 0.01)
−0.5
0
0.5
Favours Placebo
Favours Lebrikizumab Q2W

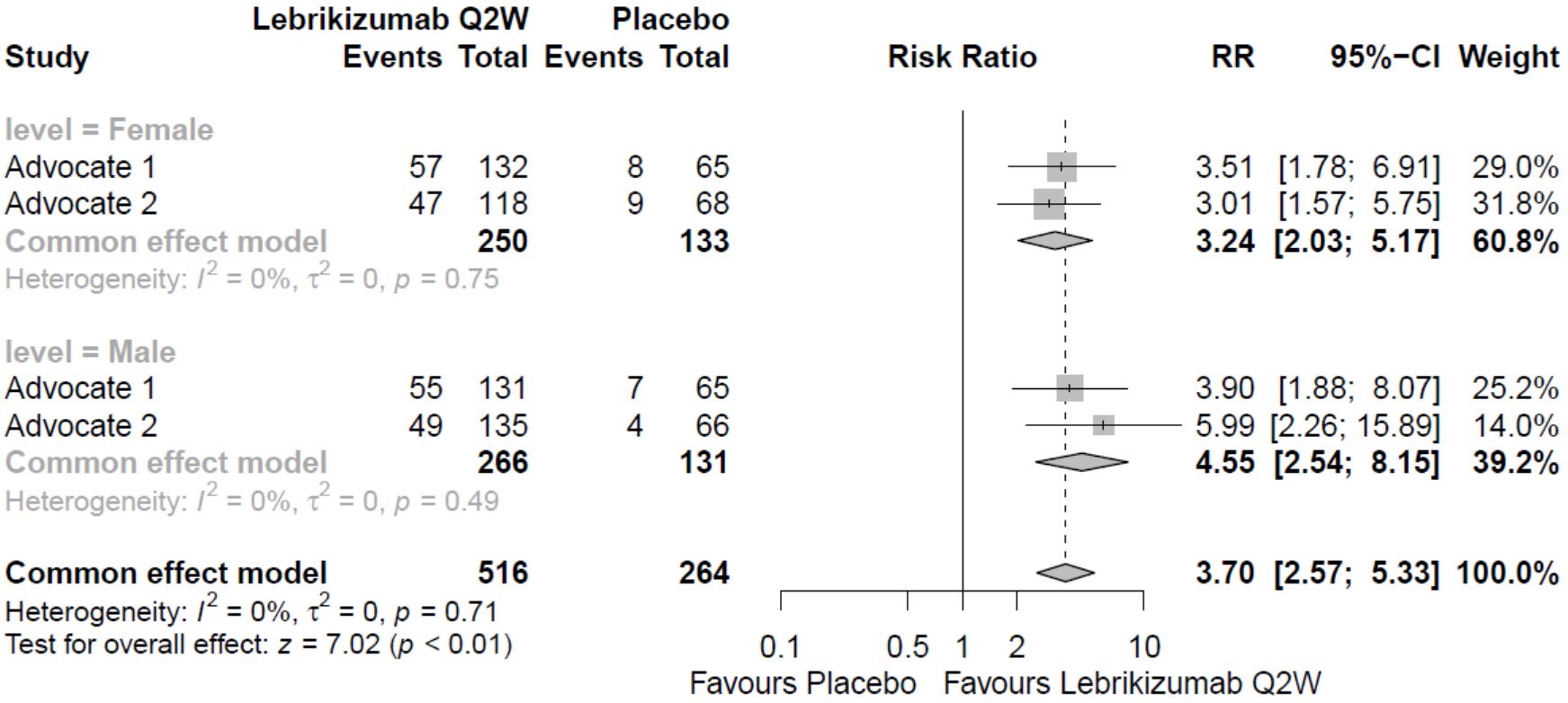
4.5.1.8.4 Region

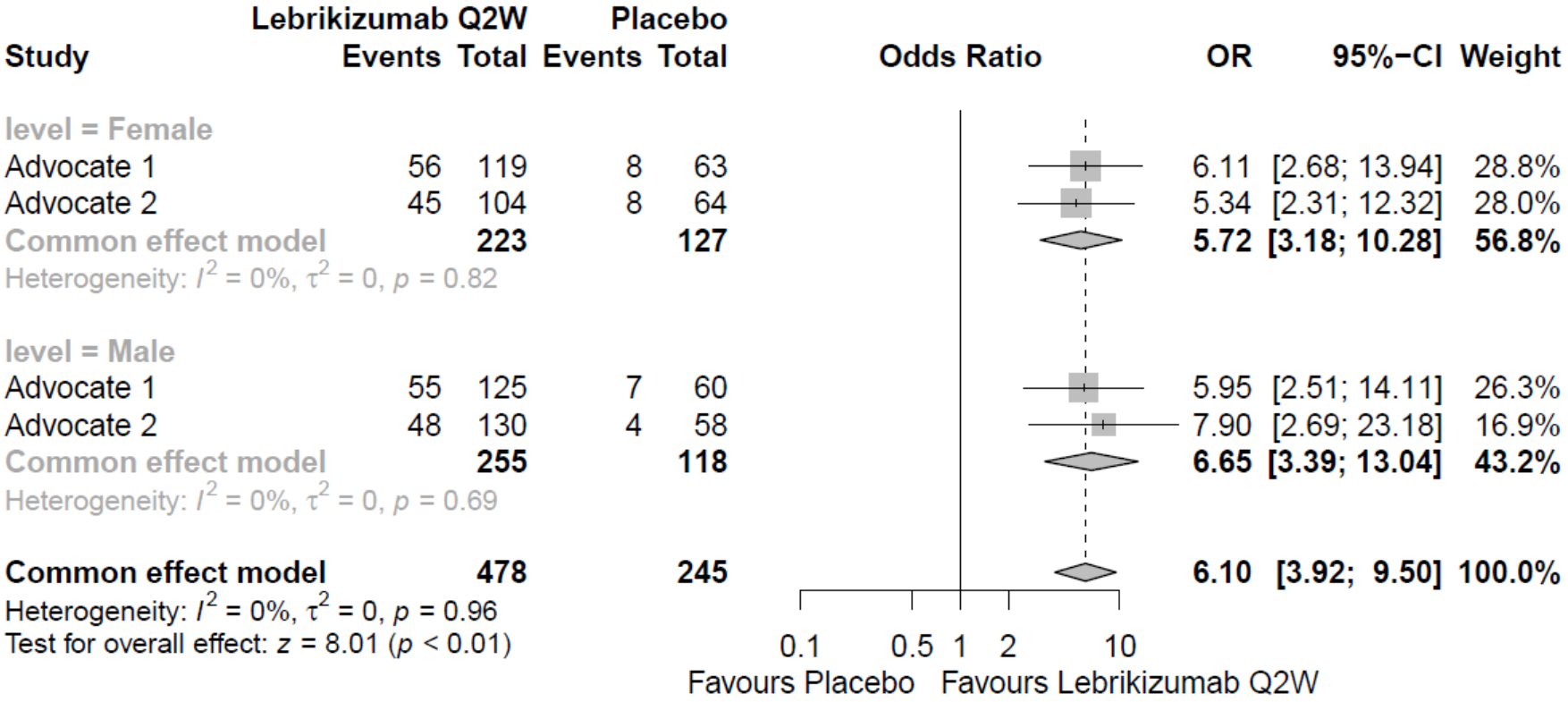


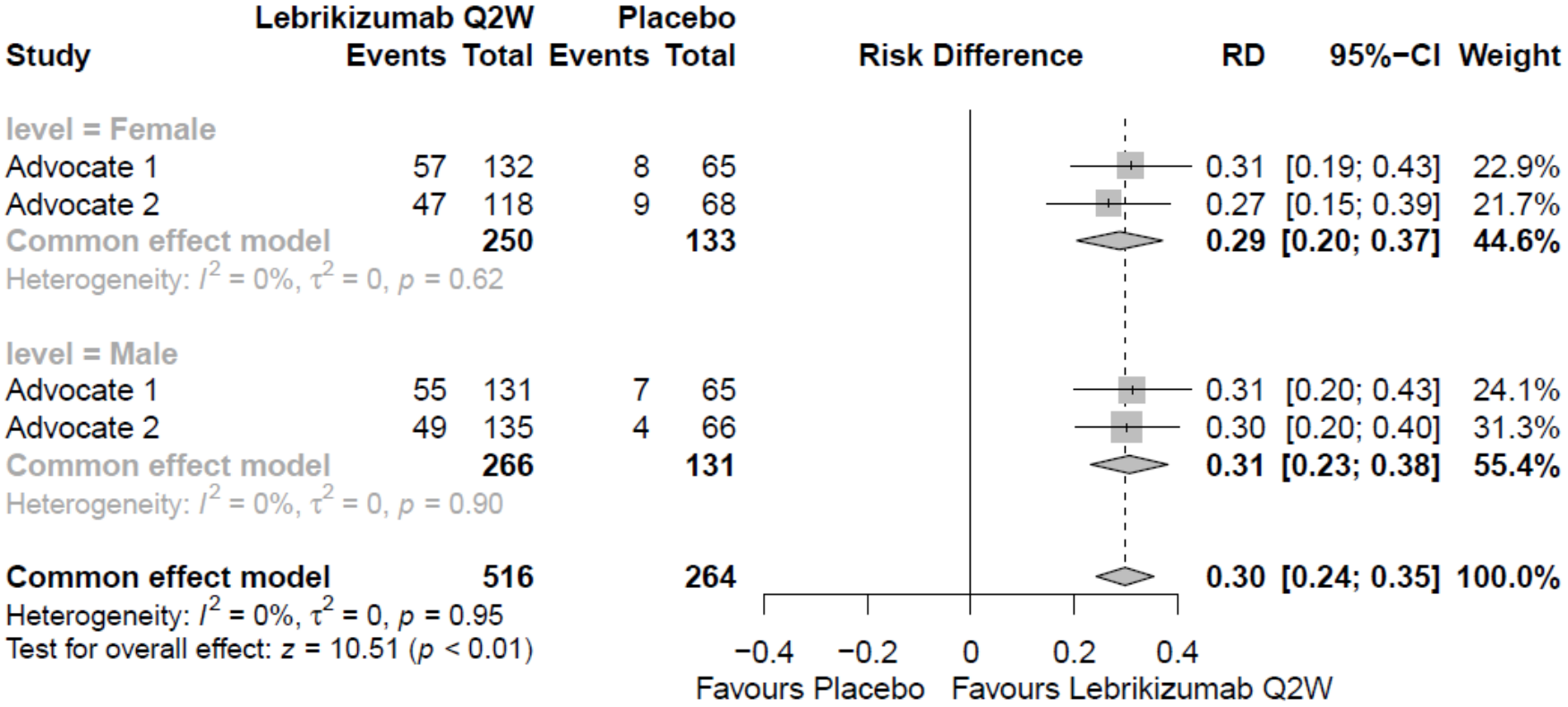

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = US
Advocate 1 48 119 9 57 3.61 [1.62; 8.03] 30.7%
Advocate 2 33 92 8 53 3.15 [1.33; 7.47] 26.3%
Common effect model 211 110 3.39 [1.88; 6.09] 57.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.82
level = EU
Advocate 1 36 84 5 40 5.25 [1.87; 14.73] 18.5%
Advocate 2 31 67 4 36 6.89 [2.19; 21.65] 15.0%
Common effect model 151 76 5.93 [2.76; 12.76] 33.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.73
level = Rest of World
Advocate 1 28 60 1 33 28.00 [3.59; 218.36] 4.7%
Advocate 2 32 94 1 45 22.71 [2.99; 172.48] 4.8%
Common effect model 154 78 25.18 [5.95; 106.60] 9.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.89
Common effect model 516 264 4.94 [3.17; 7.70] 100.0%
Heterogeneity: I^2 = 27%, τ^2 < 0.0001, p = 0.23
Test for overall effect: z = 7.06 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = US
Advocate 1 48 119 9 57 0.25 [0.12; 0.37] 17.5%
Advocate 2 33 92 8 53 0.21 [0.07; 0.35] 15.5%
Common effect model 211 110 0.23 [0.13; 0.32] 33.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.70
level = EU
Advocate 1 36 84 5 40 0.30 [0.16; 0.45] 13.5%
Advocate 2 31 67 4 36 0.35 [0.19; 0.51] 11.8%
Common effect model 151 76 0.33 [0.22; 0.43] 25.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.66
level = Rest of World
Advocate 1 28 60 1 33 0.44 [0.30; 0.58] 15.1%
Advocate 2 32 94 1 45 0.32 [0.21; 0.42] 26.6%
Common effect model 154 78 0.36 [0.28; 0.44] 41.7%
Heterogeneity: I^2 = 43%, τ^2 = 0.0030, p = 0.18
Common effect model 516 264 0.31 [0.25; 0.36] 100.0%
Heterogeneity: I^2 = 24%, τ^2 = 0.0013, p = 0.26
Test for overall effect: z = 11.16 (p < 0.01)
−0.4 −0.2 0 0.2 0.4
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.8.5 Geschlecht

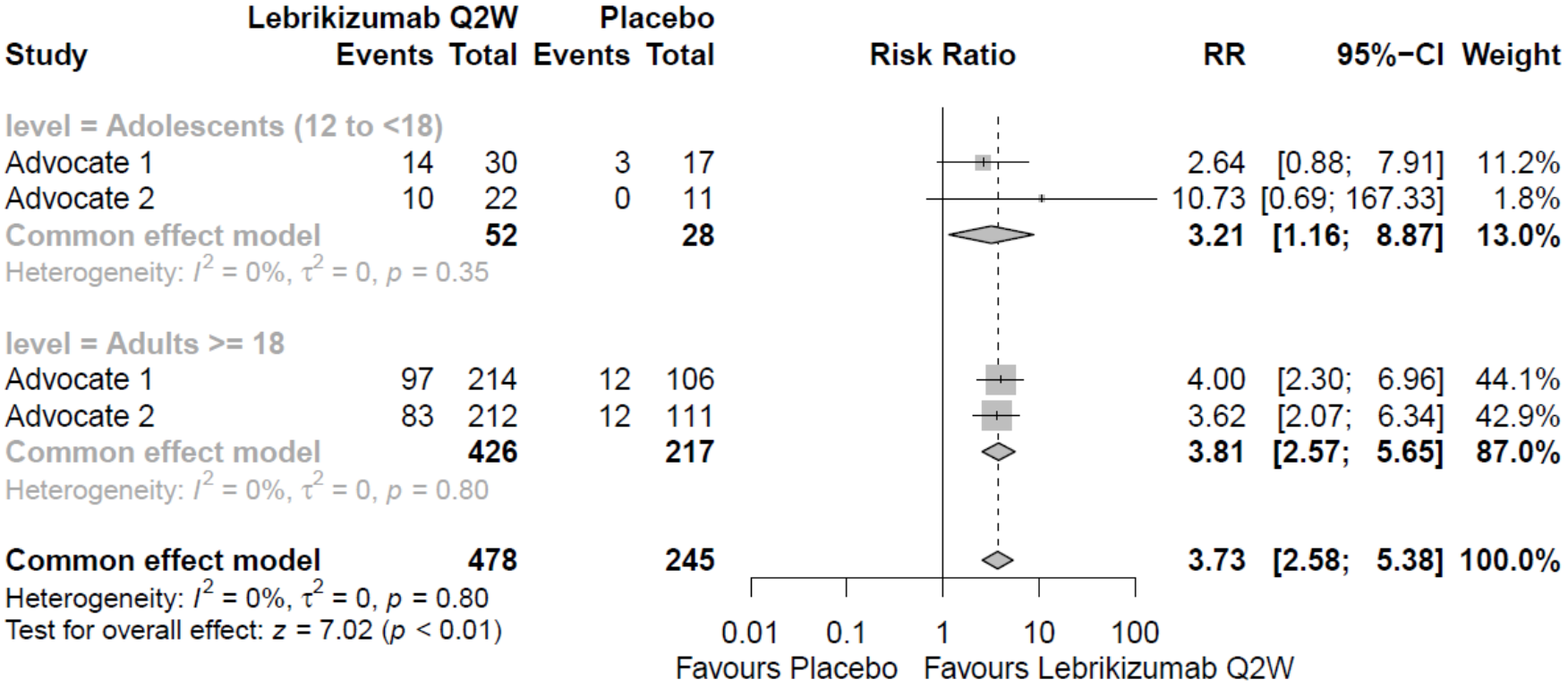


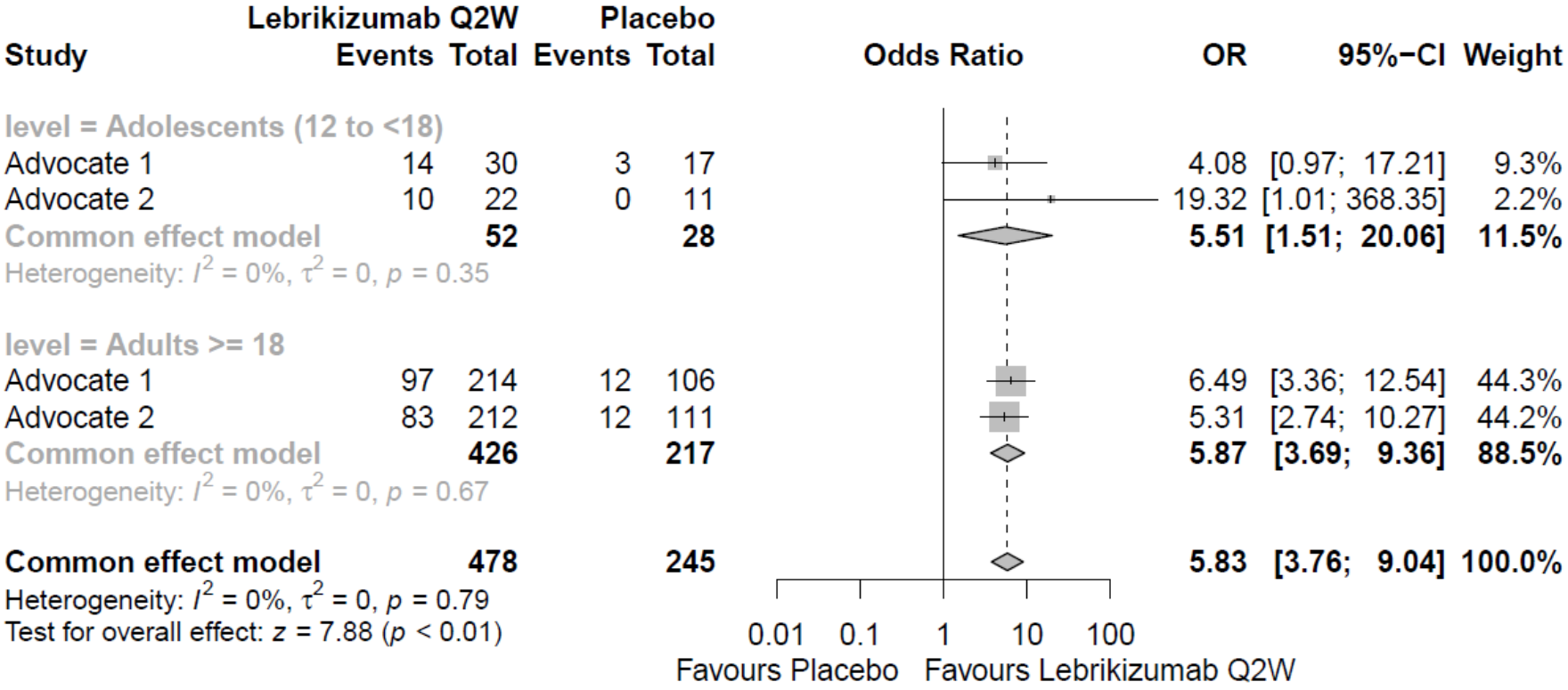

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Female
Advocate 1 56 119 8 63 6.11 [2.68; 13.94] 28.8%
Advocate 2 45 104 8 64 5.34 [2.31; 12.32] 28.0%
Common effect model 223 127 5.72 [3.18; 10.28] 56.8%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.82
level = Male
Advocate 1 55 125 7 60 5.95 [2.51; 14.11] 26.3%
Advocate 2 48 130 4 58 7.90 [2.69; 23.18] 16.9%
Common effect model 255 118 6.65 [3.39; 13.04] 43.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.69
Common effect model 478 245 6.10 [3.92; 9.50] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.96
Test for overall effect: z = 8.01 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo
Favours Lebrikizumab Q2W

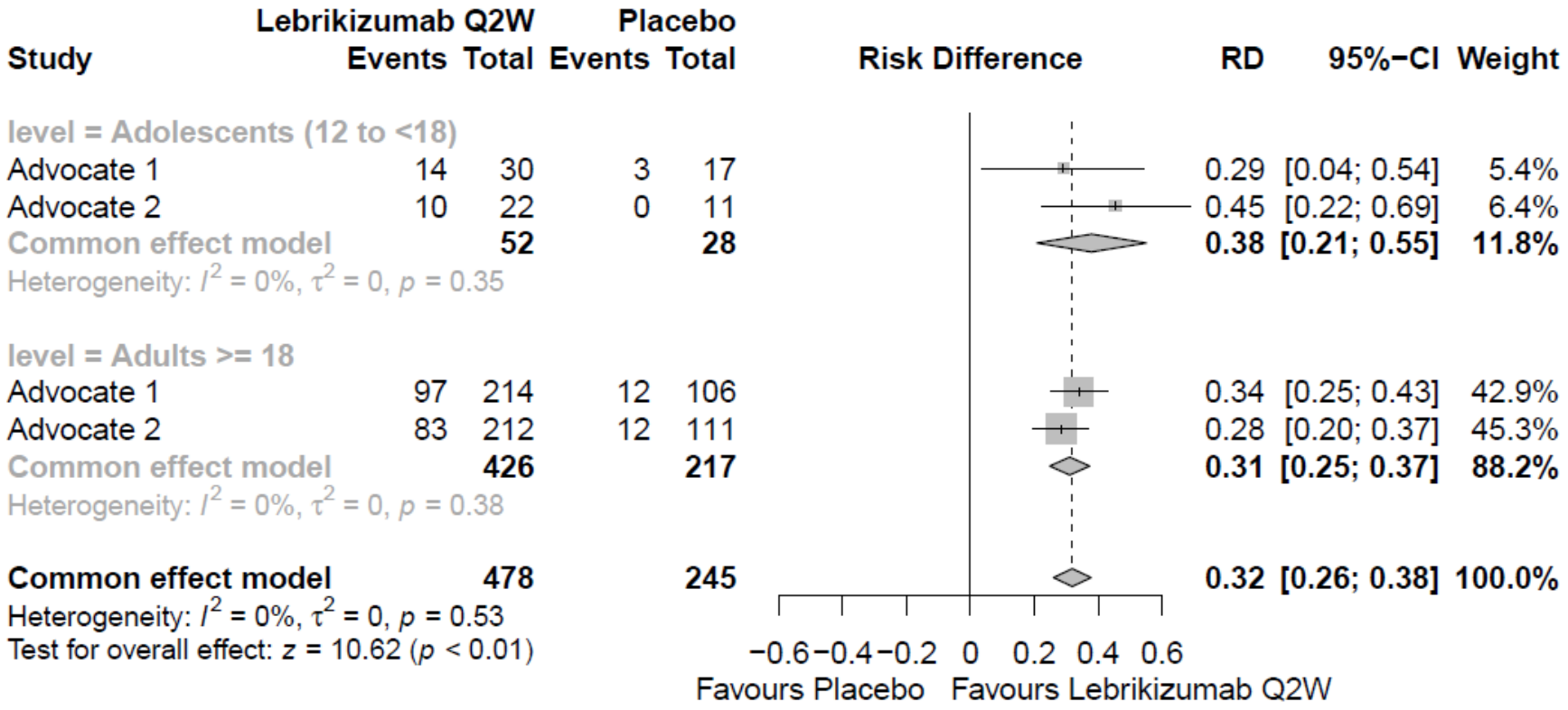

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Female
Advocate 1 57 132 8 65 0.31 [0.19; 0.43] 22.9%
Advocate 2 47 118 9 68 0.27 [0.15; 0.39] 21.7%
Common effect model 250 133 0.29 [0.20; 0.37] 44.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.62
level = Male
Advocate 1 55 131 7 65 0.31 [0.20; 0.43] 24.1%
Advocate 2 49 135 4 66 0.30 [0.20; 0.40] 31.3%
Common effect model 266 131 0.31 [0.23; 0.38] 55.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.90
Common effect model 516 264 0.30 [0.24; 0.35] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.95
Test for overall effect: z = 10.51 (p < 0.01)
−0.4
−0.2
0
0.2
0.4
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.9 Pruritus NRS Reduktion um 4 Punkte (Baseline 5)

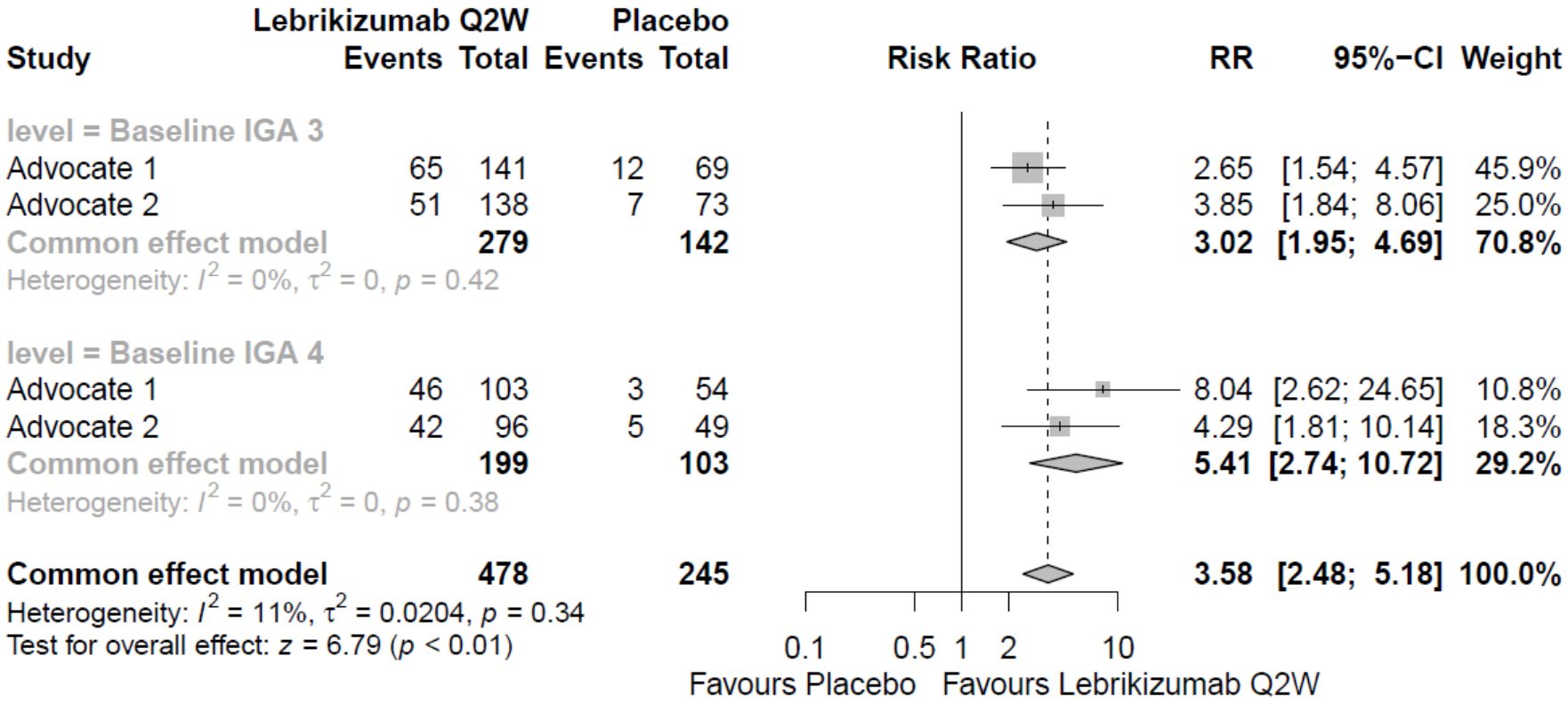
4.5.1.9.1 Altersgruppe

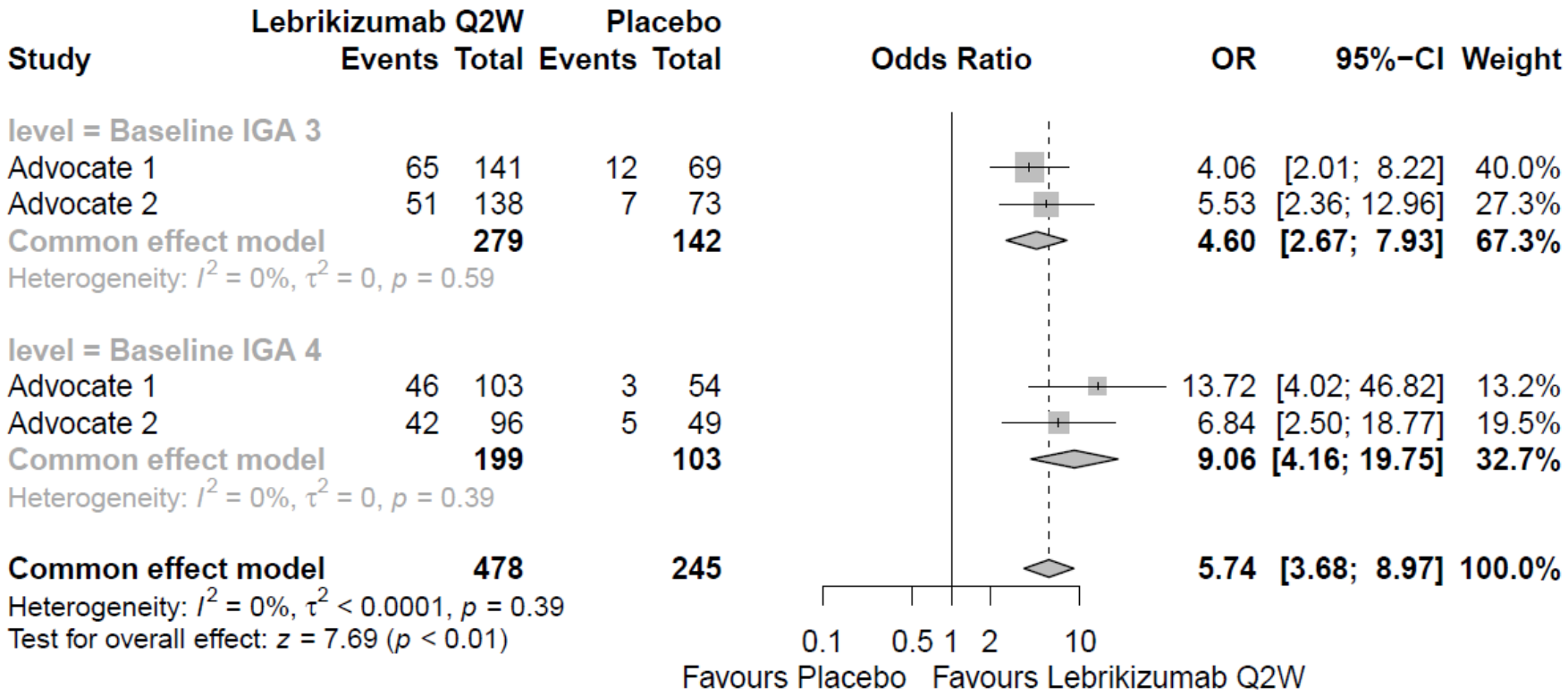


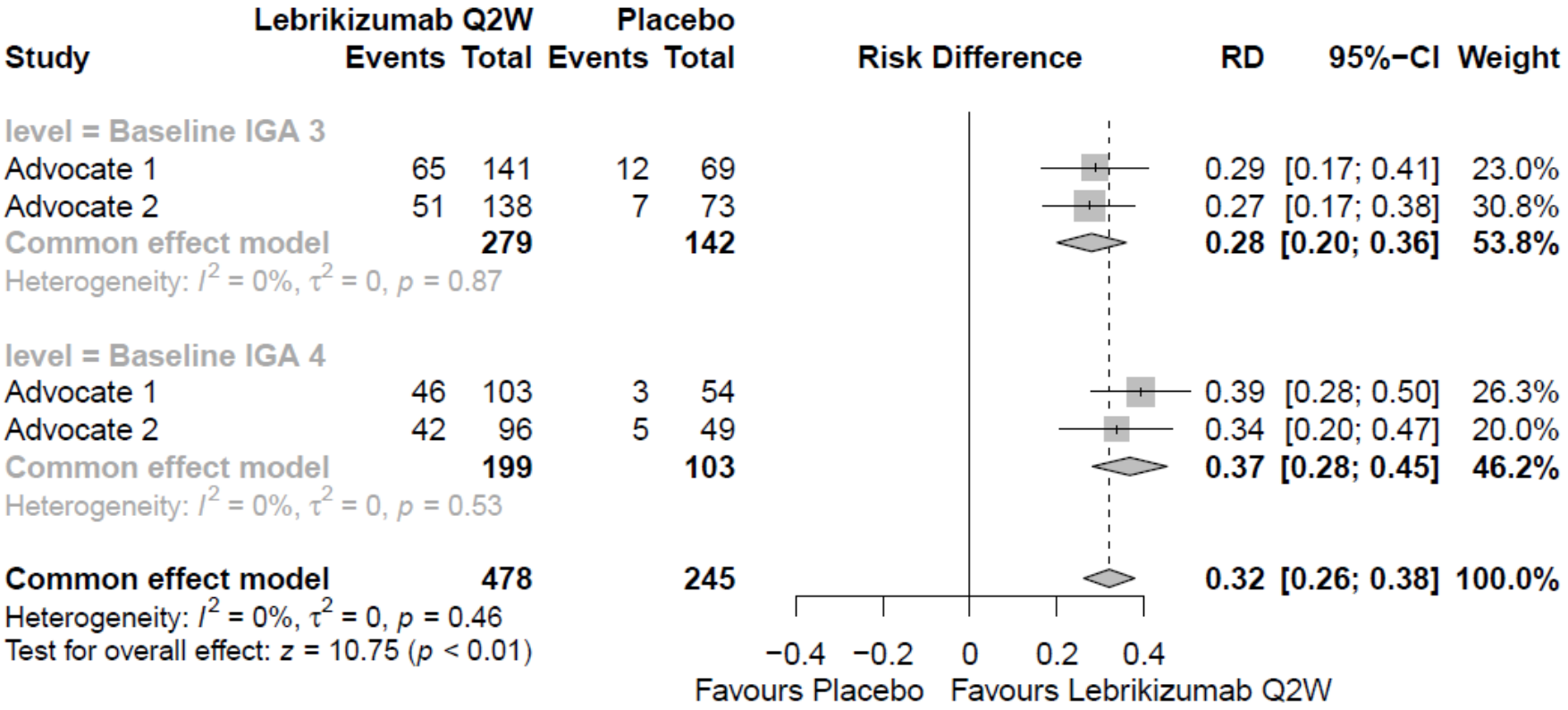

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 14 30 3 17 4.08 [0.97; 17.21] 9.3%
Advocate 2 10 22 0 11 19.32 [1.01; 368.35] 2.2%
Common effect model 52 28 5.51 [1.51; 20.06] 11.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.35
level = Adults >= 18
Advocate 1 97 214 12 106 6.49 [3.36; 12.54] 44.3%
Advocate 2 83 212 12 111 5.31 [2.74; 10.27] 44.2%
Common effect model 426 217 5.87 [3.69; 9.36] 88.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.67
Common effect model 478 245 5.83 [3.76; 9.04] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.79
Test for overall effect: z = 7.88 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 14 30 3 17 0.29 [0.04; 0.54] 5.4%
Advocate 2 10 22 0 11 0.45 [0.22; 0.69] 6.4%
Common effect model 52 28 0.38 [0.21; 0.55] 11.8%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.35
level = Adults >= 18
Advocate 1 97 214 12 106 0.34 [0.25; 0.43] 42.9%
Advocate 2 83 212 12 111 0.28 [0.20; 0.37] 45.3%
Common effect model 426 217 0.31 [0.25; 0.37] 88.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.38
Common effect model 478 245 0.32 [0.26; 0.38] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.53
Test for overall effect: z = 10.62 (p < 0.01)
−0.6 −0.4 −0.2 0 0.2 0.4 0.6
Favours Placebo
Favours Lebrikizumab Q2W

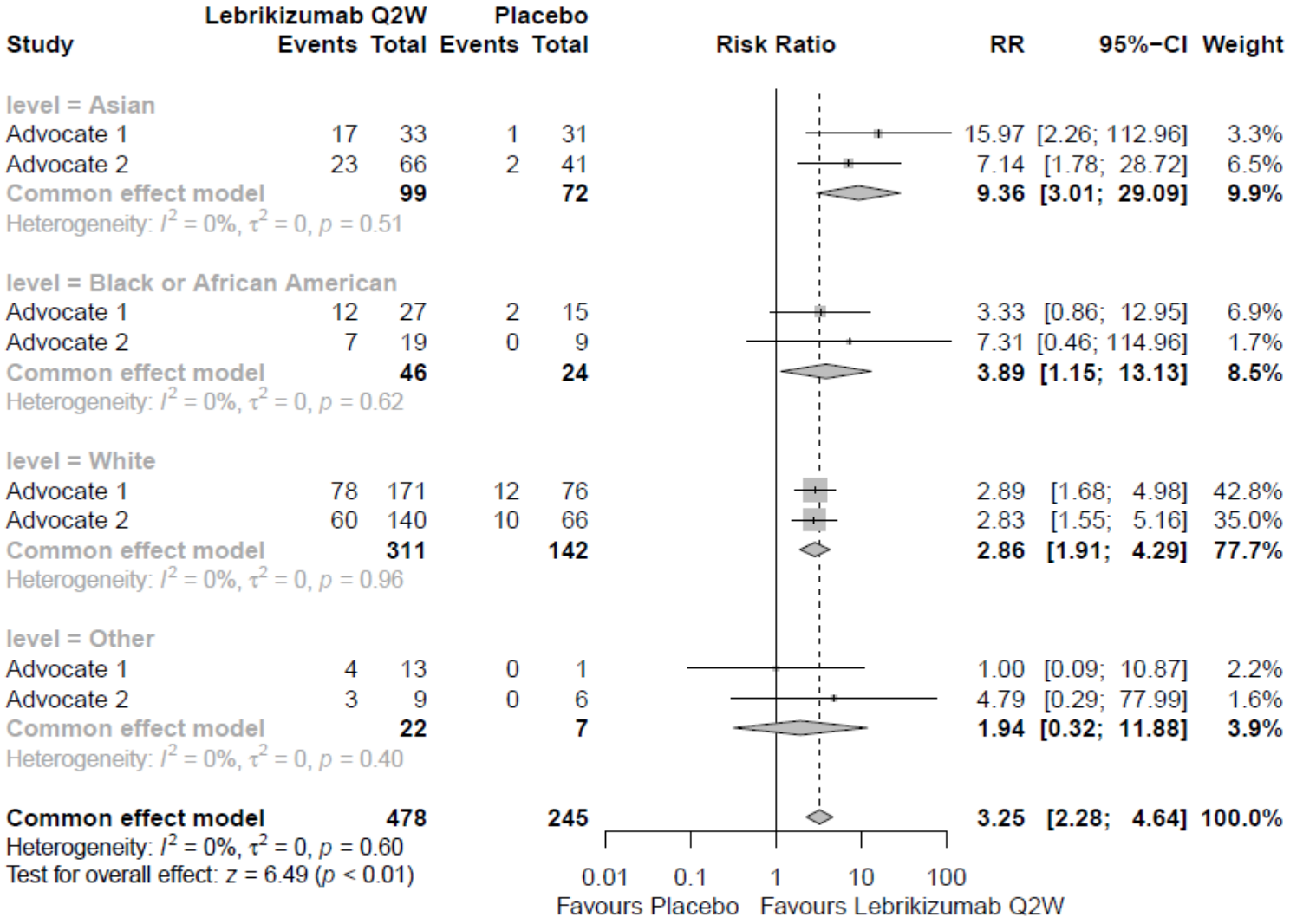
4.5.1.9.2 Krankheitsschwere

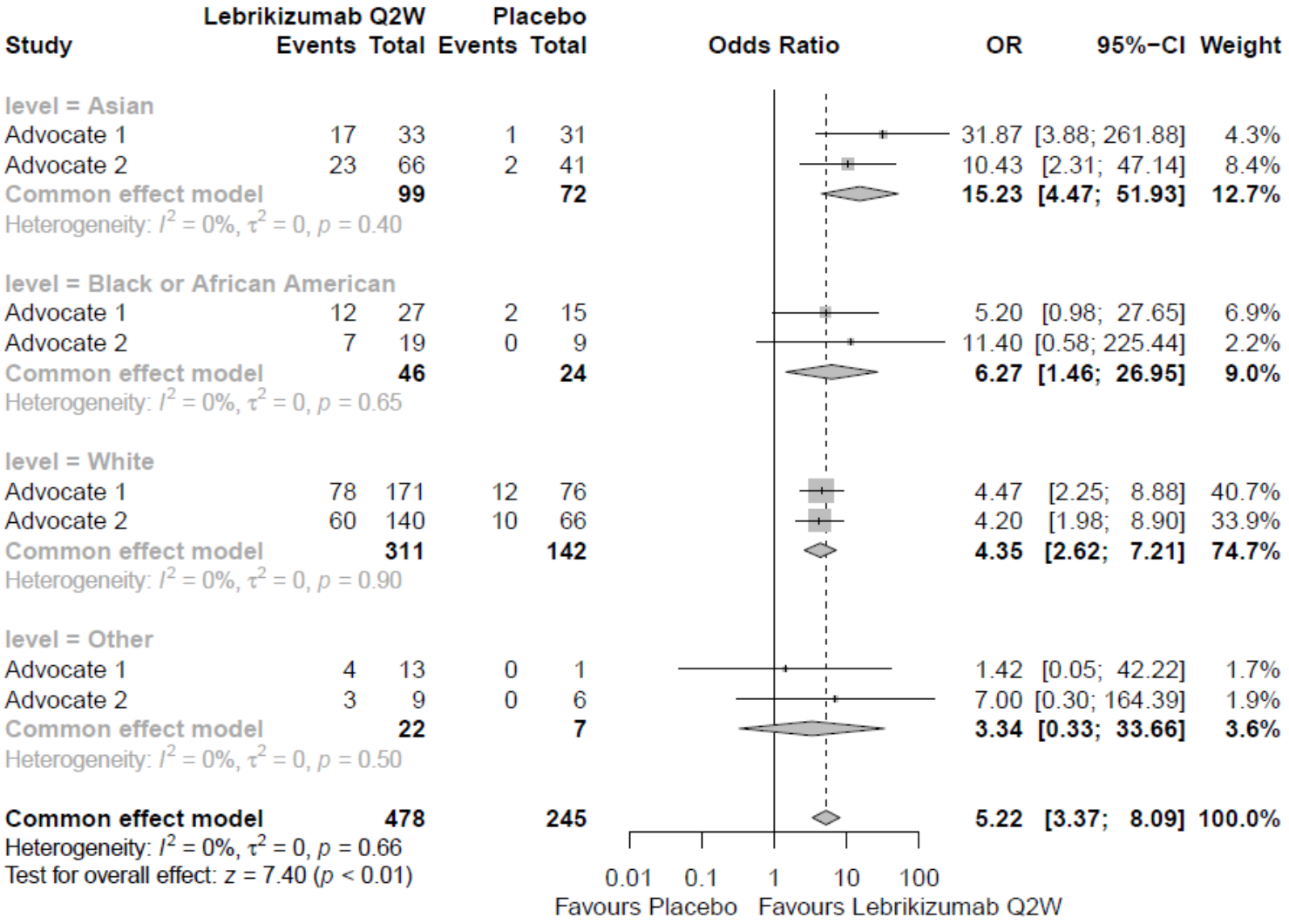


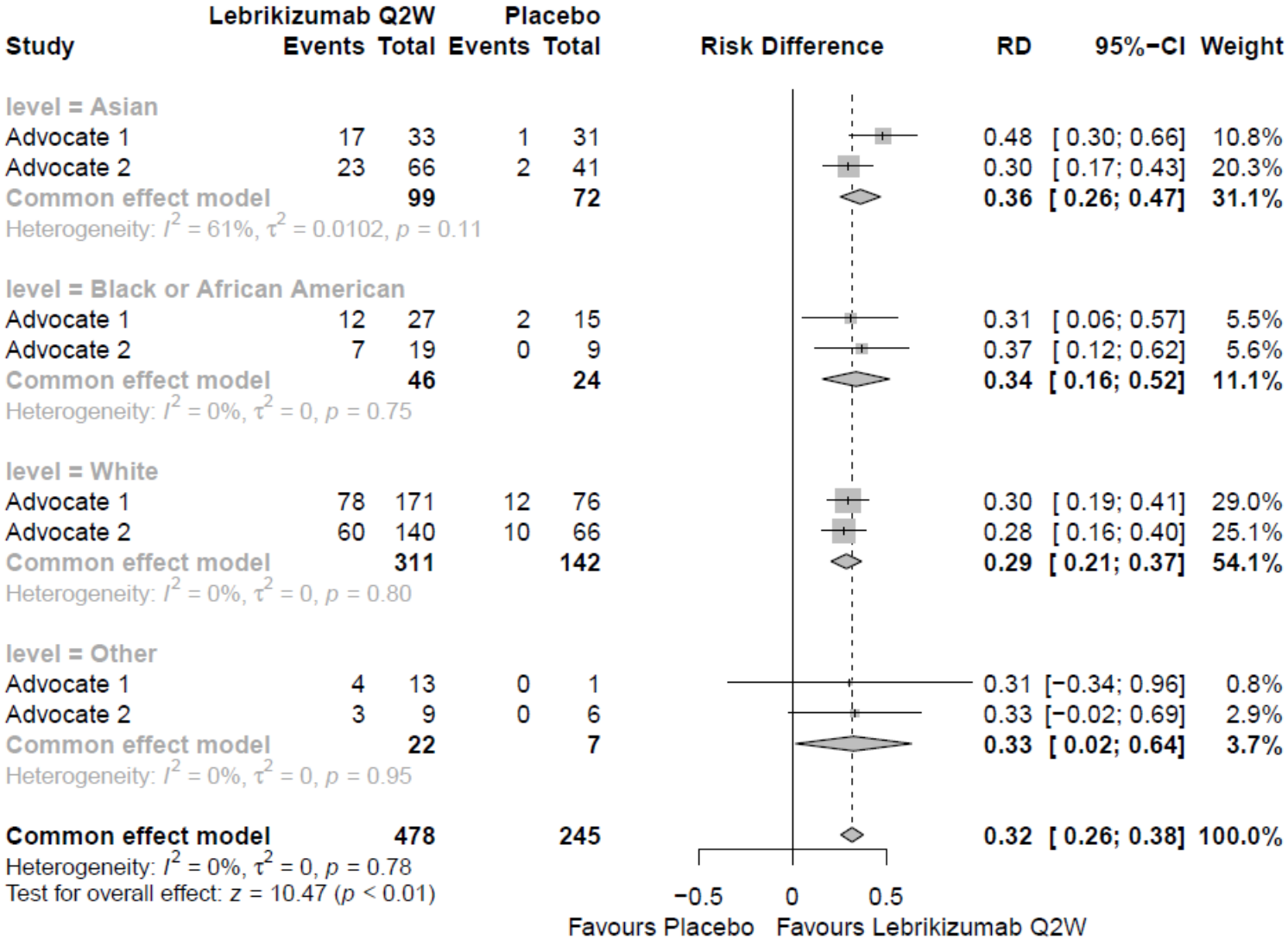

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Baseline IGA 3
Advocate 1 65 141 12 69 4.06 [2.01; 8.22] 40.0%
Advocate 2 51 138 7 73 5.53 [2.36; 12.96] 27.3%
Common effect model 279 142 4.60 [2.67; 7.93] 67.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.59
level = Baseline IGA 4
Advocate 1 46 103 3 54 13.72 [4.02; 46.82] 13.2%
Advocate 2 42 96 5 49 6.84 [2.50; 18.77] 19.5%
Common effect model 199 103 9.06 [4.16; 19.75] 32.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.39
Common effect model 478 245 5.74 [3.68; 8.97] 100.0%
Heterogeneity: I^2 = 0%, τ^2 < 0.0001, p = 0.39
Test for overall effect: z = 7.69 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Baseline IGA 3
Advocate 1 65 141 12 69 0.29 [0.17; 0.41] 23.0%
Advocate 2 51 138 7 73 0.27 [0.17; 0.38] 30.8%
Common effect model 279 142 0.28 [0.20; 0.36] 53.8%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.87
level = Baseline IGA 4
Advocate 1 46 103 3 54 0.39 [0.28; 0.50] 26.3%
Advocate 2 42 96 5 49 0.34 [0.20; 0.47] 20.0%
Common effect model 199 103 0.37 [0.28; 0.45] 46.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.53
Common effect model 478 245 0.32 [0.26; 0.38] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.46
Test for overall effect: z = 10.75 (p < 0.01)
−0.4 −0.2 0 0.2 0.4
Favours Placebo
Favours Lebrikizumab Q2W

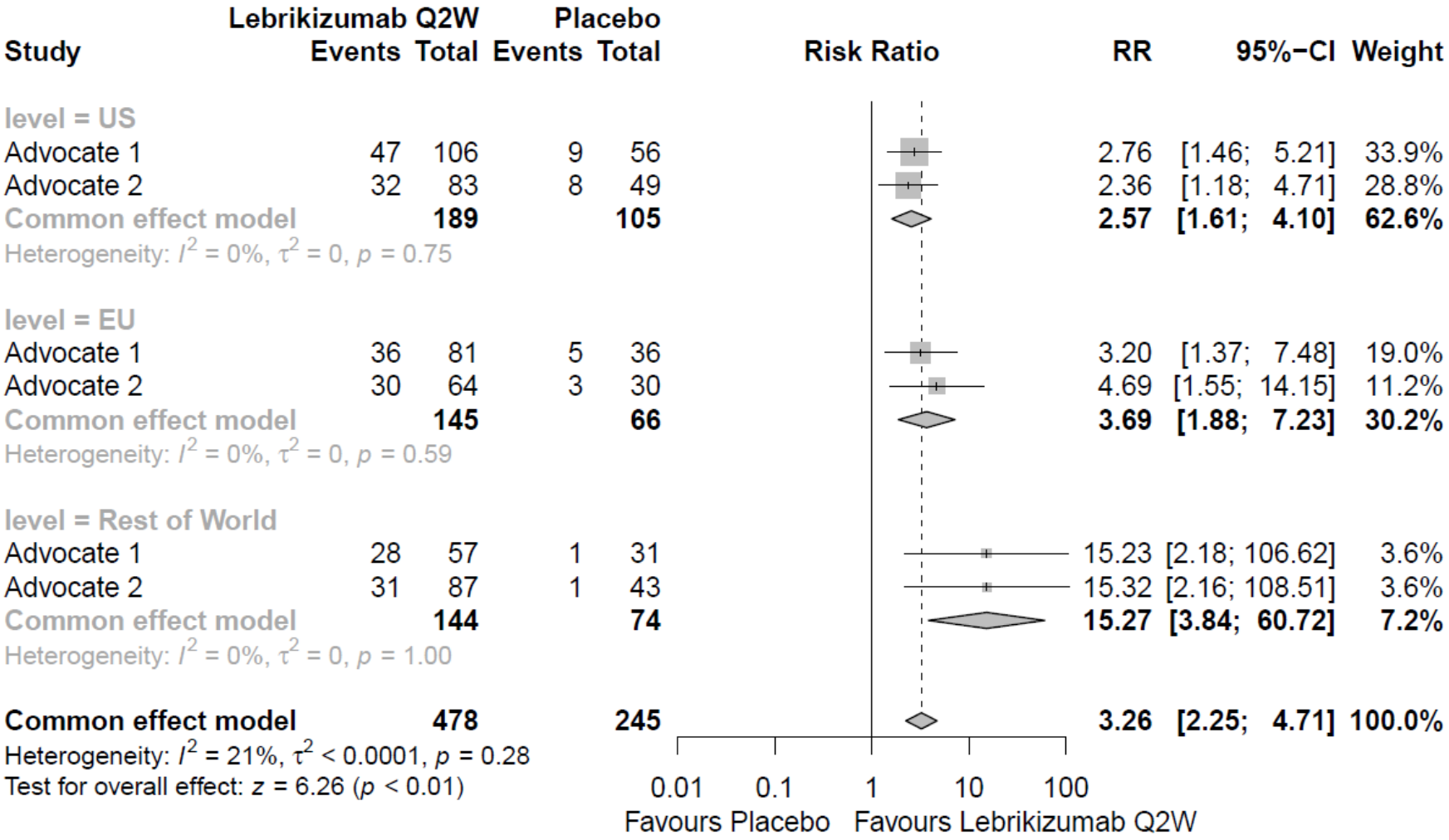
4.5.1.9.3 Ethnie

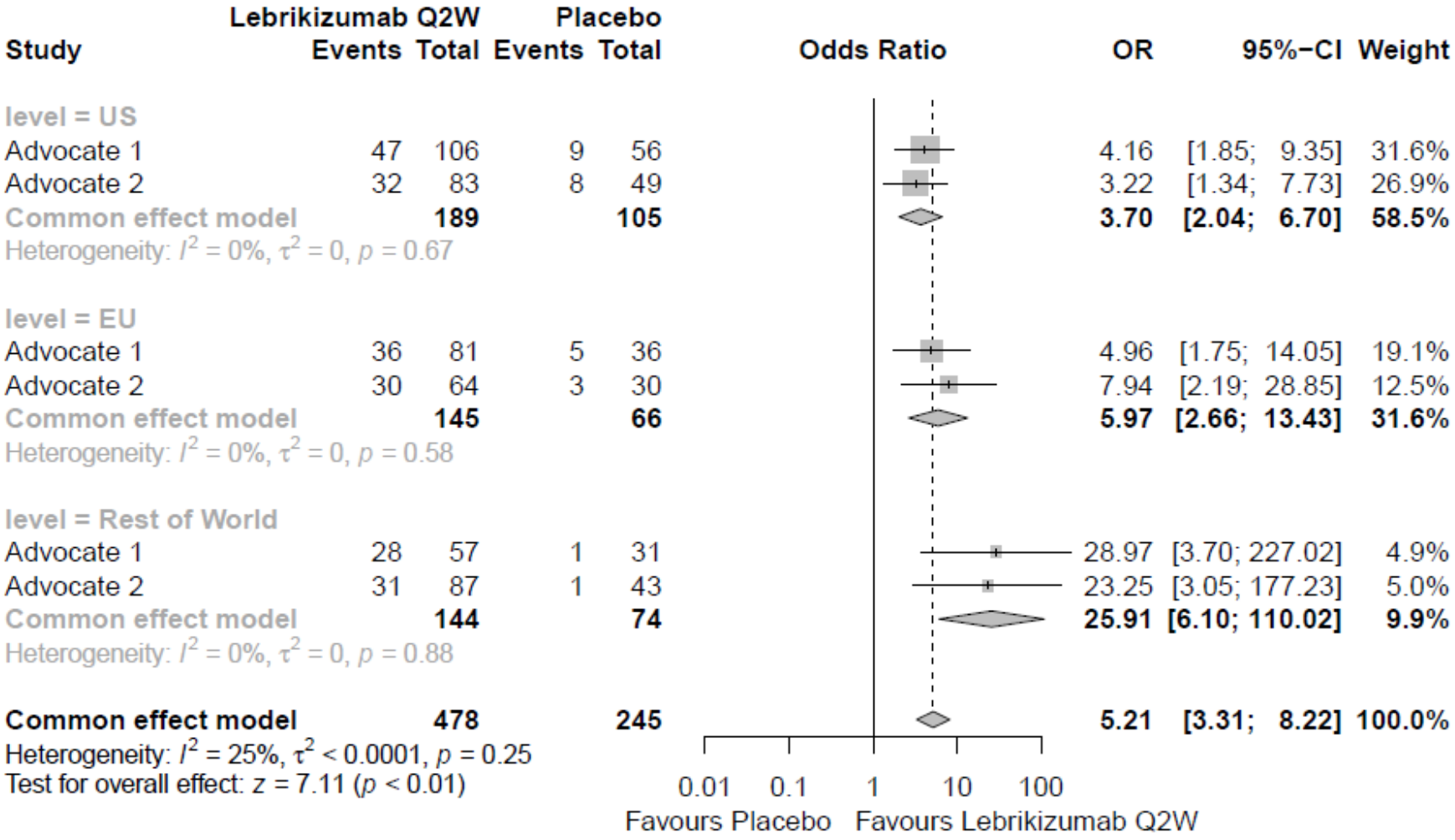


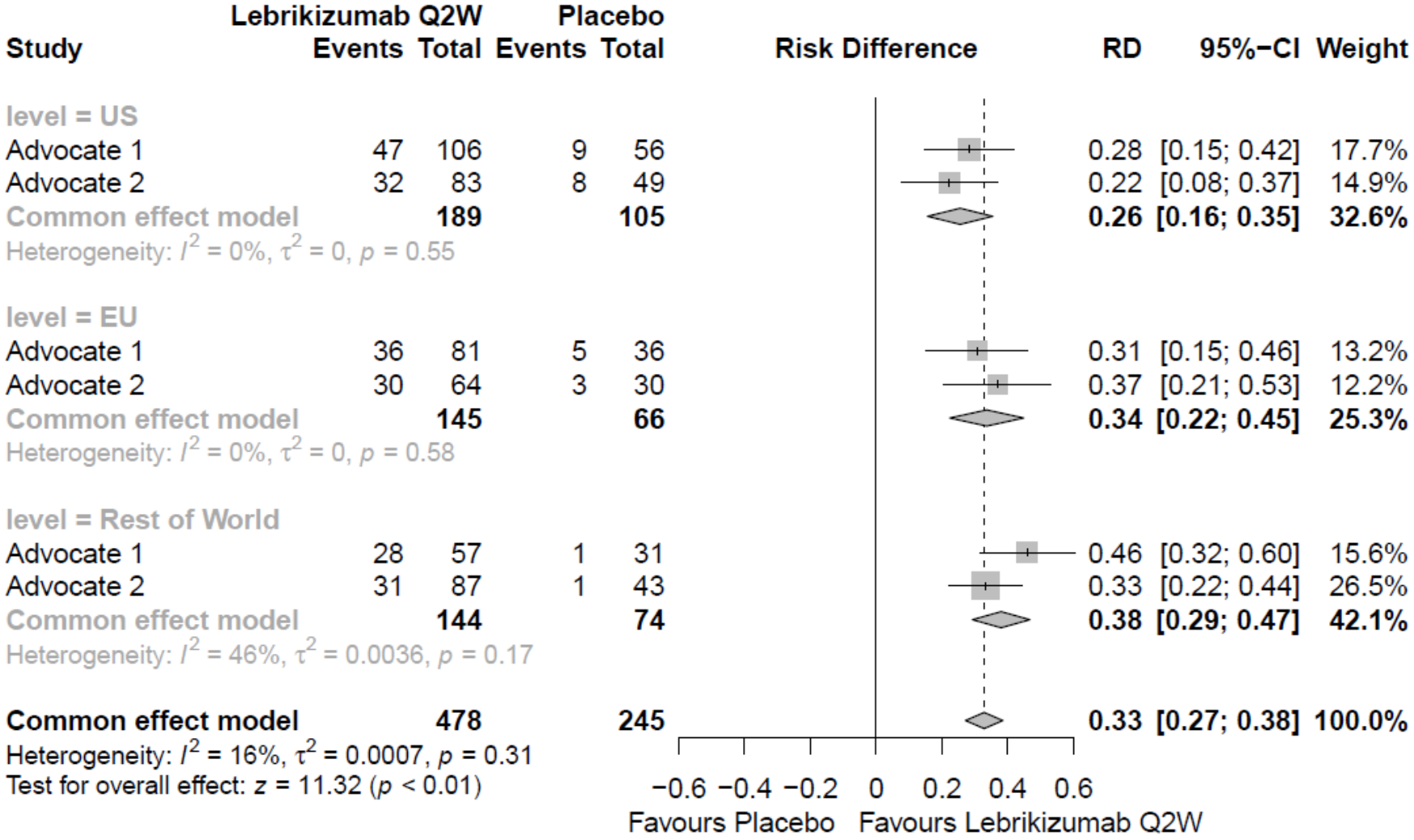

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Asian
Advocate 1 17 33 1 31 31.87 [3.88; 261.88] 4.3%
Advocate 2 23 66 2 41 10.43 [2.31; 47.14] 8.4%
Common effect model 99 72 15.23 [4.47; 51.93] 12.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.40
level = Black or African American
Advocate 1 12 27 2 15 5.20 [0.98; 27.65] 6.9%
Advocate 2 7 19 0 9 11.40 [0.58; 225.44] 2.2%
Common effect model 46 24 6.27 [1.46; 26.95] 9.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.65
level = White
Advocate 1 78 171 12 76 4.47 [2.25; 8.88] 40.7%
Advocate 2 60 140 10 66 4.20 [1.98; 8.90] 33.9%
Common effect model 311 142 4.35 [2.62; 7.21] 74.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.90
level = Other
Advocate 1 4 13 0 1 1.42 [0.05; 42.22] 1.7%
Advocate 2 3 9 0 6 7.00 [0.30; 164.39] 1.9%
Common effect model 22 7 3.34 [0.33; 33.66] 3.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.50
Common effect model 478 245 5.22 [3.37; 8.09] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.66
Test for overall effect: z = 7.40 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Asian
Advocate 1 17 33 1 31 0.48 [0.30; 0.66] 10.8%
Advocate 2 23 66 2 41 0.30 [0.17; 0.43] 20.3%
Common effect model 99 72 0.36 [0.26; 0.47] 31.1%
Heterogeneity: I^2 = 61%, τ^2 = 0.0102, p = 0.11
level = Black or African American
Advocate 1 12 27 2 15 0.31 [0.06; 0.57] 5.5%
Advocate 2 7 19 0 9 0.37 [0.12; 0.62] 5.6%
Common effect model 46 24 0.34 [0.16; 0.52] 11.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.75
level = White
Advocate 1 78 171 12 76 0.30 [0.19; 0.41] 29.0%
Advocate 2 60 140 10 66 0.28 [0.16; 0.40] 25.1%
Common effect model 311 142 0.29 [0.21; 0.37] 54.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.80
level = Other
Advocate 1 4 13 0 1 0.31 [−0.34; 0.96] 0.8%
Advocate 2 3 9 0 6 0.33 [−0.02; 0.69] 2.9%
Common effect model 22 7 0.33 [0.02; 0.64] 3.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.95
Common effect model 478 245 0.32 [0.26; 0.38] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.78
Test for overall effect: z = 10.47 (p < 0.01)
−0.5
0
0.5
Favours Placebo
Favours Lebrikizumab Q2W

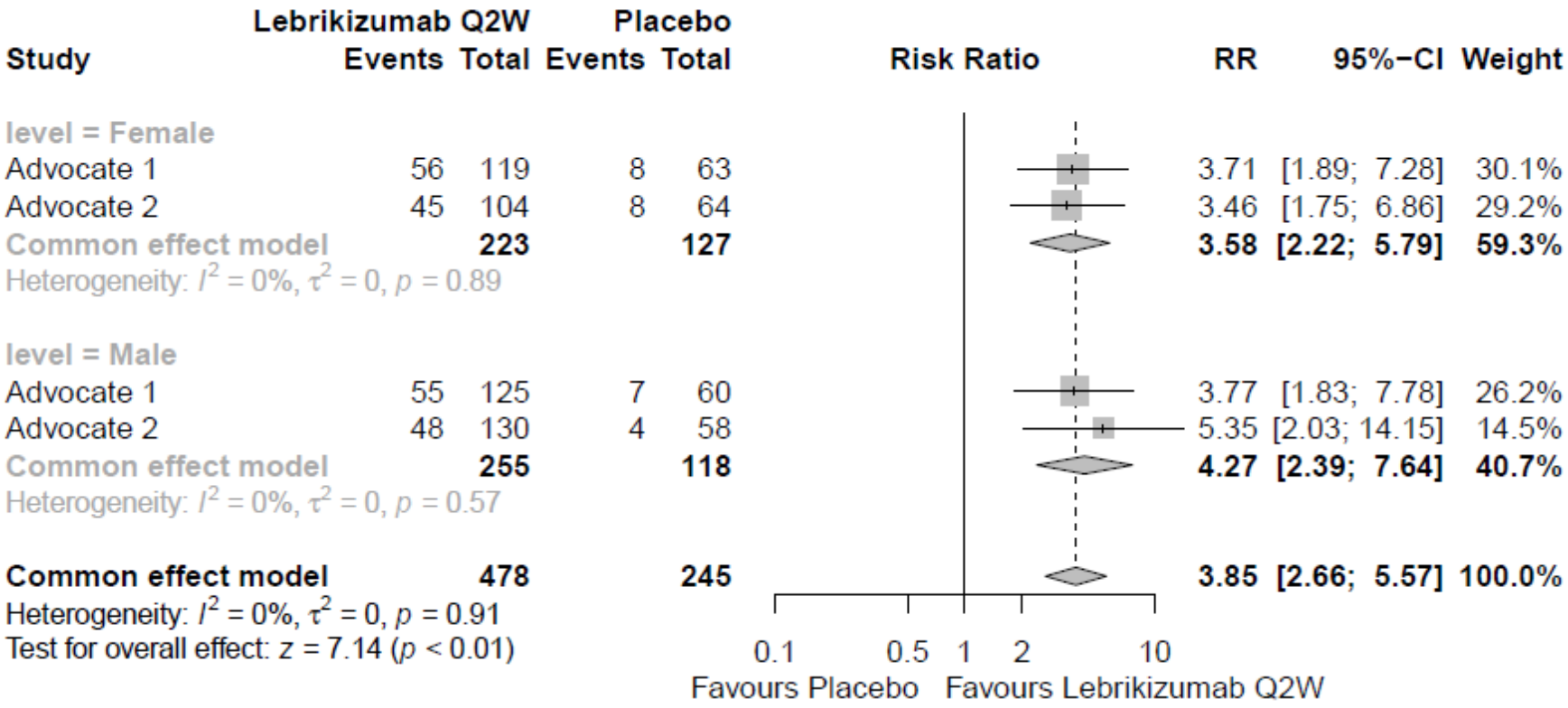
4.5.1.9.4 Region

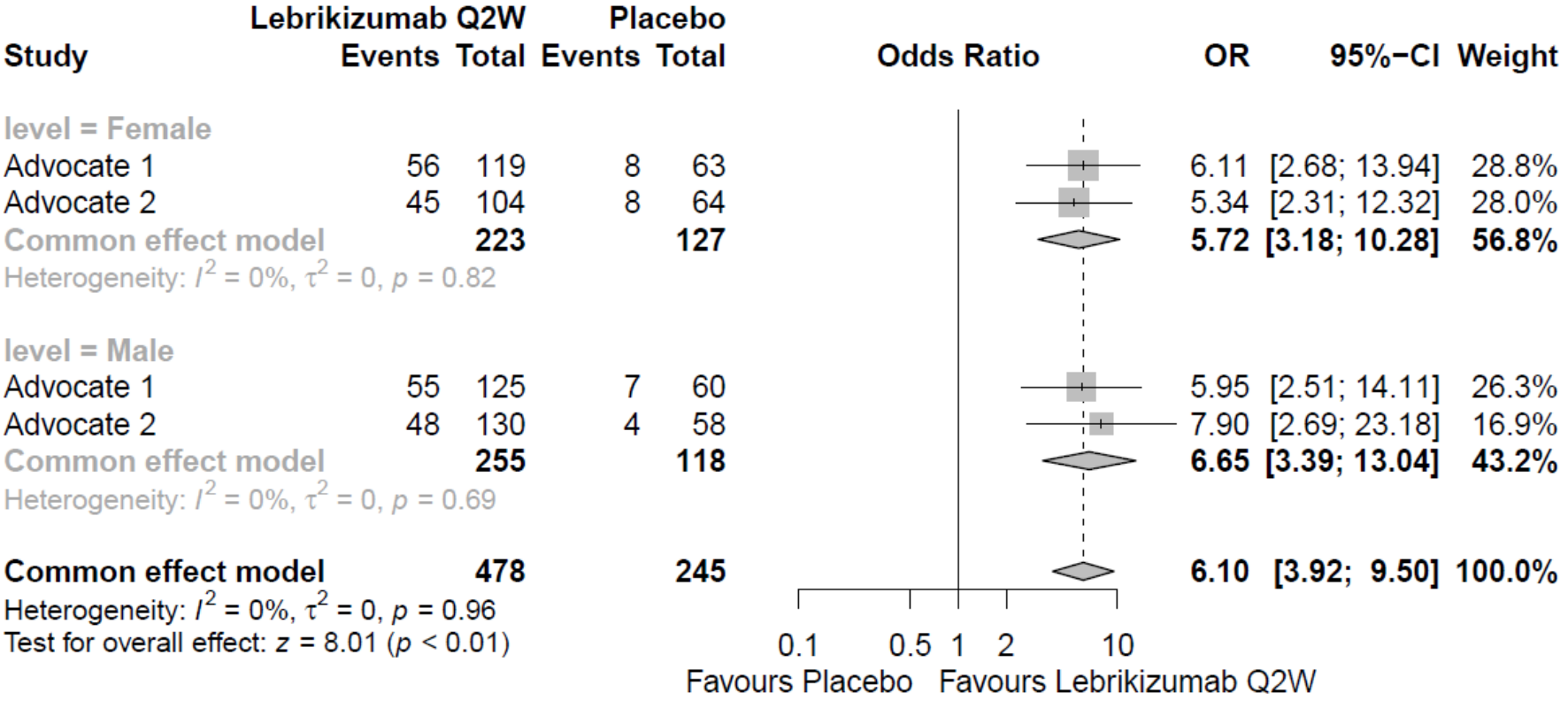


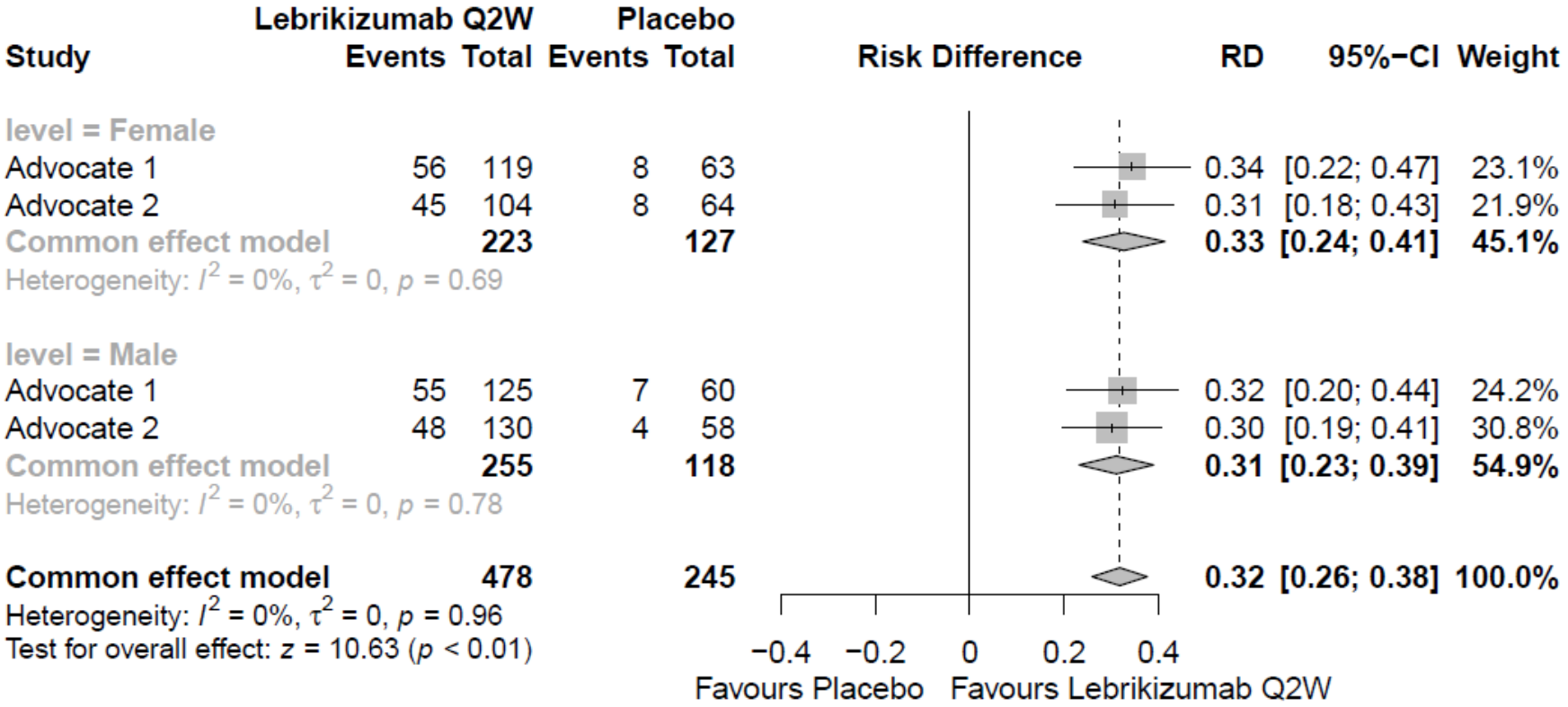

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = US
Advocate 1 47 106 9 56 4.16 [1.85; 9.35] 31.6%
Advocate 2 32 83 8 49 3.22 [1.34; 7.73] 26.9%
Common effect model 189 105 3.70 [2.04; 6.70] 58.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.67
level = EU
Advocate 1 36 81 5 36 4.96 [1.75; 14.05] 19.1%
Advocate 2 30 64 3 30 7.94 [2.19; 28.85] 12.5%
Common effect model 145 66 5.97 [2.66; 13.43] 31.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.58
level = Rest of World
Advocate 1 28 57 1 31 28.97 [3.70; 227.02] 4.9%
Advocate 2 31 87 1 43 23.25 [3.05; 177.23] 5.0%
Common effect model 144 74 25.91 [6.10; 110.02] 9.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.88
Common effect model 478 245 5.21 [3.31; 8.22] 100.0%
Heterogeneity: I^2 = 25%, τ^2 < 0.0001, p = 0.25
Test for overall effect: z = 7.11 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = US
Advocate 1 47 106 9 56 0.28 [0.15; 0.42] 17.7%
Advocate 2 32 83 8 49 0.22 [0.08; 0.37] 14.9%
Common effect model 189 105 0.26 [0.16; 0.35] 32.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.55
level = EU
Advocate 1 36 81 5 36 0.31 [0.15; 0.46] 13.2%
Advocate 2 30 64 3 30 0.37 [0.21; 0.53] 12.2%
Common effect model 145 66 0.34 [0.22; 0.45] 25.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.58
level = Rest of World
Advocate 1 28 57 1 31 0.46 [0.32; 0.60] 15.6%
Advocate 2 31 87 1 43 0.33 [0.22; 0.44] 26.5%
Common effect model 144 74 0.38 [0.29; 0.47] 42.1%
Heterogeneity: I^2 = 46%, τ^2 = 0.0036, p = 0.17
Common effect model 478 245 0.33 [0.27; 0.38] 100.0%
Heterogeneity: I^2 = 16%, τ^2 = 0.0007, p = 0.31
Test for overall effect: z = 11.32 (p < 0.01)
−0.6 −0.4 −0.2 0 0.2 0.4 0.6
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.9.5 Geschlecht

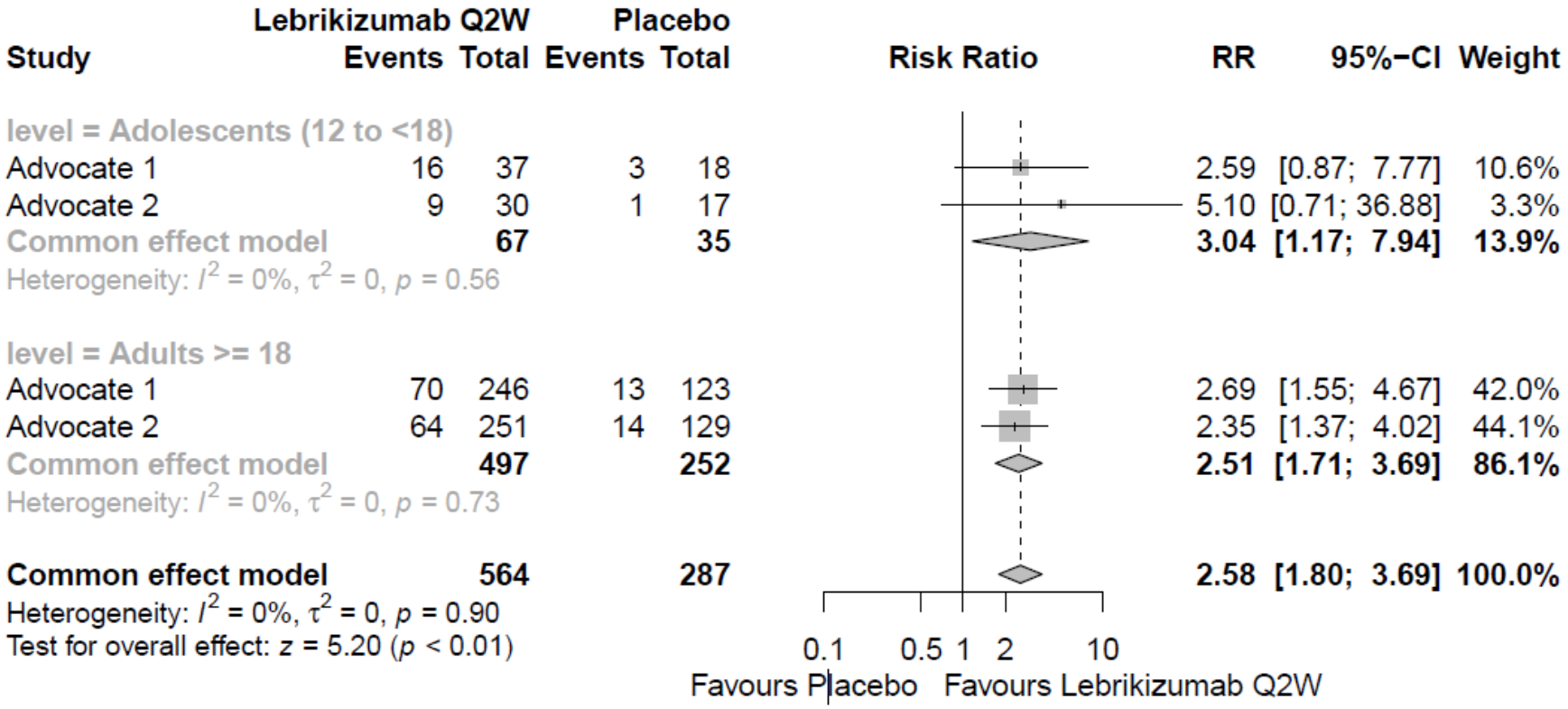


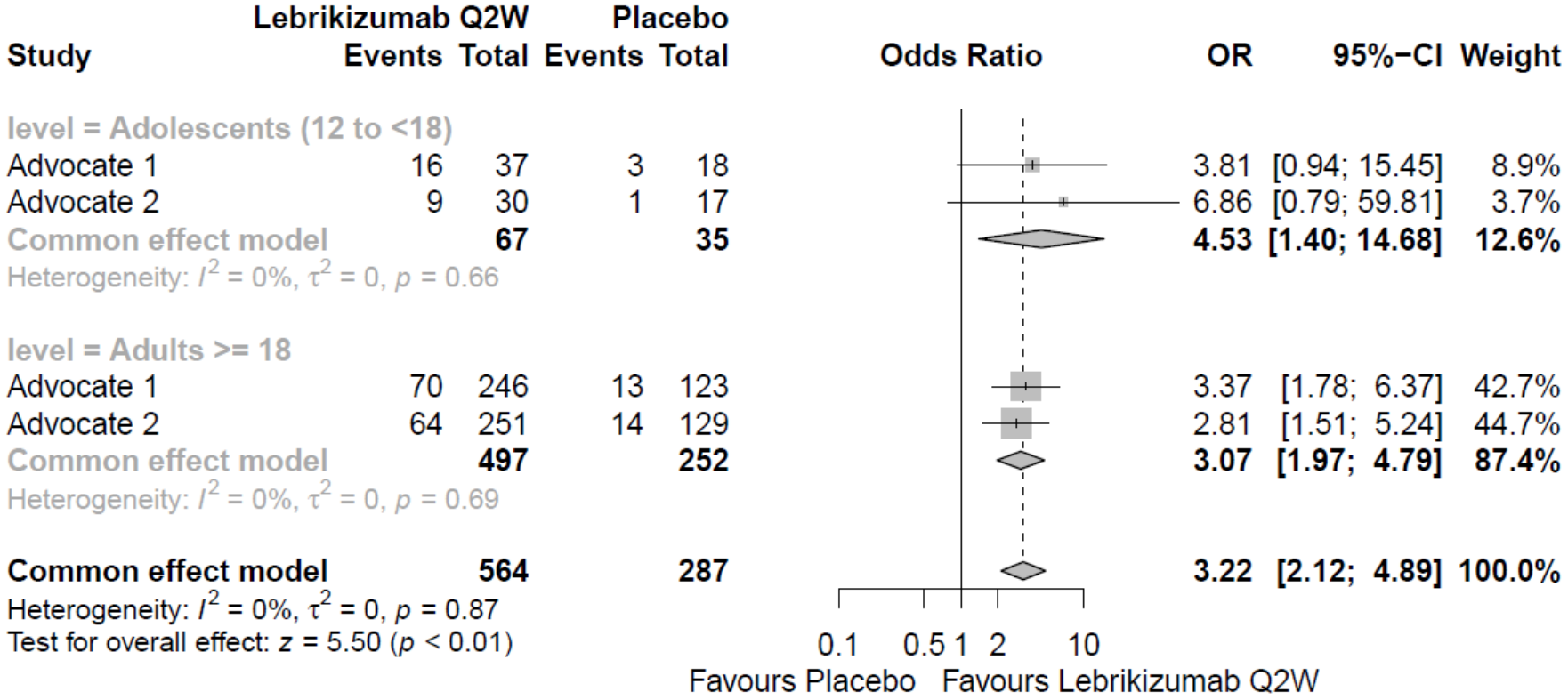

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Female
Advocate 1 56 119 8 63 6.11 [2.68; 13.94] 28.8%
Advocate 2 45 104 8 64 5.34 [2.31; 12.32] 28.0%
Common effect model 223 127 5.72 [3.18; 10.28] 56.8%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.82
level = Male
Advocate 1 55 125 7 60 5.95 [2.51; 14.11] 26.3%
Advocate 2 48 130 4 58 7.90 [2.69; 23.18] 16.9%
Common effect model 255 118 6.65 [3.39; 13.04] 43.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.69
Common effect model 478 245 6.10 [3.92; 9.50] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.96
Test for overall effect: z = 8.01 (p < 0.01)
0.1
0.5
1
2
10
Favours Placebo
Favours Lebrikizumab Q2W

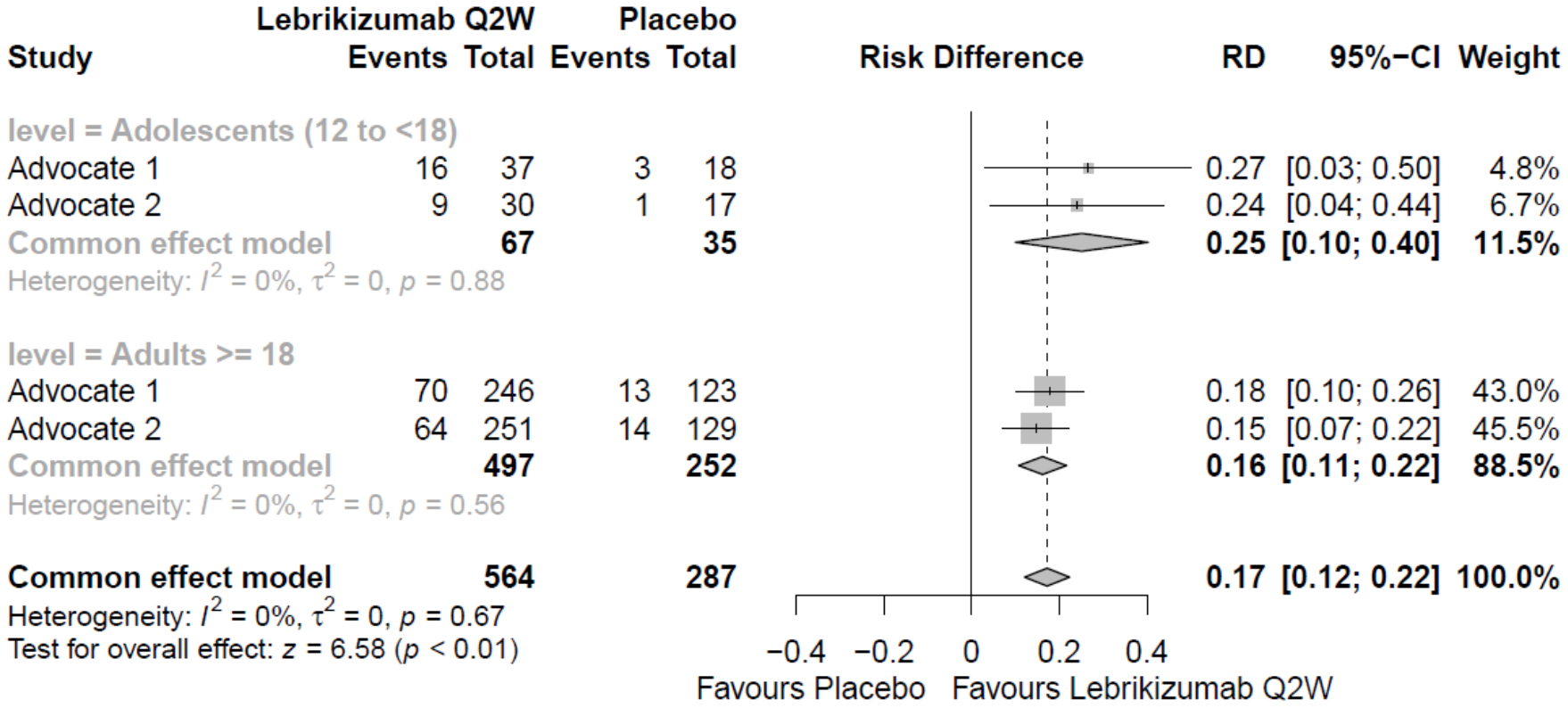

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Female
Advocate 1 56 119 8 63 0.34 [0.22; 0.47] 23.1%
Advocate 2 45 104 8 64 0.31 [0.18; 0.43] 21.9%
Common effect model 223 127 0.33 [0.24; 0.41] 45.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.69
level = Male
Advocate 1 55 125 7 60 0.32 [0.20; 0.44] 24.2%
Advocate 2 48 130 4 58 0.30 [0.19; 0.41] 30.8%
Common effect model 255 118 0.31 [0.23; 0.39] 54.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.78
Common effect model 478 245 0.32 [0.26; 0.38] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.96
Test for overall effect: z = 10.63 (p < 0.01)
−0.4 −0.2 0 0.2 0.4
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.10 EQ-5D VAS Verbesserung um 15 Punkte

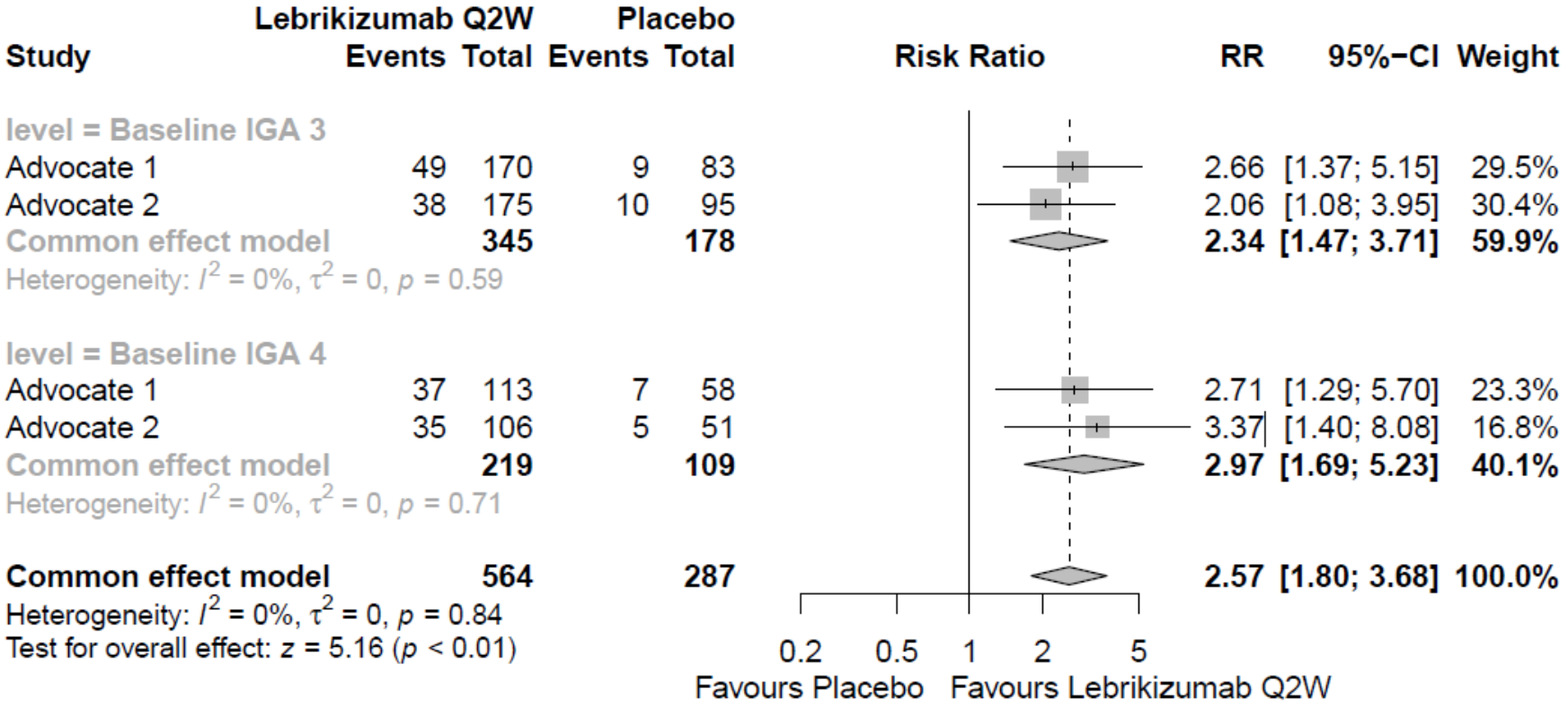
4.5.1.10.1 Altersgruppe

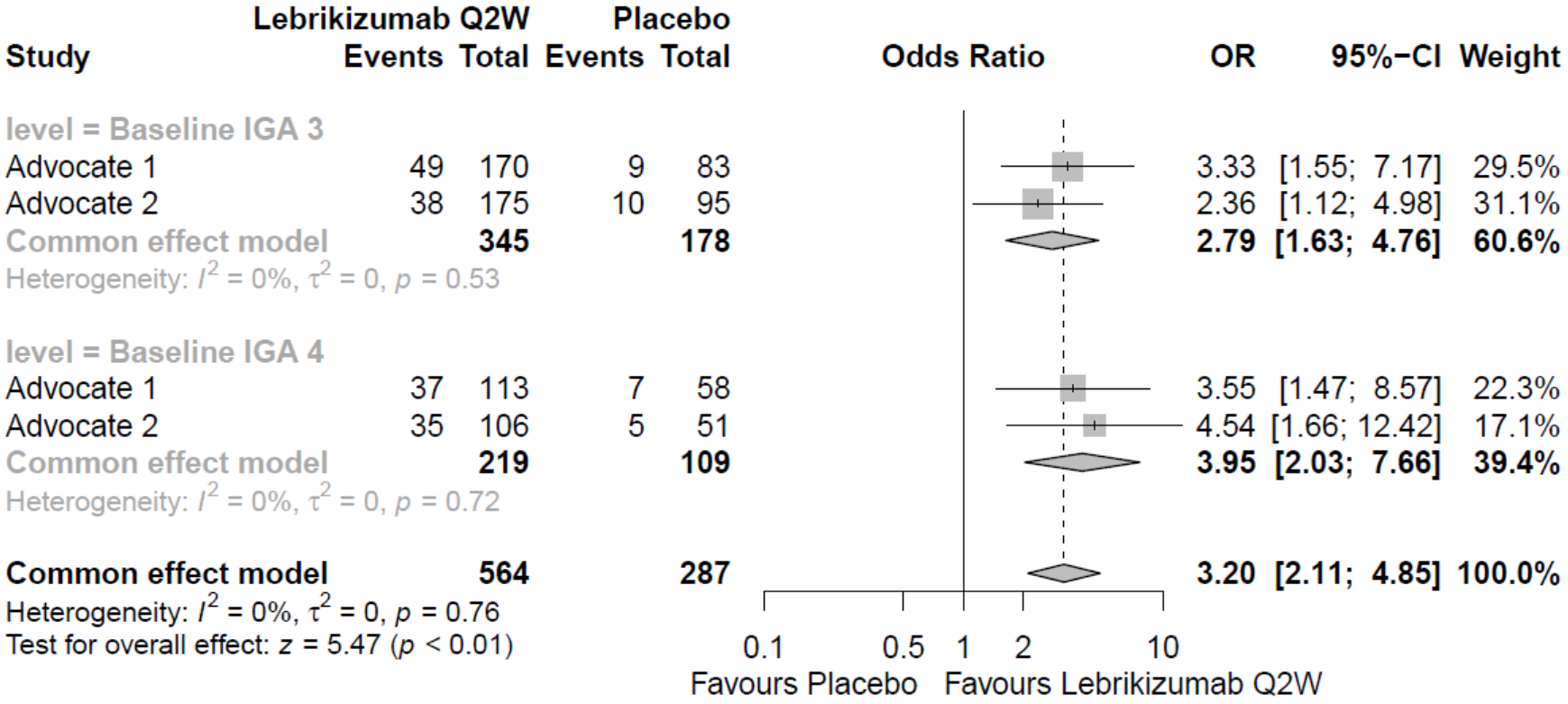


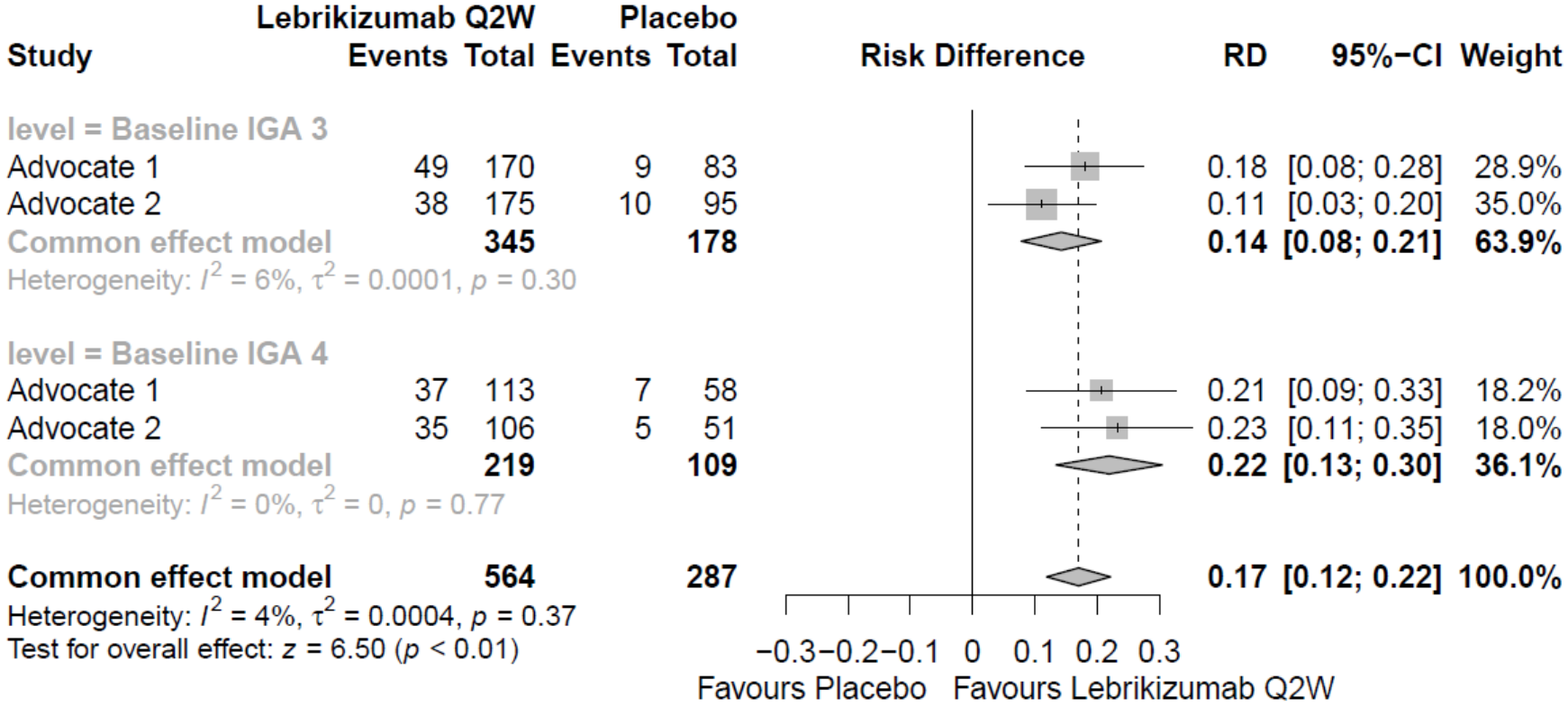

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 16 37 3 18 3.81 [0.94; 15.45] 8.9%
Advocate 2 9 30 1 17 6.86 [0.79; 59.81] 3.7%
Common effect model 67 35 4.53 [1.40; 14.68] 12.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.66
level = Adults >= 18
Advocate 1 70 246 13 123 3.37 [1.78; 6.37] 42.7%
Advocate 2 64 251 14 129 2.81 [1.51; 5.24] 44.7%
Common effect model 497 252 3.07 [1.97; 4.79] 87.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.69
Common effect model 564 287 3.22 [2.12; 4.89] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.87
Test for overall effect: z = 5.50 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 16 37 3 18 0.27 [0.03; 0.50] 4.8%
Advocate 2 9 30 1 17 0.24 [0.04; 0.44] 6.7%
Common effect model 67 35 0.25 [0.10; 0.40] 11.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.88
level = Adults >= 18
Advocate 1 70 246 13 123 0.18 [0.10; 0.26] 43.0%
Advocate 2 64 251 14 129 0.15 [0.07; 0.22] 45.5%
Common effect model 497 252 0.16 [0.11; 0.22] 88.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.56
Common effect model 564 287 0.17 [0.12; 0.22] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.67
Test for overall effect: z = 6.58 (p < 0.01)
−0.4 −0.2 0 0.2 0.4
Favours Placebo
Favours Lebrikizumab Q2W

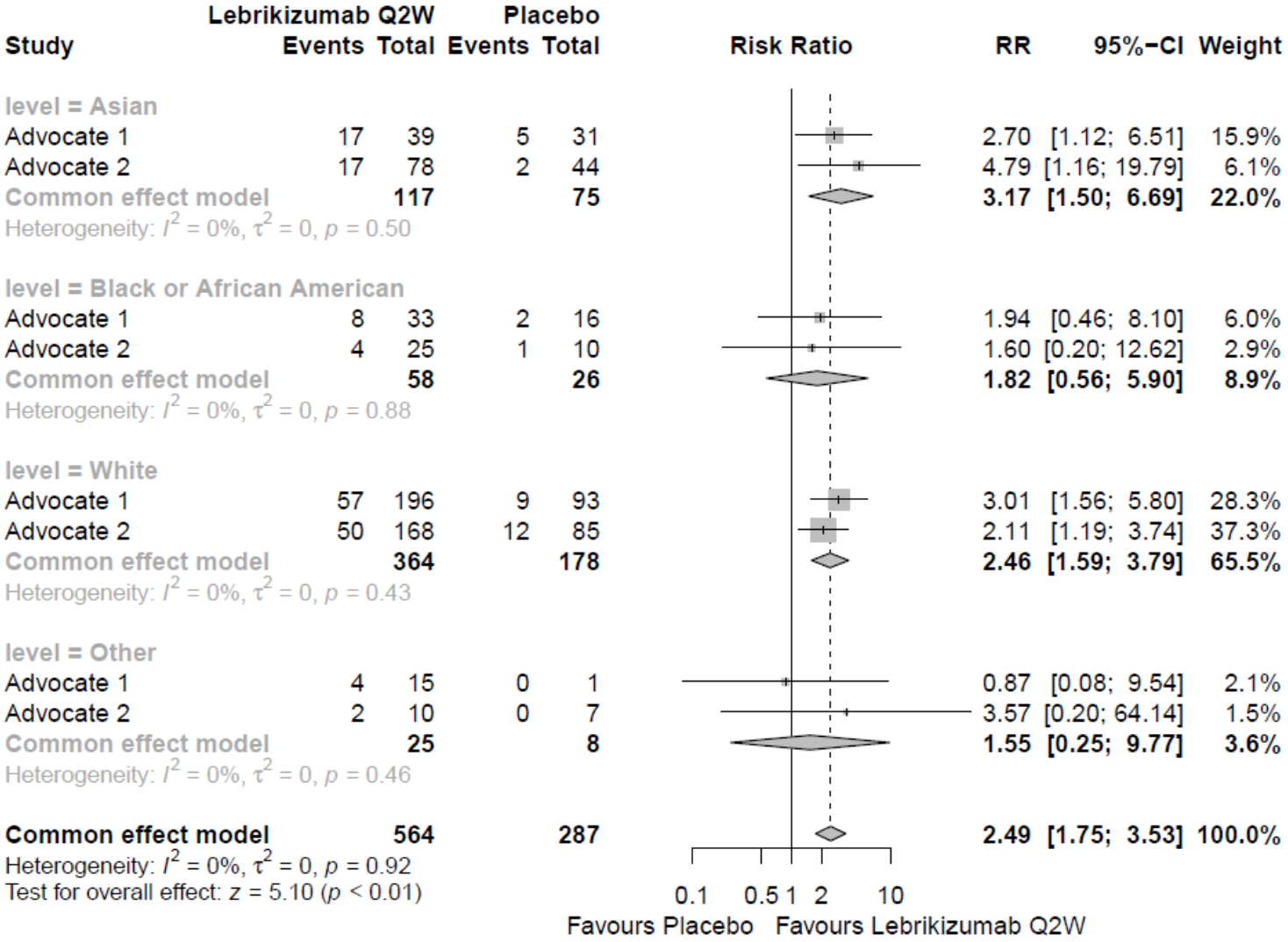
4.5.1.10.2 Krankheitsschwere

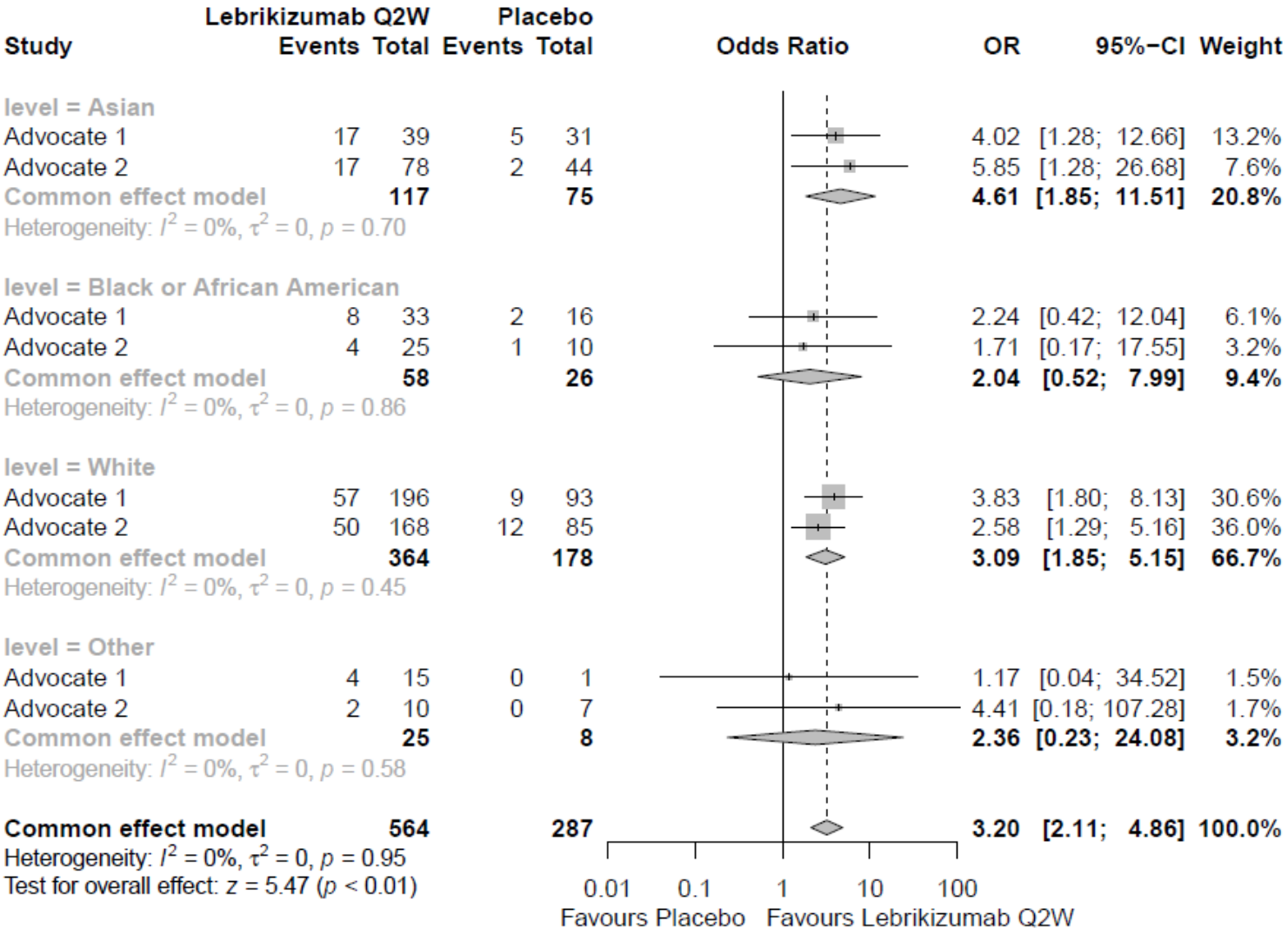


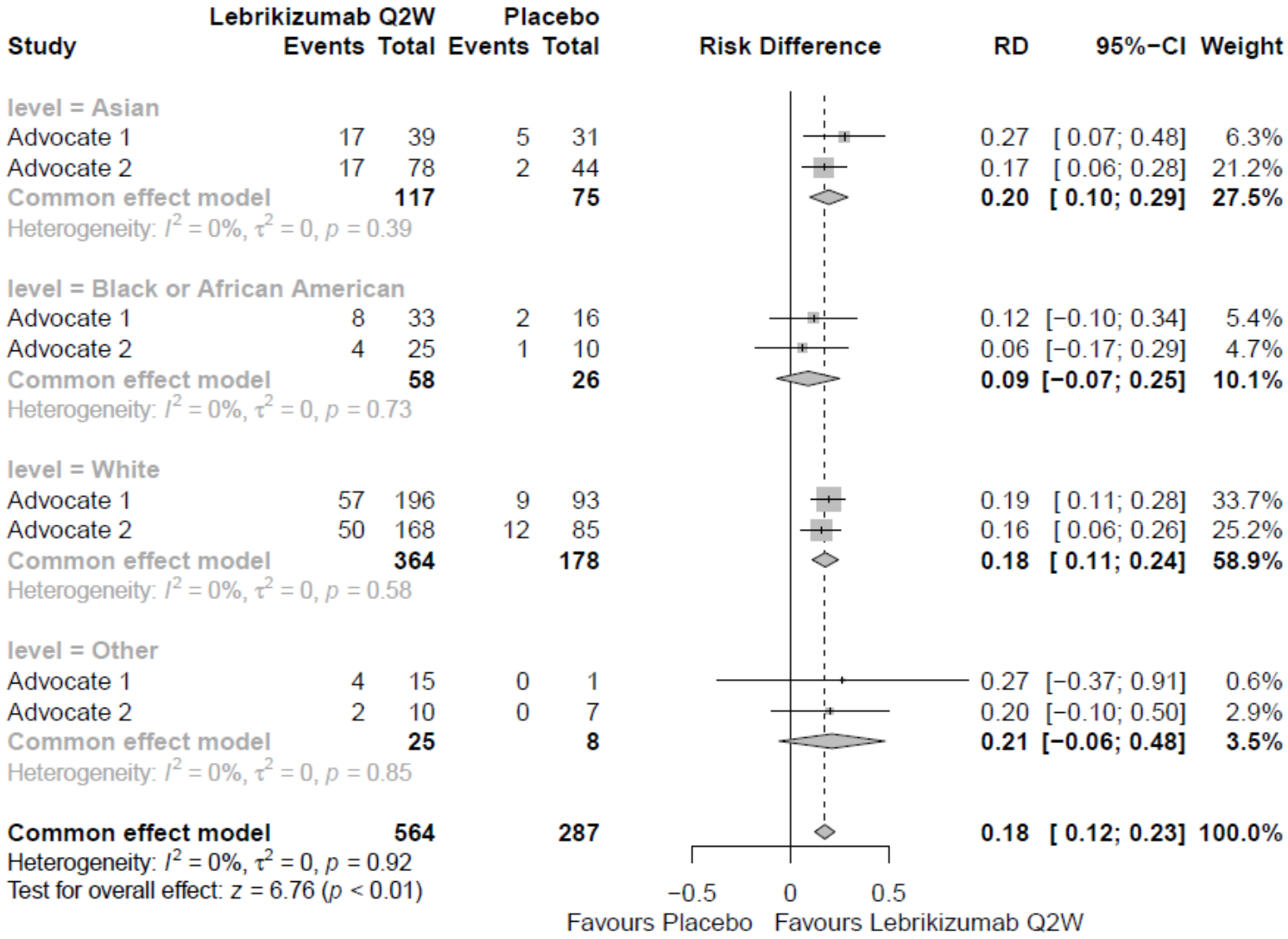

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Baseline IGA 3
Advocate 1 49 170 9 83 3.33 [1.55; 7.17] 29.5%
Advocate 2 38 175 10 95 2.36 [1.12; 4.98] 31.1%
Common effect model 345 178 2.79 [1.63; 4.76] 60.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.53
level = Baseline IGA 4
Advocate 1 37 113 7 58 3.55 [1.47; 8.57] 22.3%
Advocate 2 35 106 5 51 4.54 [1.66; 12.42] 17.1%
Common effect model 219 109 3.95 [2.03; 7.66] 39.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.72
Common effect model 564 287 3.20 [2.11; 4.85] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.76
Test for overall effect: z = 5.47 (p < 0.01)
0.1
0.5
1
2
10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Baseline IGA 3
Advocate 1 49 170 9 83 0.18 [0.08; 0.28] 28.9%
Advocate 2 38 175 10 95 0.11 [0.03; 0.20] 35.0%
Common effect model 345 178 0.14 [0.08; 0.21] 63.9%
Heterogeneity: I^2 = 6%, τ^2 = 0.0001, p = 0.30
level = Baseline IGA 4
Advocate 1 37 113 7 58 0.21 [0.09; 0.33] 18.2%
Advocate 2 35 106 5 51 0.23 [0.11; 0.35] 18.0%
Common effect model 219 109 0.22 [0.13; 0.30] 36.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.77
Common effect model 564 287 0.17 [0.12; 0.22] 100.0%
Heterogeneity: I^2 = 4%, τ^2 = 0.0004, p = 0.37
Test for overall effect: z = 6.50 (p < 0.01)
−0.3 −0.2 −0.1 0 0.1 0.2 0.3
Favours Placebo
Favours Lebrikizumab Q2W

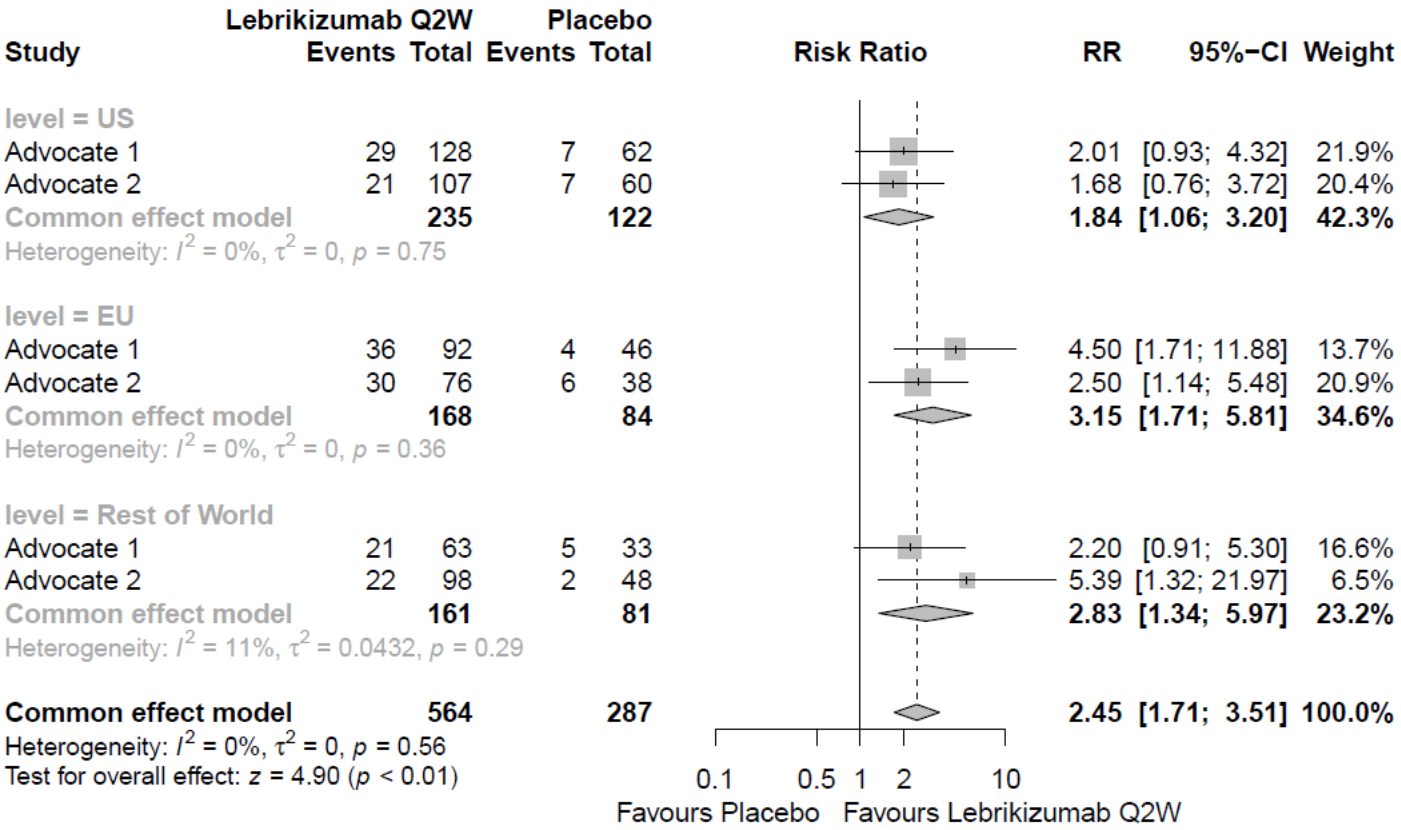
4.5.1.10.3 Ethnie

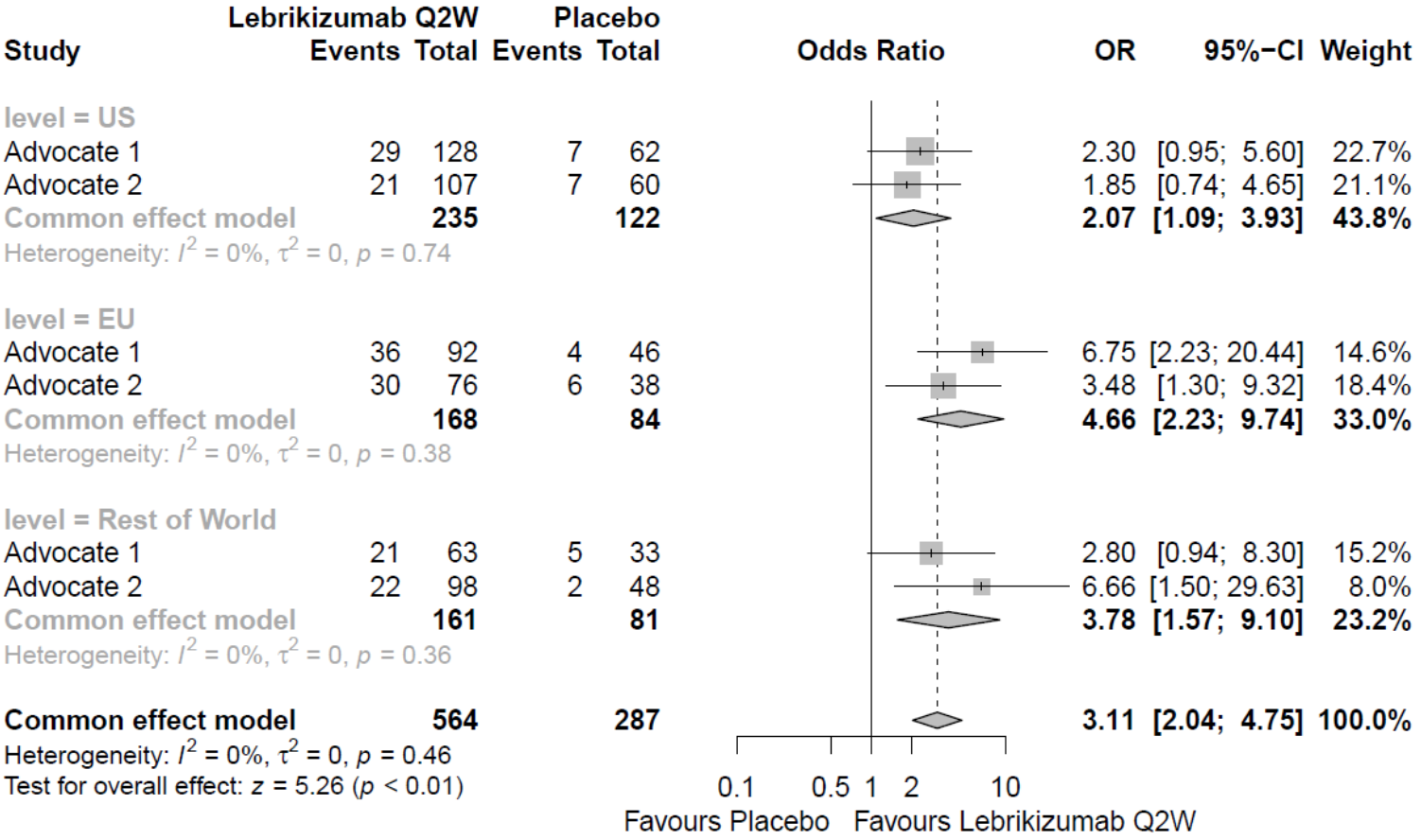


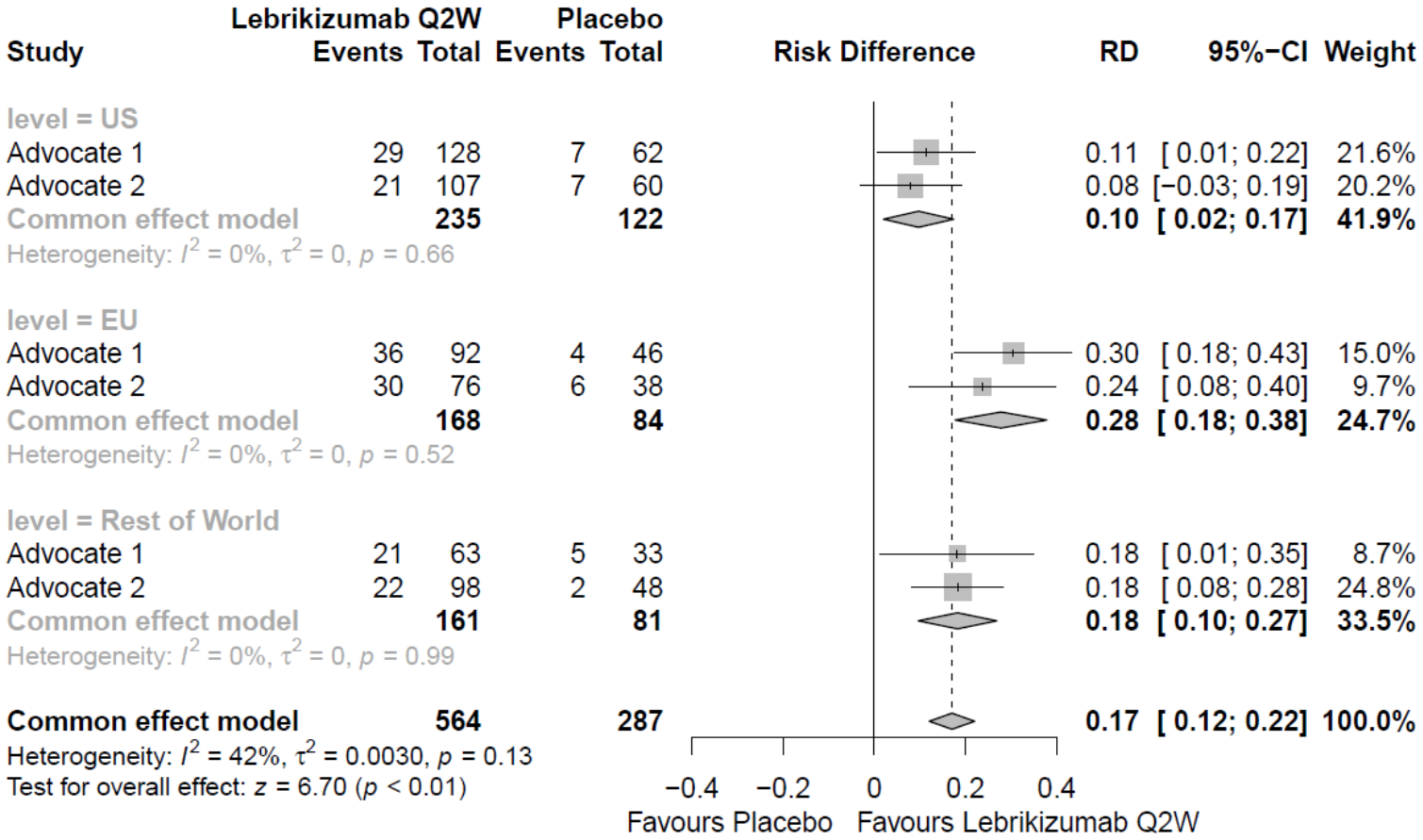

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Asian
Advocate 1 17 39 5 31 4.02 [1.28; 12.66] 13.2%
Advocate 2 17 78 2 44 5.85 [1.28; 26.68] 7.6%
Common effect model 117 75 4.61 [1.85; 11.51] 20.8%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.70
level = Black or African American
Advocate 1 8 33 2 16 2.24 [0.42; 12.04] 6.1%
Advocate 2 4 25 1 10 1.71 [0.17; 17.55] 3.2%
Common effect model 58 26 2.04 [0.52; 7.99] 9.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.86
level = White
Advocate 1 57 196 9 93 3.83 [1.80; 8.13] 30.6%
Advocate 2 50 168 12 85 2.58 [1.29; 5.16] 36.0%
Common effect model 364 178 3.09 [1.85; 5.15] 66.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.45
level = Other
Advocate 1 4 15 0 1 1.17 [0.04; 34.52] 1.5%
Advocate 2 2 10 0 7 4.41 [0.18; 107.28] 1.7%
Common effect model 25 8 2.36 [0.23; 24.08] 3.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.58
Common effect model 564 287 3.20 [2.11; 4.86] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.95
Test for overall effect: z = 5.47 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Asian
Advocate 1 17 39 5 31 0.27 [0.07; 0.48] 6.3%
Advocate 2 17 78 2 44 0.17 [0.06; 0.28] 21.2%
Common effect model 117 75 0.20 [0.10; 0.29] 27.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.39
level = Black or African American
Advocate 1 8 33 2 16 0.12 [−0.10; 0.34] 5.4%
Advocate 2 4 25 1 10 0.06 [−0.17; 0.29] 4.7%
Common effect model 58 26 0.09 [−0.07; 0.25] 10.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.73
level = White
Advocate 1 57 196 9 93 0.19 [0.11; 0.28] 33.7%
Advocate 2 50 168 12 85 0.16 [0.06; 0.26] 25.2%
Common effect model 364 178 0.18 [0.11; 0.24] 58.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.58
level = Other
Advocate 1 4 15 0 1 0.27 [−0.37; 0.91] 0.6%
Advocate 2 2 10 0 7 0.20 [−0.10; 0.50] 2.9%
Common effect model 25 8 0.21 [−0.06; 0.48] 3.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.85
Common effect model 564 287 0.18 [0.12; 0.23] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.92
Test for overall effect: z = 6.76 (p < 0.01)
−0.5
0
0.5
Favours Placebo
Favours Lebrikizumab Q2W

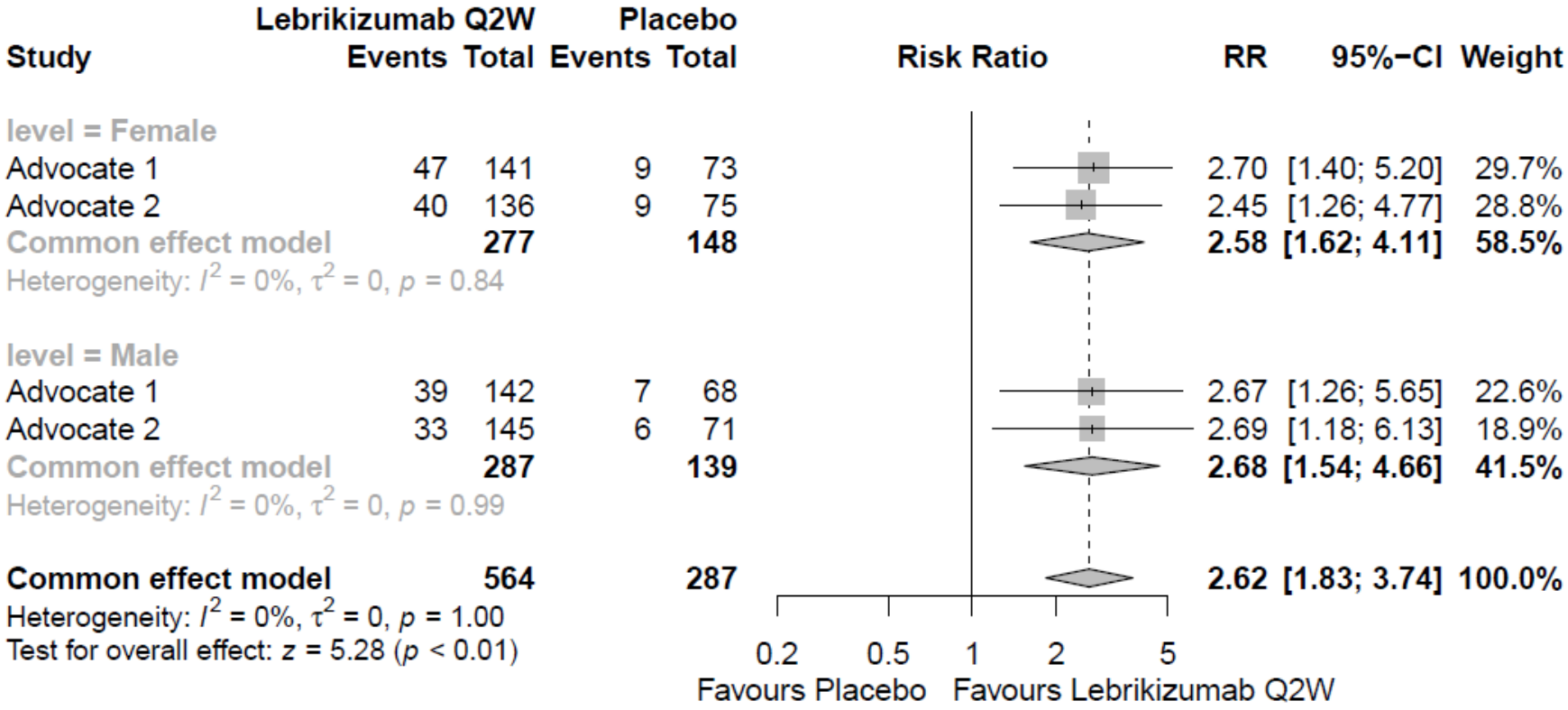
4.5.1.10.4 Region

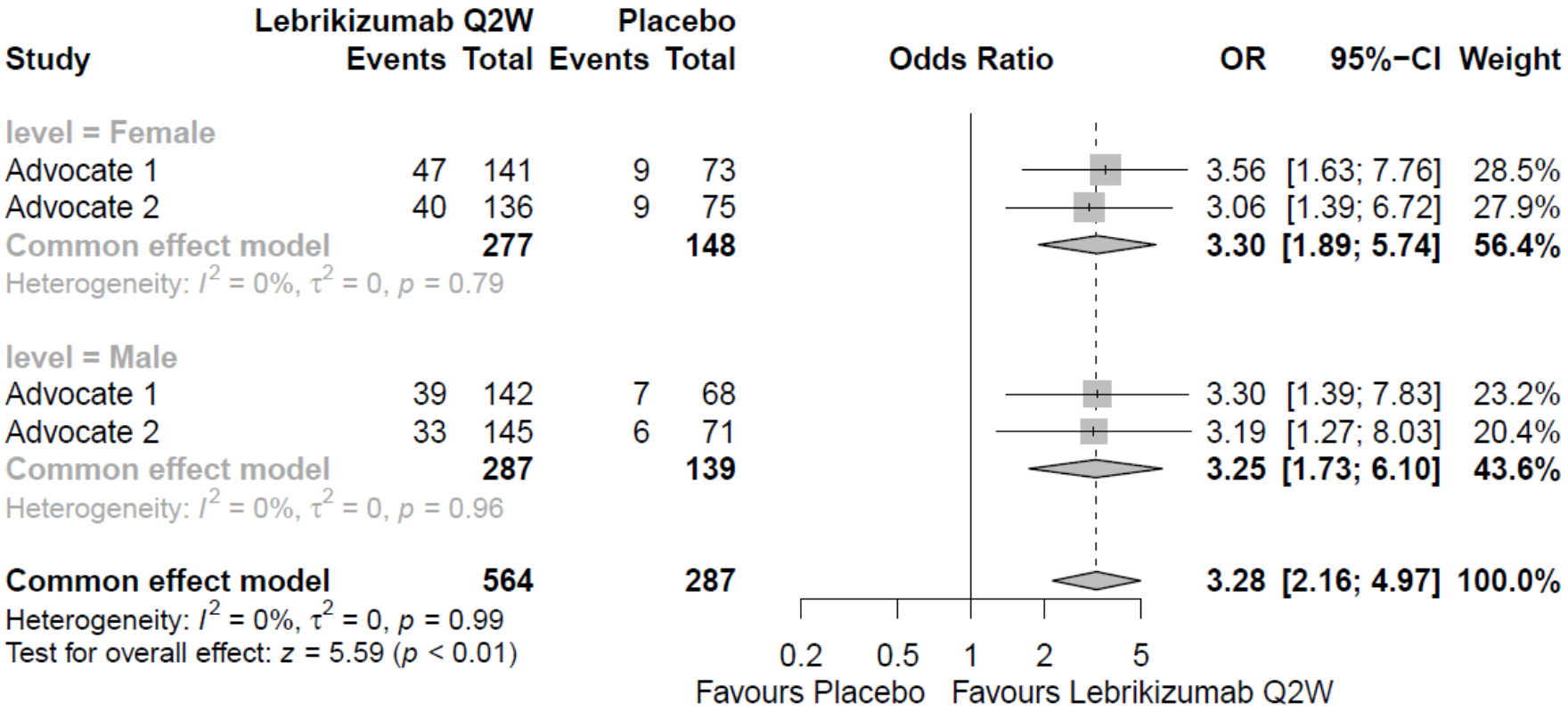


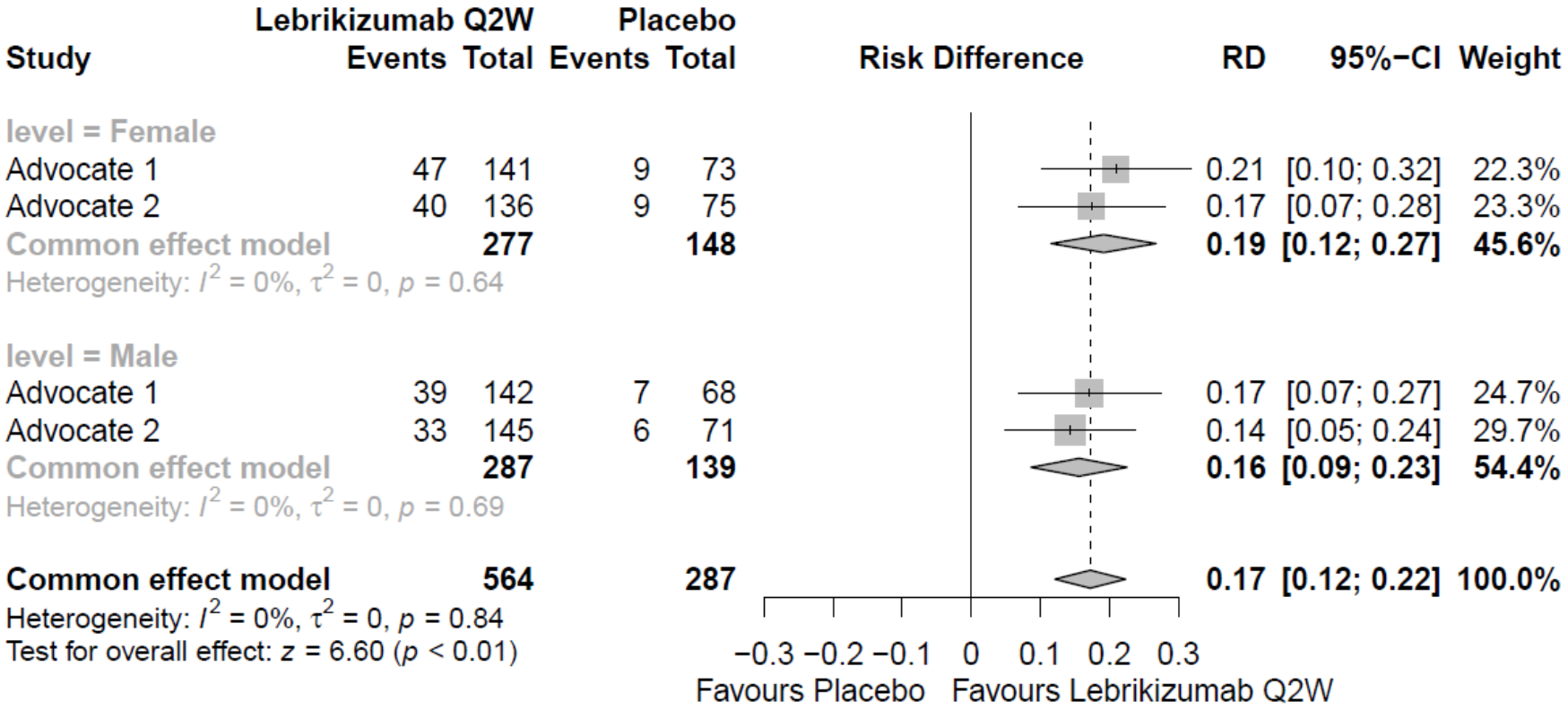

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = US
Advocate 1 29 128 7 62 2.30 [0.95; 5.60] 22.7%
Advocate 2 21 107 7 60 1.85 [0.74; 4.65] 21.1%
Common effect model 235 122 2.07 [1.09; 3.93] 43.8%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.74
level = EU
Advocate 1 36 92 4 46 6.75 [2.23; 20.44] 14.6%
Advocate 2 30 76 6 38 3.48 [1.30; 9.32] 18.4%
Common effect model 168 84 4.66 [2.23; 9.74] 33.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.38
level = Rest of World
Advocate 1 21 63 5 33 2.80 [0.94; 8.30] 15.2%
Advocate 2 22 98 2 48 6.66 [1.50; 29.63] 8.0%
Common effect model 161 81 3.78 [1.57; 9.10] 23.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.36
Common effect model 564 287 3.11 [2.04; 4.75] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.46
Test for overall effect: z = 5.26 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = US
Advocate 1 29 128 7 62 0.11 [0.01; 0.22] 21.6%
Advocate 2 21 107 7 60 0.08 [−0.03; 0.19] 20.2%
Common effect model 235 122 0.10 [0.02; 0.17] 41.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.66
level = EU
Advocate 1 36 92 4 46 0.30 [0.18; 0.43] 15.0%
Advocate 2 30 76 6 38 0.24 [0.08; 0.40] 9.7%
Common effect model 168 84 0.28 [0.18; 0.38] 24.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.52
level = Rest of World
Advocate 1 21 63 5 33 0.18 [0.01; 0.35] 8.7%
Advocate 2 22 98 2 48 0.18 [0.08; 0.28] 24.8%
Common effect model 161 81 0.18 [0.10; 0.27] 33.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.99
Common effect model 564 287 0.17 [0.12; 0.22] 100.0%
Heterogeneity: I^2 = 42%, τ^2 = 0.0030, p = 0.13
Test for overall effect: z = 6.70 (p < 0.01)
−0.4
−0.2
0
0.2
0.4
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.10.5 Geschlecht

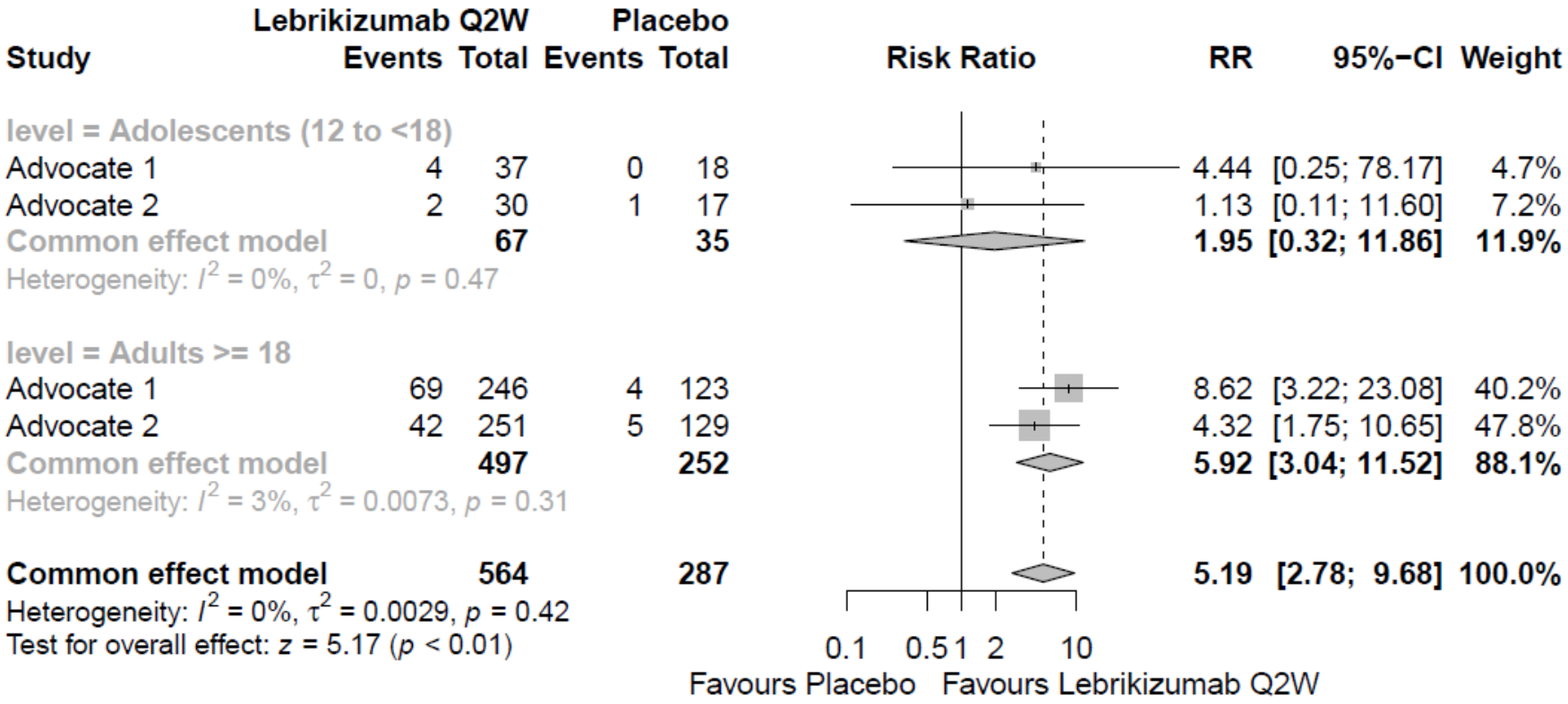


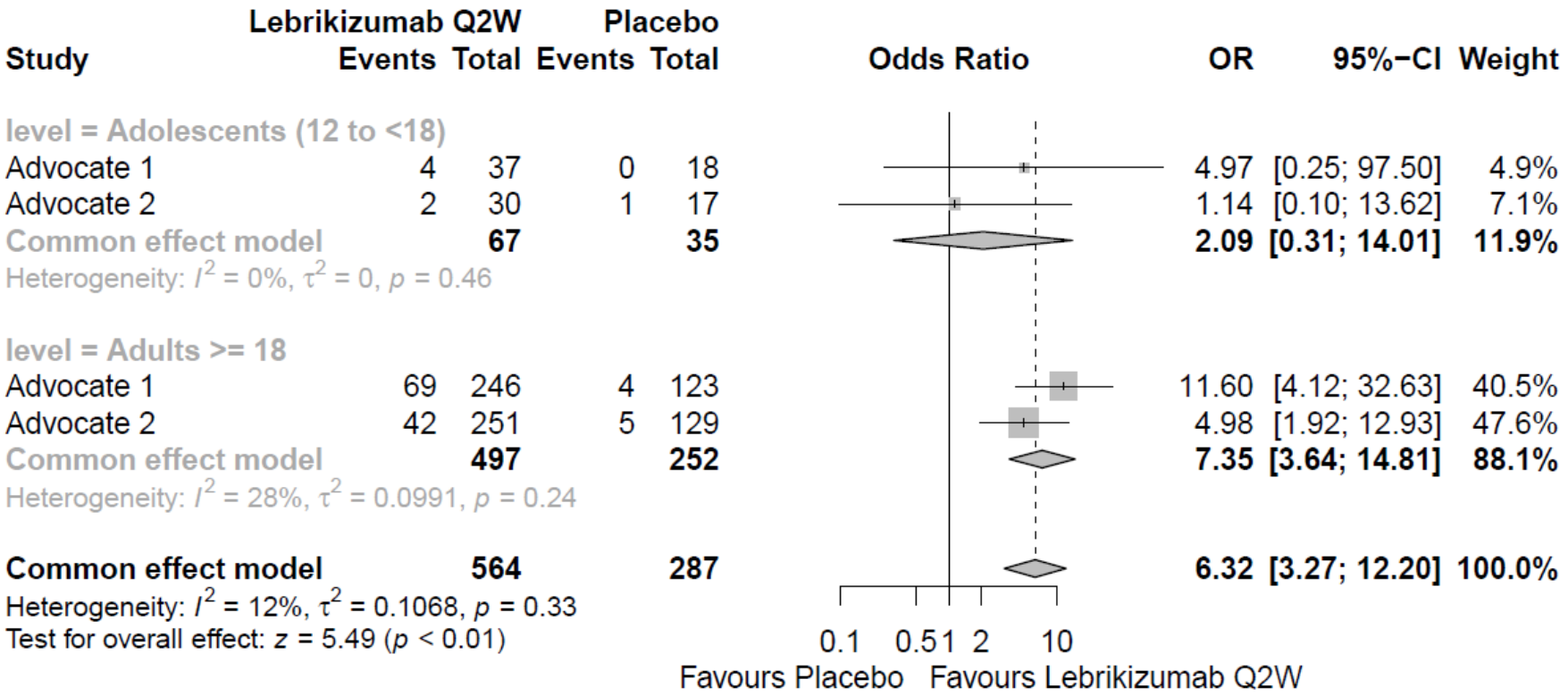

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Female
Advocate 1 47 141 9 73 3.56 [1.63; 7.76] 28.5%
Advocate 2 40 136 9 75 3.06 [1.39; 6.72] 27.9%
Common effect model 277 148 3.30 [1.89; 5.74] 56.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.79
level = Male
Advocate 1 39 142 7 68 3.30 [1.39; 7.83] 23.2%
Advocate 2 33 145 6 71 3.19 [1.27; 8.03] 20.4%
Common effect model 287 139 3.25 [1.73; 6.10] 43.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.96
Common effect model 564 287 3.28 [2.16; 4.97] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.99
Test for overall effect: z = 5.59 (p < 0.01)
0.2
0.5
1
2
5
Favours Placebo
Favours Lebrikizumab Q2W

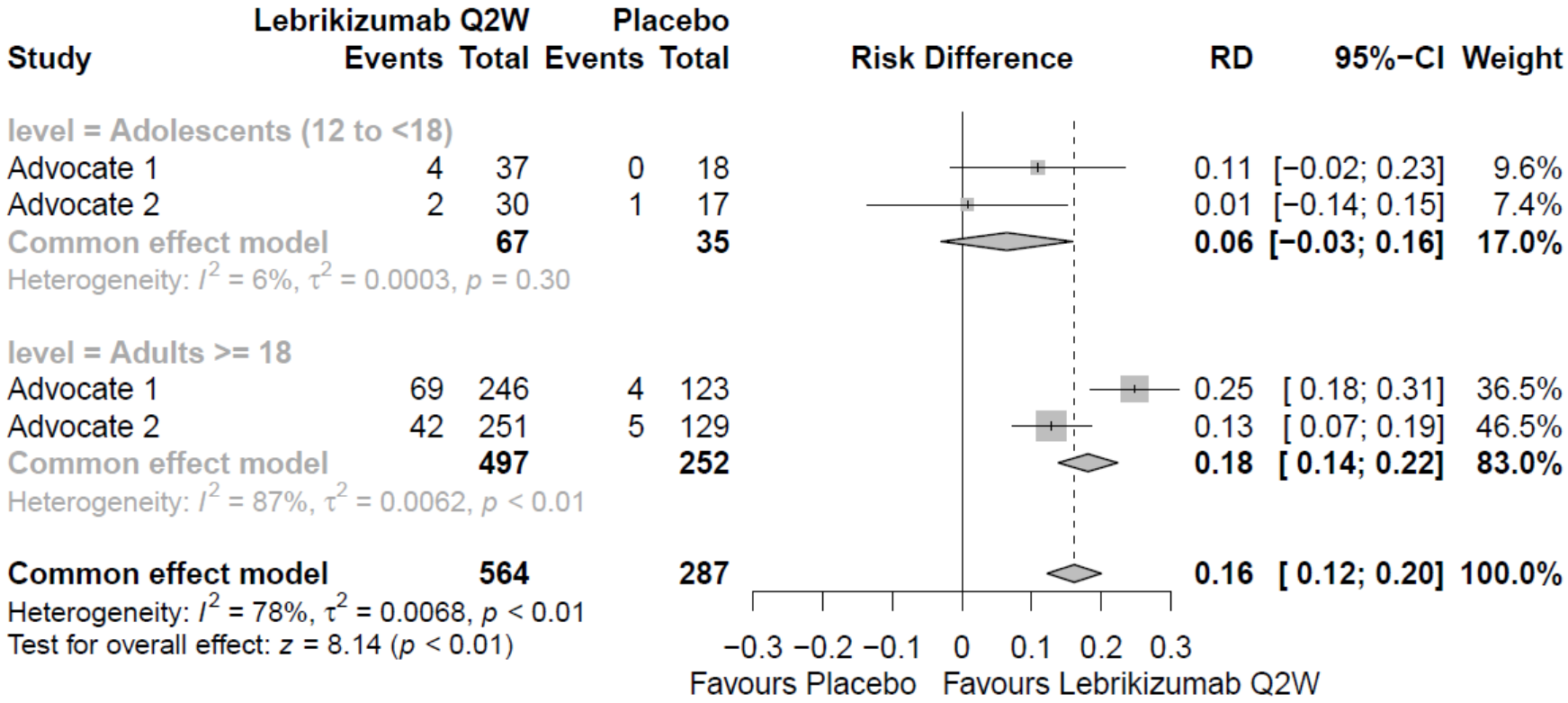

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Female
Advocate 1 47 141 9 73 0.21 [0.10; 0.32] 22.3%
Advocate 2 40 136 9 75 0.17 [0.07; 0.28] 23.3%
Common effect model 277 148 0.19 [0.12; 0.27] 45.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.64
level = Male
Advocate 1 39 142 7 68 0.17 [0.07; 0.27] 24.7%
Advocate 2 33 145 6 71 0.14 [0.05; 0.24] 29.7%
Common effect model 287 139 0.16 [0.09; 0.23] 54.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.69
Common effect model 564 287 0.17 [0.12; 0.22] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.84
Test for overall effect: z = 6.60 (p < 0.01)
−0.3 −0.2 −0.1 0 0.1 0.2 0.3
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.11 Sleep-Loss-Score Verbesserung um 2 Punkte

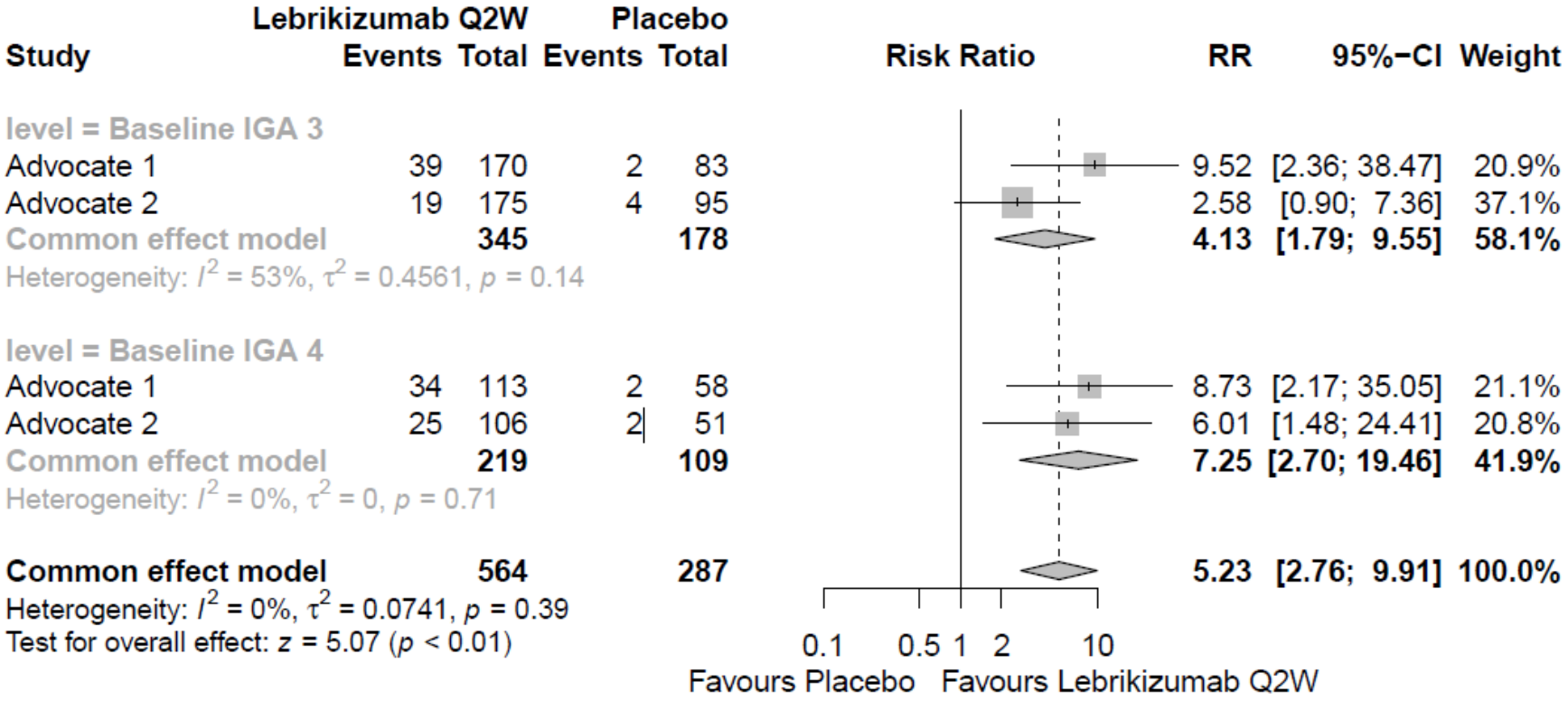
4.5.1.11.1 Altersgruppe

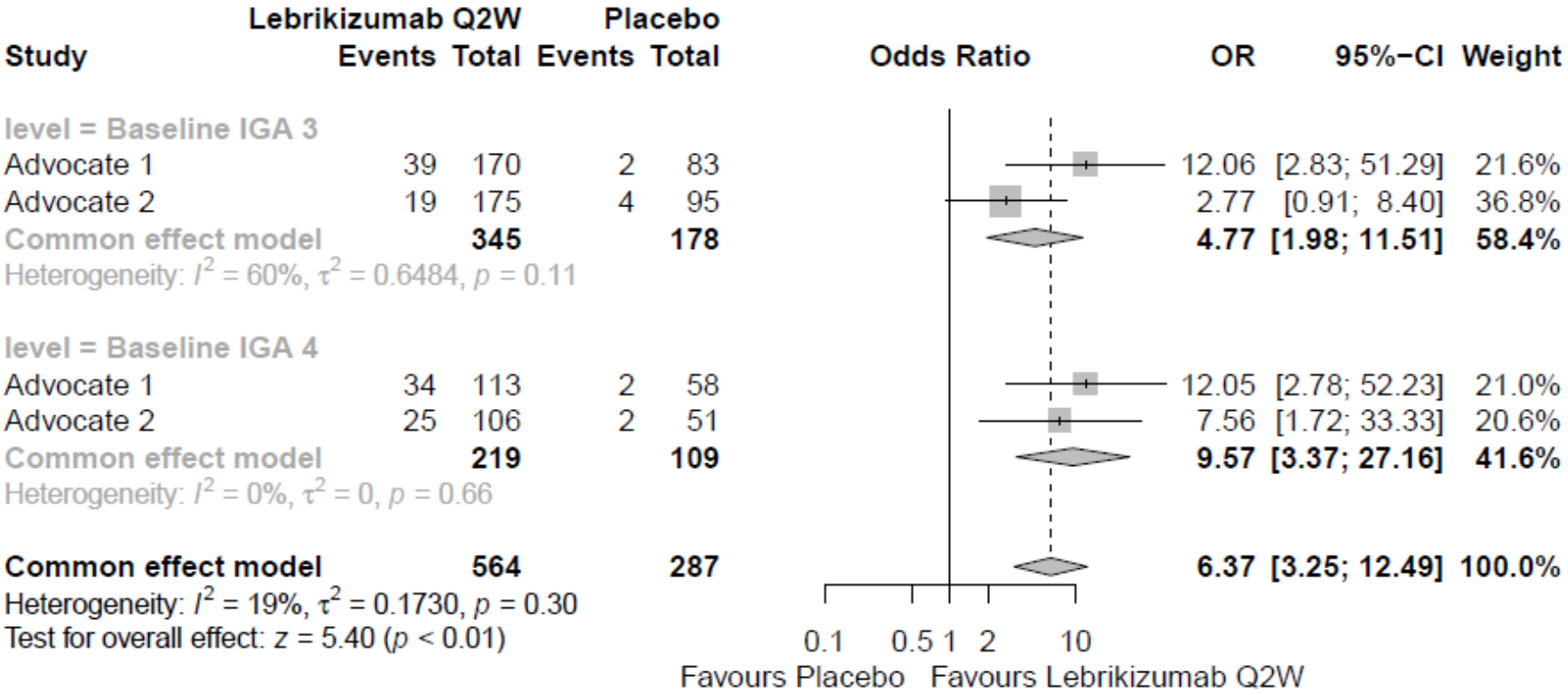


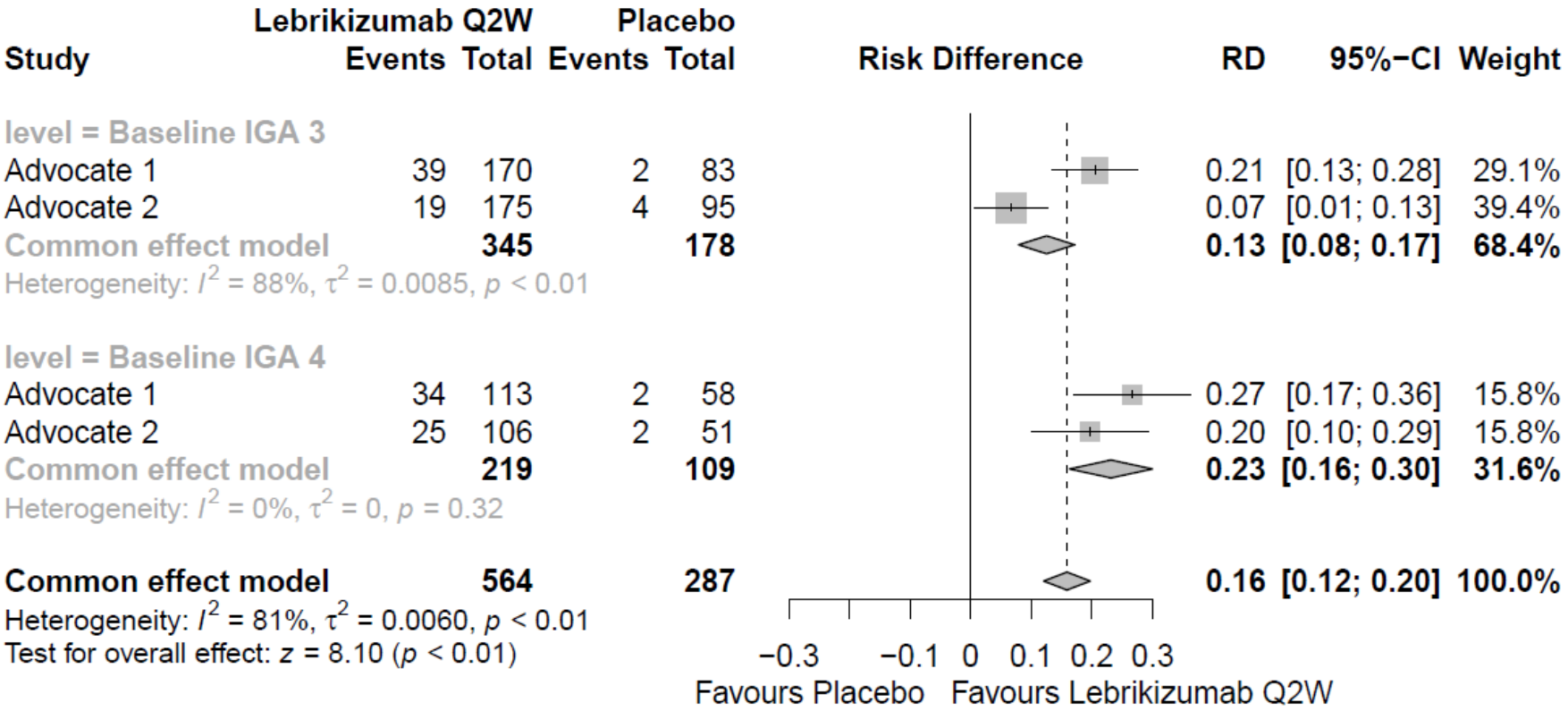

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 4 37 0 18 4.97 [0.25; 97.50] 4.9%
Advocate 2 2 30 1 17 1.14 [0.10; 13.62] 7.1%
Common effect model 67 35 2.09 [0.31; 14.01] 11.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.46
level = Adults >= 18
Advocate 1 69 246 4 123 11.60 [4.12; 32.63] 40.5%
Advocate 2 42 251 5 129 4.98 [1.92; 12.93] 47.6%
Common effect model 497 252 7.35 [3.64; 14.81] 88.1%
Heterogeneity: I^2 = 28%, τ^2 = 0.0991, p = 0.24
Common effect model 564 287 6.32 [3.27; 12.20] 100.0%
Heterogeneity: I^2 = 12%, τ^2 = 0.1068, p = 0.33
Test for overall effect: z = 5.49 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Adolescents (12 to <18)
Advocate 1 4 37 0 18 0.11 [−0.02; 0.23] 9.6%
Advocate 2 2 30 1 17 0.01 [−0.14; 0.15] 7.4%
Common effect model 67 35 0.06 [−0.03; 0.16] 17.0%
Heterogeneity: I^2 = 6%, τ^2 = 0.0003, p = 0.30
level = Adults >= 18
Advocate 1 69 246 4 123 0.25 [0.18; 0.31] 36.5%
Advocate 2 42 251 5 129 0.13 [0.07; 0.19] 46.5%
Common effect model 497 252 0.18 [0.14; 0.22] 83.0%
Heterogeneity: I^2 = 87%, τ^2 = 0.0062, p < 0.01
Common effect model 564 287 0.16 [0.12; 0.20] 100.0%
Heterogeneity: I^2 = 78%, τ^2 = 0.0068, p < 0.01
Test for overall effect: z = 8.14 (p < 0.01)
−0.3 −0.2 −0.1 0 0.1 0.2 0.3
Favours Placebo
Favours Lebrikizumab Q2W

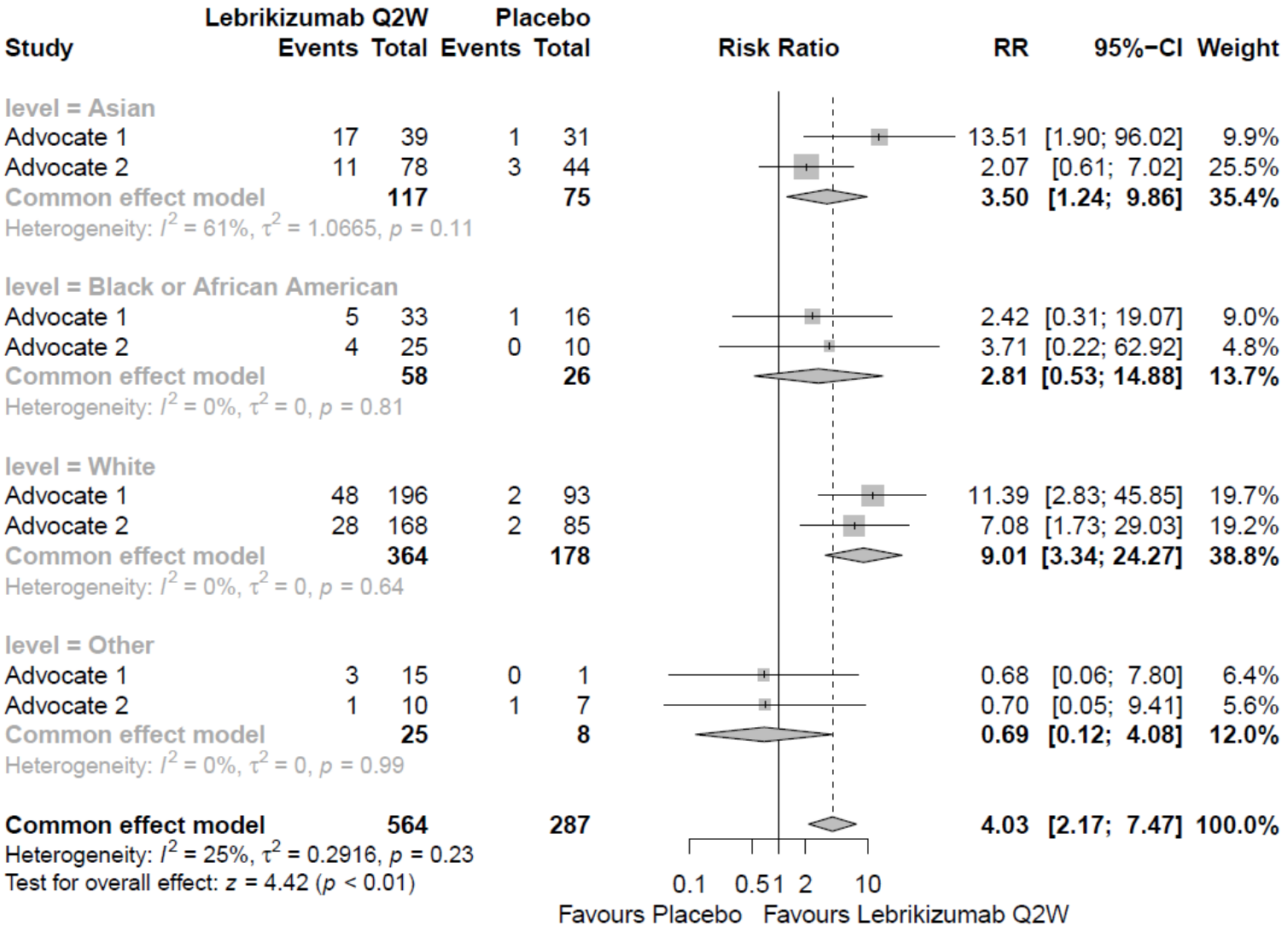
4.5.1.11.2 Krankheitsschwere

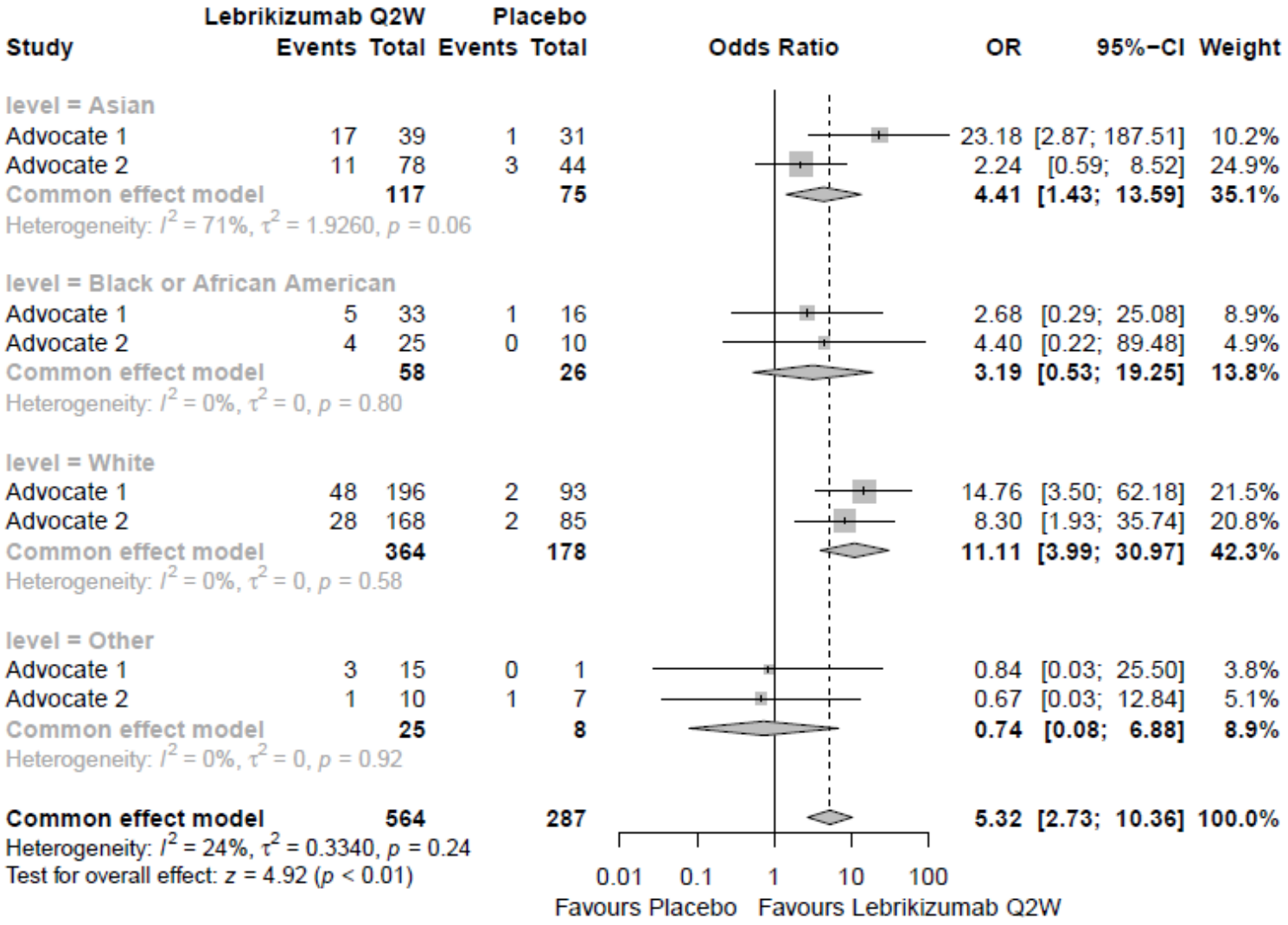


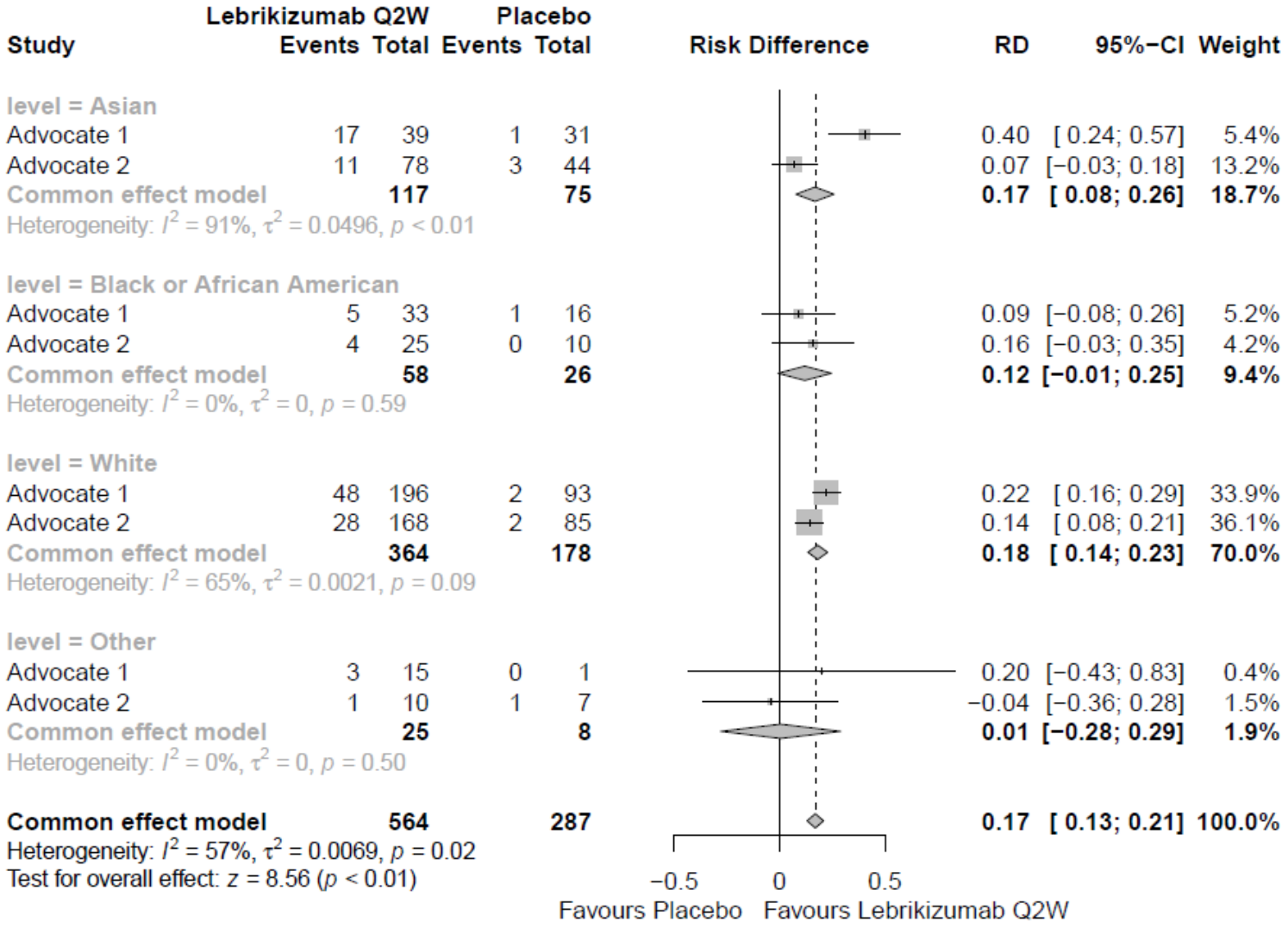

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Baseline IGA 3
Advocate 1 39 170 2 83 12.06 [2.83; 51.29] 21.6%
Advocate 2 19 175 4 95 2.77 [0.91; 8.40] 36.8%
Common effect model 345 178 4.77 [1.98; 11.51] 58.4%
Heterogeneity: I^2 = 60%, τ^2 = 0.6484, p = 0.11
level = Baseline IGA 4
Advocate 1 34 113 2 58 12.05 [2.78; 52.23] 21.0%
Advocate 2 25 106 2 51 7.56 [1.72; 33.33] 20.6%
Common effect model 219 109 9.57 [3.37; 27.16] 41.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.66
Common effect model 564 287 6.37 [3.25; 12.49] 100.0%
Heterogeneity: I^2 = 19%, τ^2 = 0.1730, p = 0.30
Test for overall effect: z = 5.40 (p < 0.01)
0.1
0.5
1
2
10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Baseline IGA 3
Advocate 1 39 170 2 83 0.21 [0.13; 0.28] 29.1%
Advocate 2 19 175 4 95 0.07 [0.01; 0.13] 39.4%
Common effect model 345 178 0.13 [0.08; 0.17] 68.4%
Heterogeneity: I^2 = 88%, τ^2 = 0.0085, p < 0.01
level = Baseline IGA 4
Advocate 1 34 113 2 58 0.27 [0.17; 0.36] 15.8%
Advocate 2 25 106 2 51 0.20 [0.10; 0.29] 15.8%
Common effect model 219 109 0.23 [0.16; 0.30] 31.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.32
Common effect model 564 287 0.16 [0.12; 0.20] 100.0%
Heterogeneity: I^2 = 81%, τ^2 = 0.0060, p < 0.01
Test for overall effect: z = 8.10 (p < 0.01)
−0.3 −0.1 0 0.1 0.2 0.3
Favours Placebo
Favours Lebrikizumab Q2W

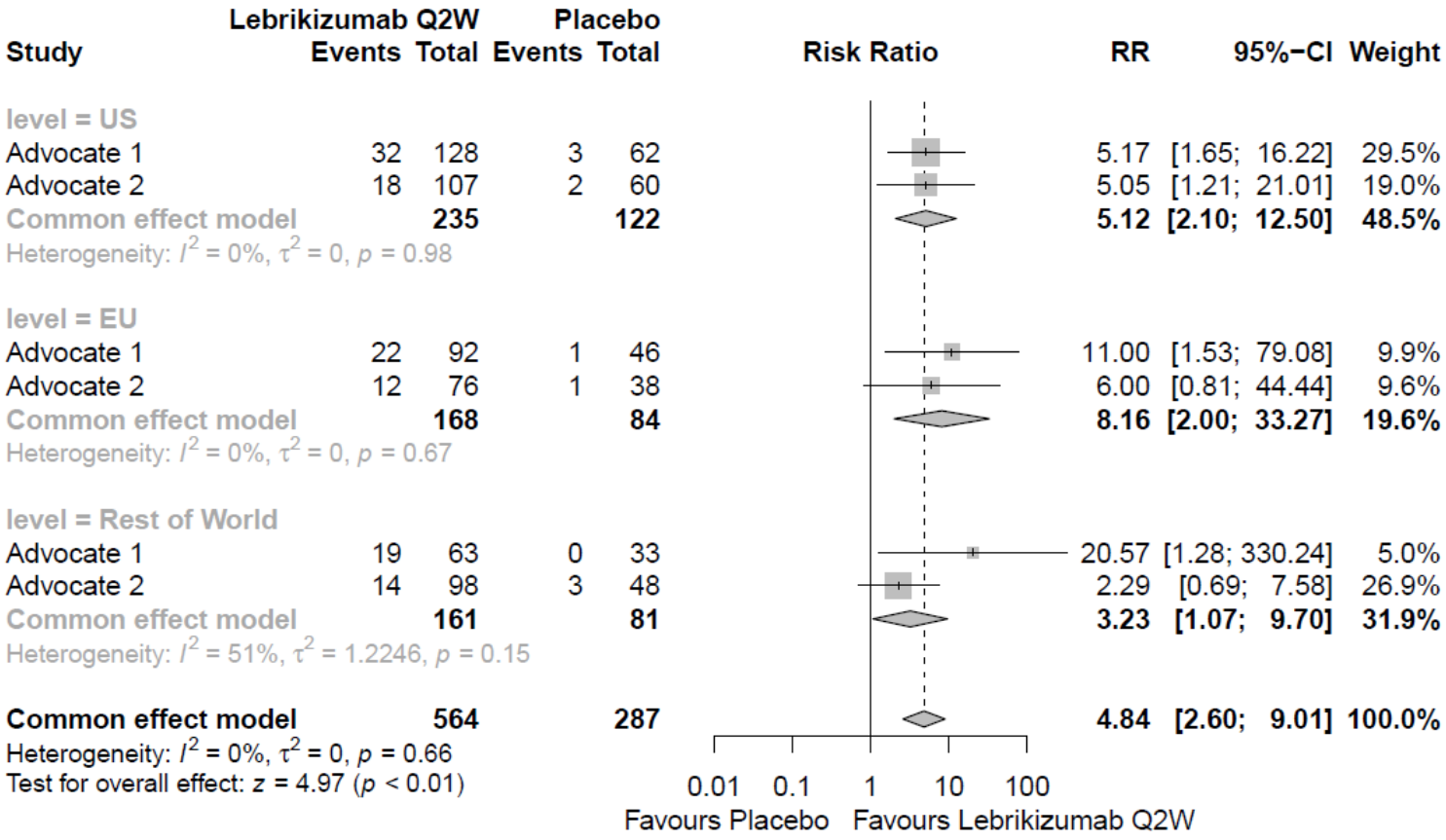
4.5.1.11.3 Ethnie

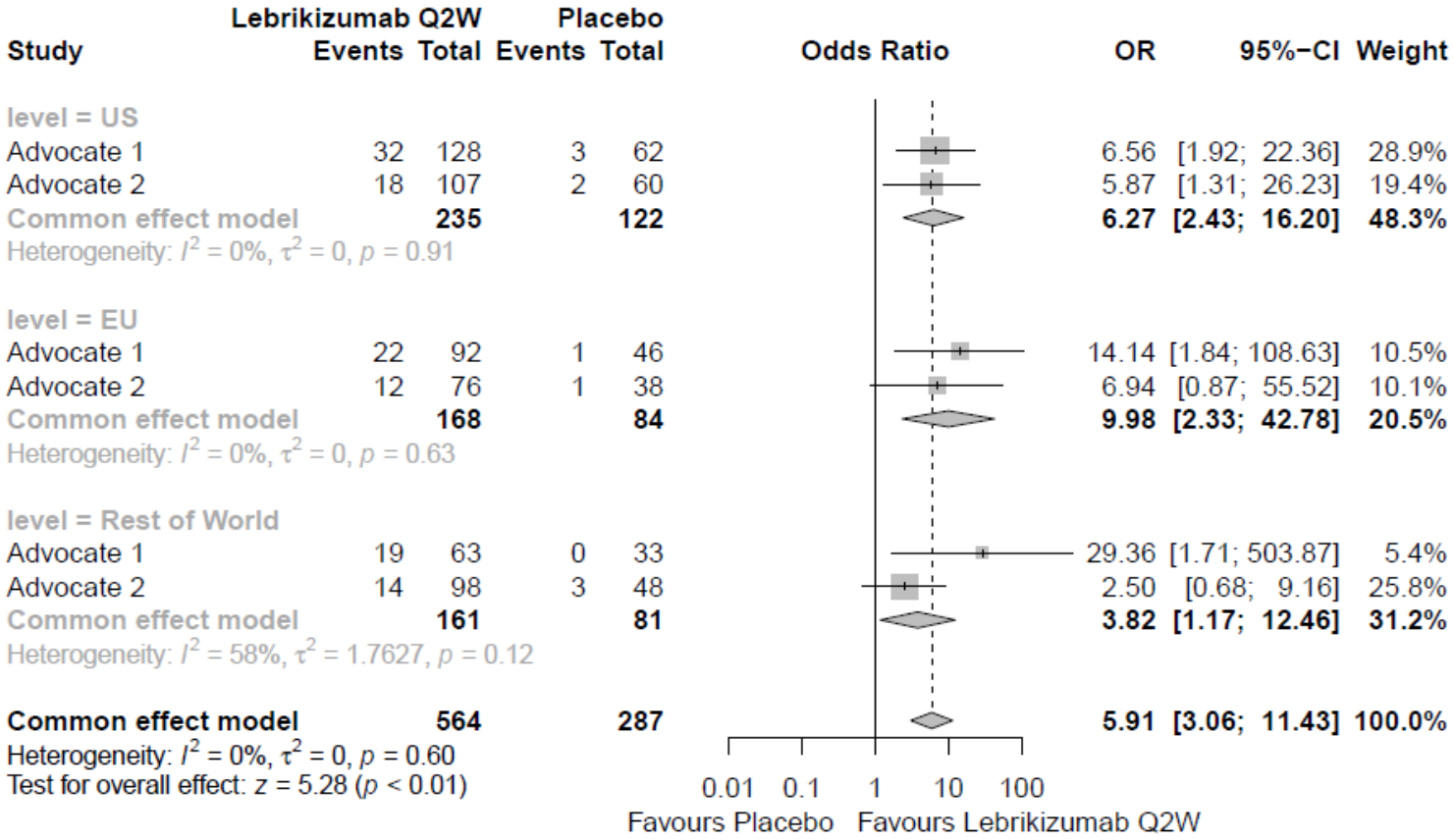


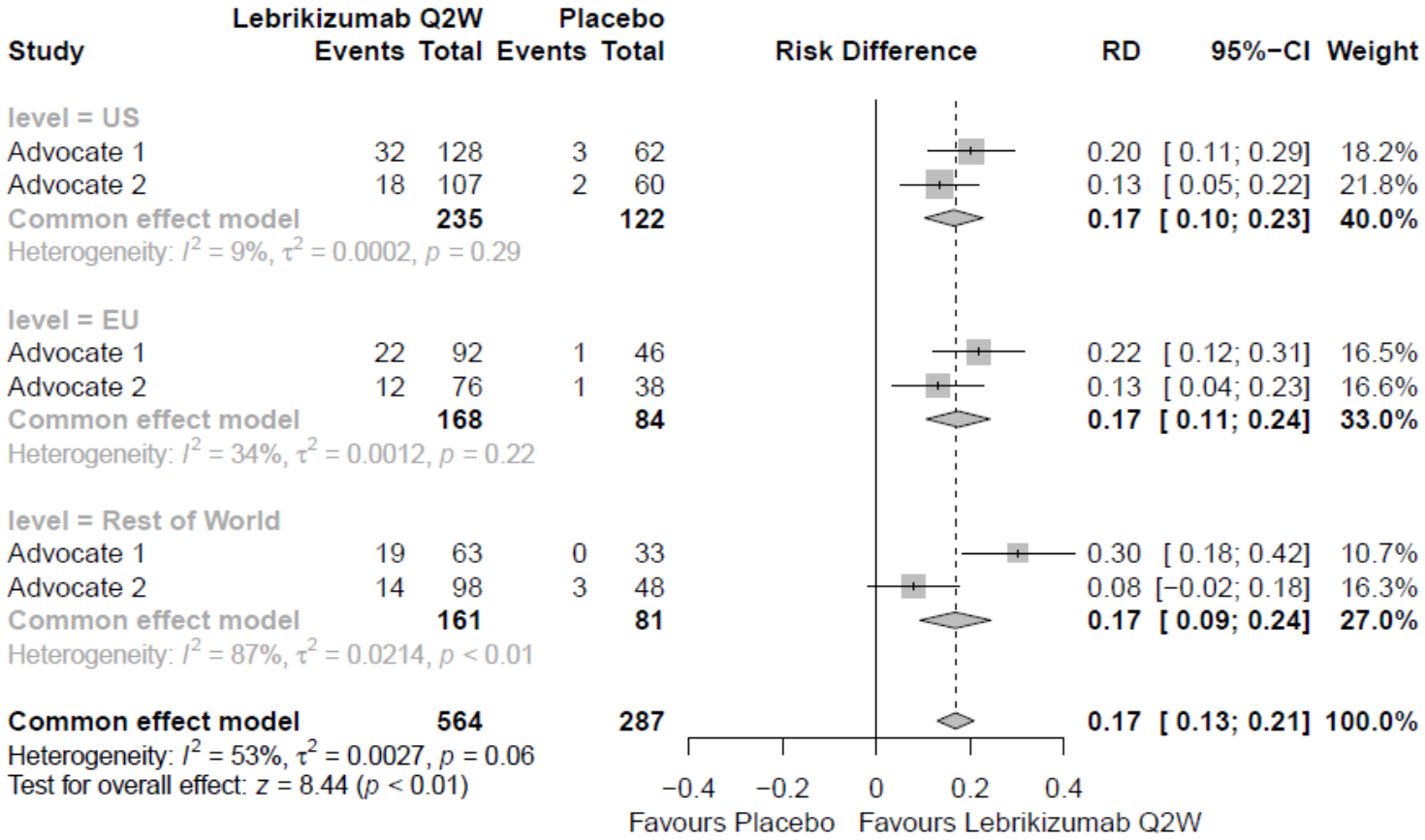

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Asian
Advocate 1 17 39 1 31 23.18 [2.87; 187.51] 10.2%
Advocate 2 11 78 3 44 2.24 [0.59; 8.52] 24.9%
Common effect model 117 75 4.41 [1.43; 13.59] 35.1%
Heterogeneity: I^2 = 71%, τ^2 = 1.9260, p = 0.06
level = Black or African American
Advocate 1 5 33 1 16 2.68 [0.29; 25.08] 8.9%
Advocate 2 4 25 0 10 4.40 [0.22; 89.48] 4.9%
Common effect model 58 26 3.19 [0.53; 19.25] 13.8%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.80
level = White
Advocate 1 48 196 2 93 14.76 [3.50; 62.18] 21.5%
Advocate 2 28 168 2 85 8.30 [1.93; 35.74] 20.8%
Common effect model 364 178 11.11 [3.99; 30.97] 42.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.58
level = Other
Advocate 1 3 15 0 1 0.84 [0.03; 25.50] 3.8%
Advocate 2 1 10 1 7 0.67 [0.03; 12.84] 5.1%
Common effect model 25 8 0.74 [0.08; 6.88] 8.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.92
Common effect model 564 287 5.32 [2.73; 10.36] 100.0%
Heterogeneity: I^2 = 24%, τ^2 = 0.3340, p = 0.24
Test for overall effect: z = 4.92 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Asian
Advocate 1 17 39 1 31 0.40 [0.24; 0.57] 5.4%
Advocate 2 11 78 3 44 0.07 [−0.03; 0.18] 13.2%
Common effect model 117 75 0.17 [0.08; 0.26] 18.7%
Heterogeneity: I^2 = 91%, τ^2 = 0.0496, p < 0.01
level = Black or African American
Advocate 1 5 33 1 16 0.09 [−0.08; 0.26] 5.2%
Advocate 2 4 25 0 10 0.16 [−0.03; 0.35] 4.2%
Common effect model 58 26 0.12 [−0.01; 0.25] 9.4%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.59
level = White
Advocate 1 48 196 2 93 0.22 [0.16; 0.29] 33.9%
Advocate 2 28 168 2 85 0.14 [0.08; 0.21] 36.1%
Common effect model 364 178 0.18 [0.14; 0.23] 70.0%
Heterogeneity: I^2 = 65%, τ^2 = 0.0021, p = 0.09
level = Other
Advocate 1 3 15 0 1 0.20 [−0.43; 0.83] 0.4%
Advocate 2 1 10 1 7 −0.04 [−0.36; 0.28] 1.5%
Common effect model 25 8 0.01 [−0.28; 0.29] 1.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.50
Common effect model 564 287 0.17 [0.13; 0.21] 100.0%
Heterogeneity: I^2 = 57%, τ^2 = 0.0069, p = 0.02
Test for overall effect: z = 8.56 (p < 0.01)
−0.5
0
0.5
Favours Placebo
Favours Lebrikizumab Q2W

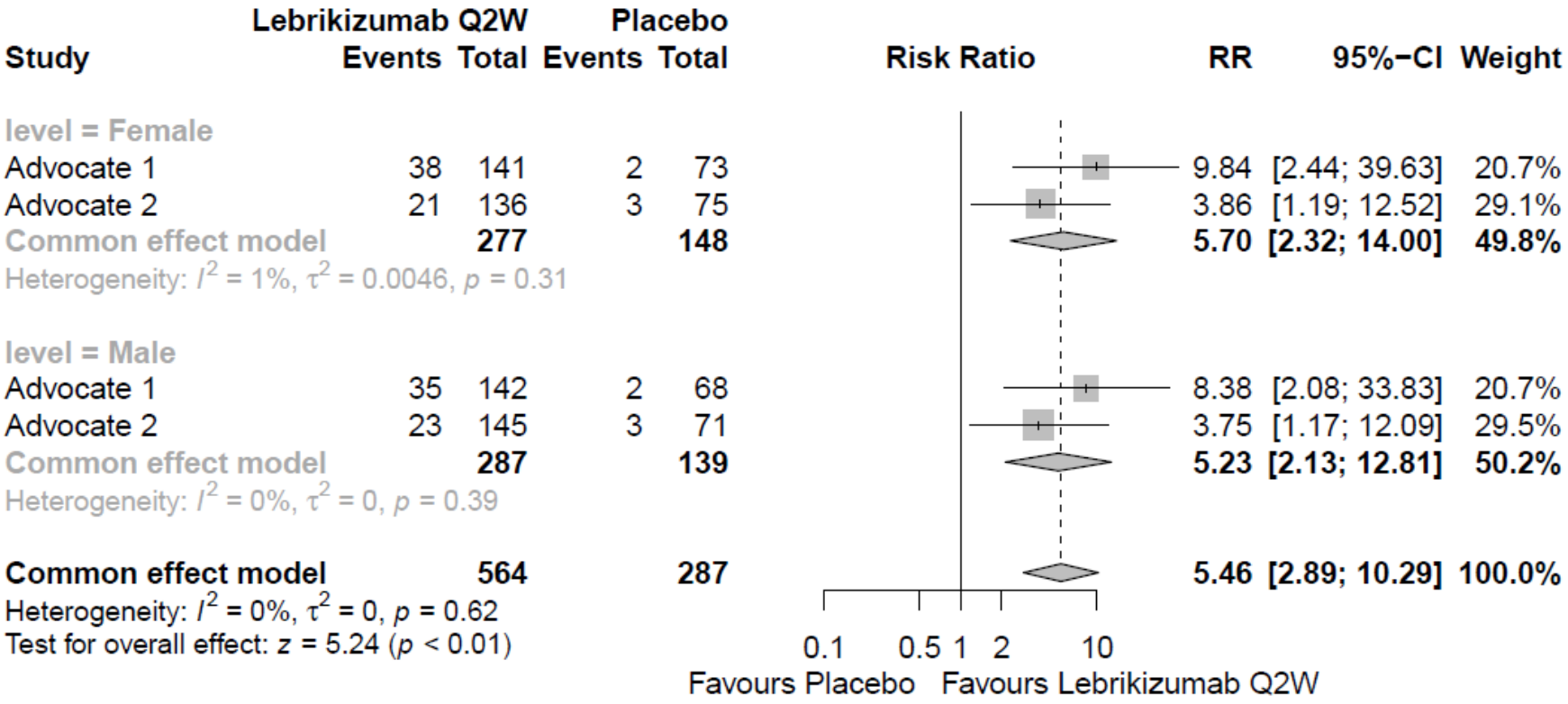
4.5.1.11.4 Region

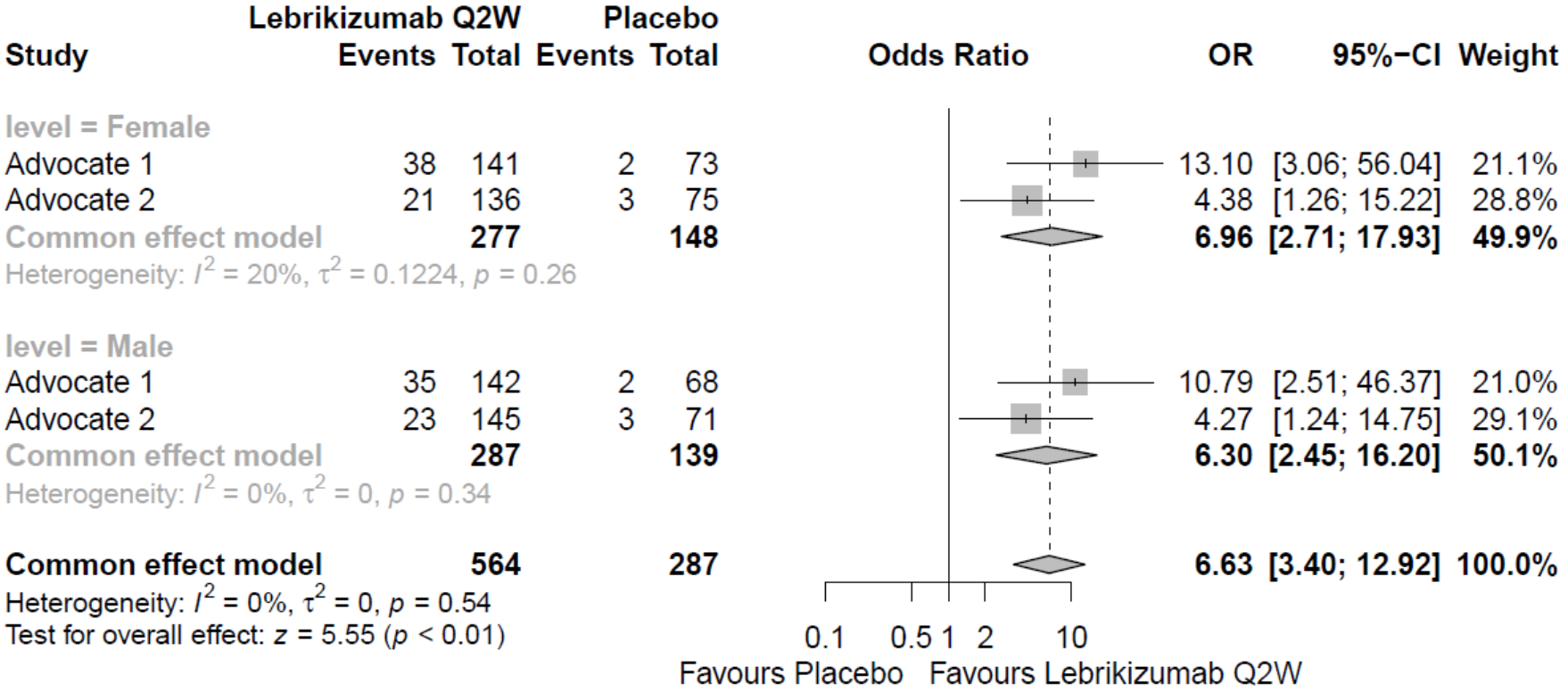


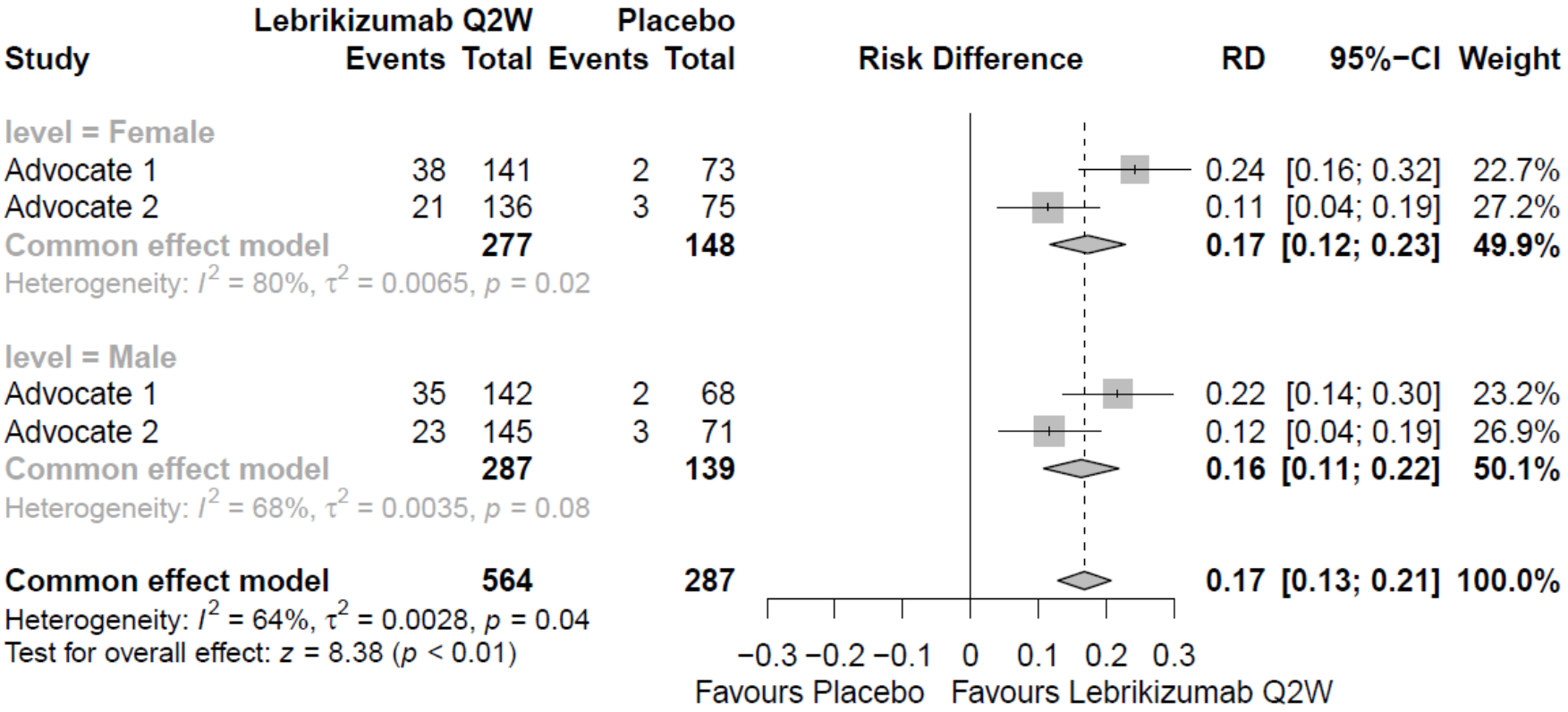

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = US
Advocate 1 32 128 3 62 6.56 [1.92; 22.36] 28.9%
Advocate 2 18 107 2 60 5.87 [1.31; 26.23] 19.4%
Common effect model 235 122 6.27 [2.43; 16.20] 48.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.91
level = EU
Advocate 1 22 92 1 46 14.14 [1.84; 108.63] 10.5%
Advocate 2 12 76 1 38 6.94 [0.87; 55.52] 10.1%
Common effect model 168 84 9.98 [2.33; 42.78] 20.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.63
level = Rest of World
Advocate 1 19 63 0 33 29.36 [1.71; 503.87] 5.4%
Advocate 2 14 98 3 48 2.50 [0.68; 9.16] 25.8%
Common effect model 161 81 3.82 [1.17; 12.46] 31.2%
Heterogeneity: I^2 = 58%, τ^2 = 1.7627, p = 0.12
Common effect model 564 287 5.91 [3.06; 11.43] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.60
Test for overall effect: z = 5.28 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = US
Advocate 1 32 128 3 62 0.20 [0.11; 0.29] 18.2%
Advocate 2 18 107 2 60 0.13 [0.05; 0.22] 21.8%
Common effect model 235 122 0.17 [0.10; 0.23] 40.0%
Heterogeneity: I^2 = 9%, τ^2 = 0.0002, p = 0.29
level = EU
Advocate 1 22 92 1 46 0.22 [0.12; 0.31] 16.5%
Advocate 2 12 76 1 38 0.13 [0.04; 0.23] 16.6%
Common effect model 168 84 0.17 [0.11; 0.24] 33.0%
Heterogeneity: I^2 = 34%, τ^2 = 0.0012, p = 0.22
level = Rest of World
Advocate 1 19 63 0 33 0.30 [0.18; 0.42] 10.7%
Advocate 2 14 98 3 48 0.08 [−0.02; 0.18] 16.3%
Common effect model 161 81 0.17 [0.09; 0.24] 27.0%
Heterogeneity: I^2 = 87%, τ^2 = 0.0214, p < 0.01
Common effect model 564 287 0.17 [0.13; 0.21] 100.0%
Heterogeneity: I^2 = 53%, τ^2 = 0.0027, p = 0.06
Test for overall effect: z = 8.44 (p < 0.01)
−0.4 −0.2 0 0.2 0.4
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.11.5 Geschlecht

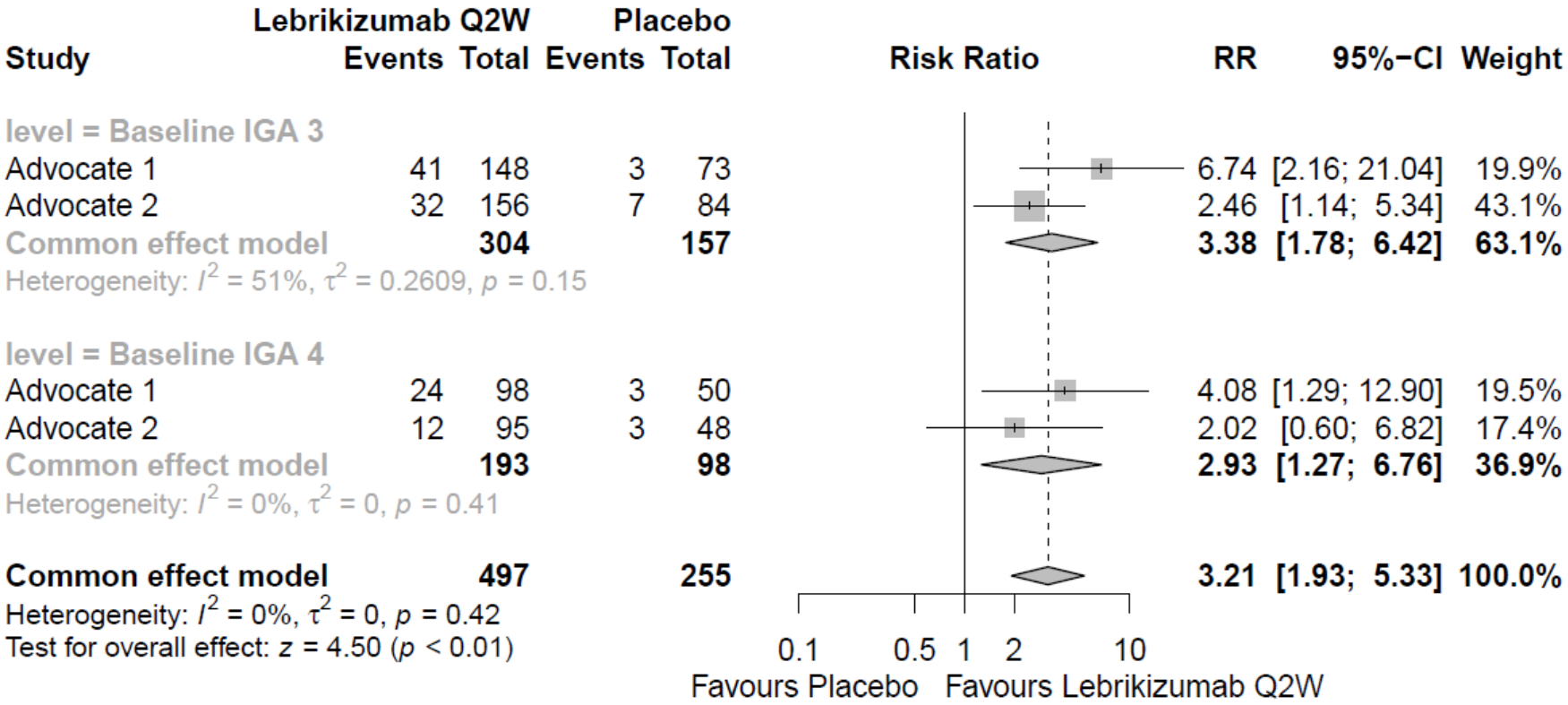


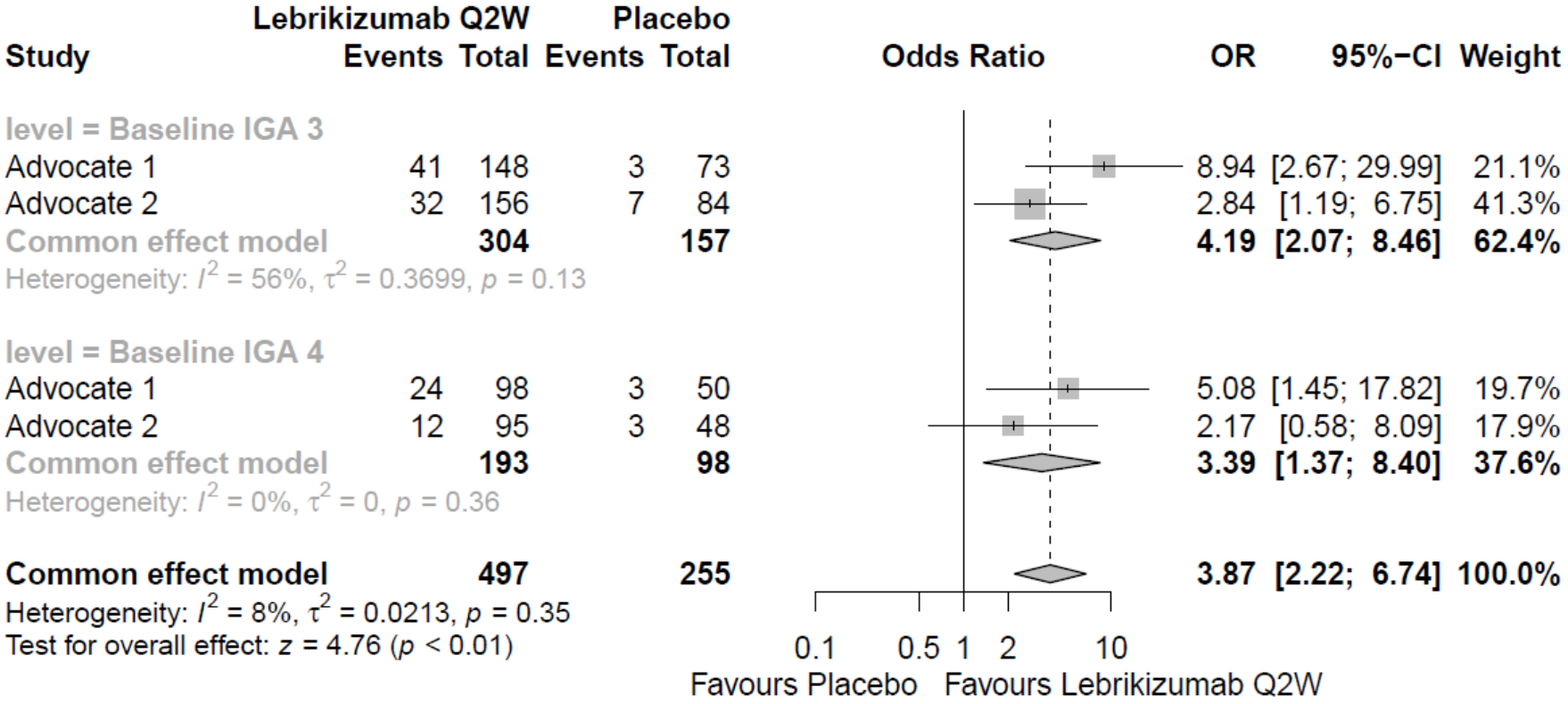

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Female
Advocate 1 38 141 2 73 13.10 [3.06; 56.04] 21.1%
Advocate 2 21 136 3 75 4.38 [1.26; 15.22] 28.8%
Common effect model 277 148 6.96 [2.71; 17.93] 49.9%
Heterogeneity: I^2 = 20%, τ^2 = 0.1224, p = 0.26
level = Male
Advocate 1 35 142 2 68 10.79 [2.51; 46.37] 21.0%
Advocate 2 23 145 3 71 4.27 [1.24; 14.75] 29.1%
Common effect model 287 139 6.30 [2.45; 16.20] 50.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.34
Common effect model 564 287 6.63 [3.40; 12.92] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.54
Test for overall effect: z = 5.55 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo
Favours Lebrikizumab Q2W

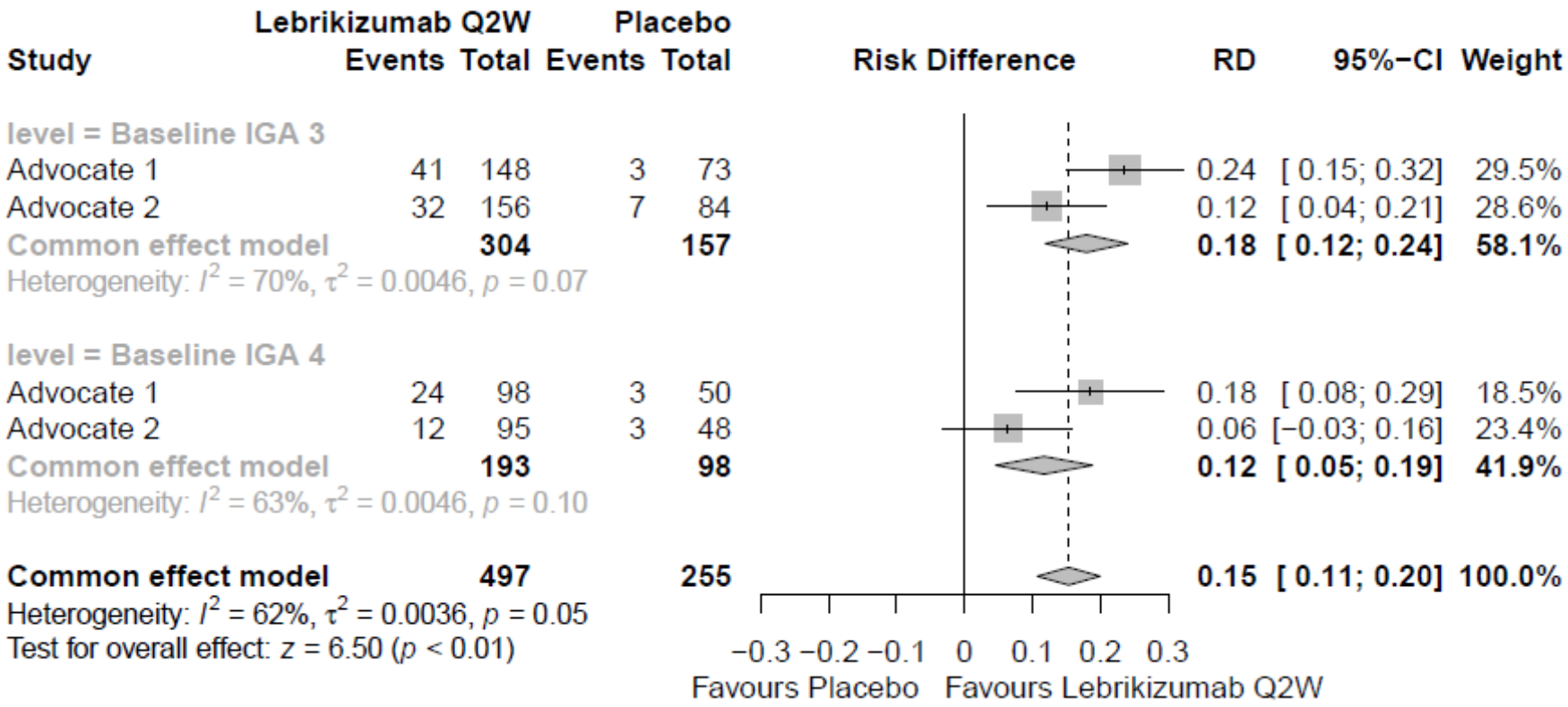

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Female
Advocate 1 38 141 2 73 0.24 [0.16; 0.32] 22.7%
Advocate 2 21 136 3 75 0.11 [0.04; 0.19] 27.2%
Common effect model 277 148 0.17 [0.12; 0.23] 49.9%
Heterogeneity: I^2 = 80%, τ^2 = 0.0065, p = 0.02
level = Male
Advocate 1 35 142 2 68 0.22 [0.14; 0.30] 23.2%
Advocate 2 23 145 3 71 0.12 [0.04; 0.19] 26.9%
Common effect model 287 139 0.16 [0.11; 0.22] 50.1%
Heterogeneity: I^2 = 68%, τ^2 = 0.0035, p = 0.08
Common effect model 564 287 0.17 [0.13; 0.21] 100.0%
Heterogeneity: I^2 = 64%, τ^2 = 0.0028, p = 0.04
Test for overall effect: z = 8.38 (p < 0.01)
−0.3 −0.2 −0.1 0 0.1 0.2 0.3
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.12 DLQI 0 / 1

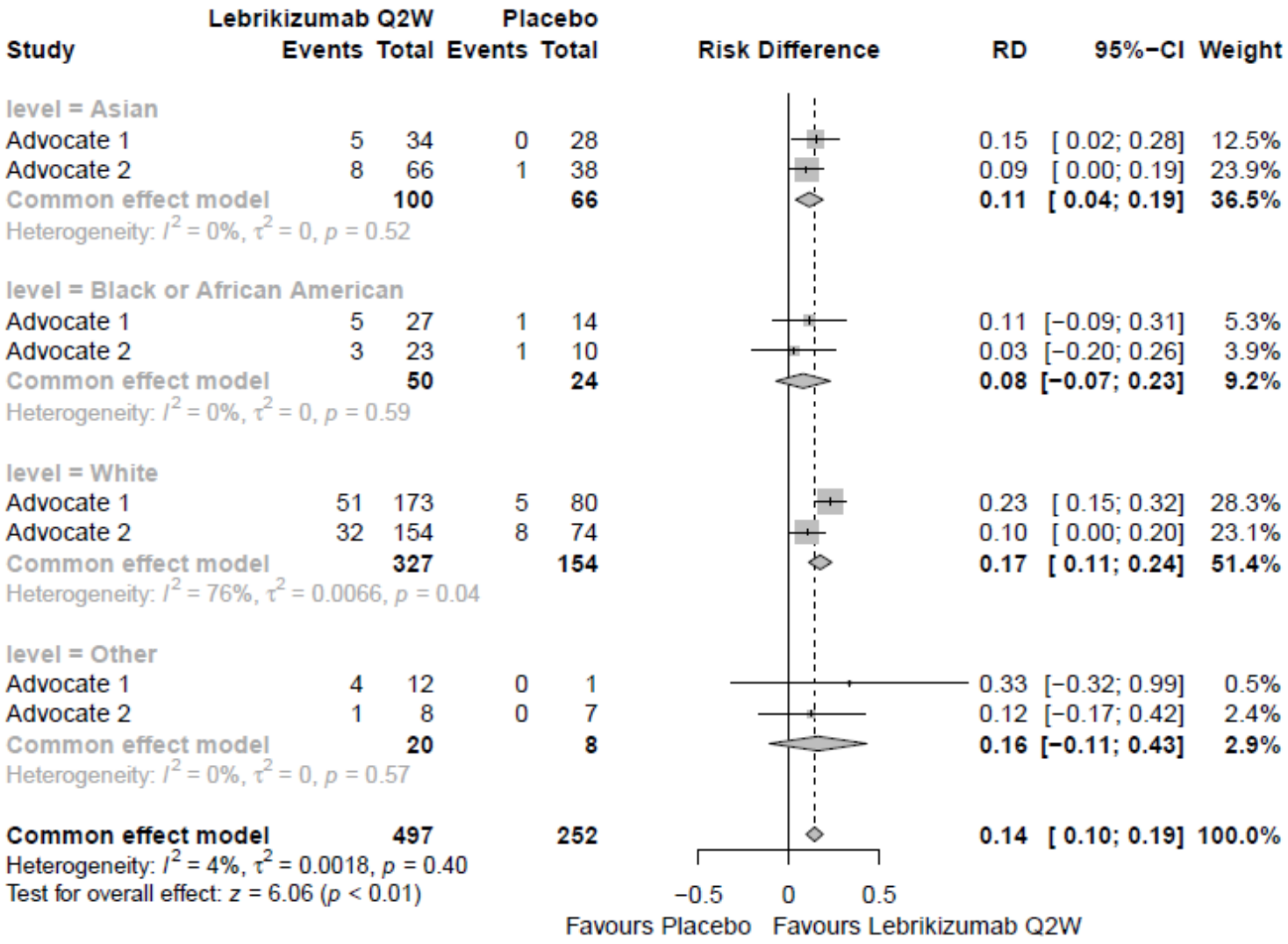
4.5.1.12.1 Krankheitsschwere



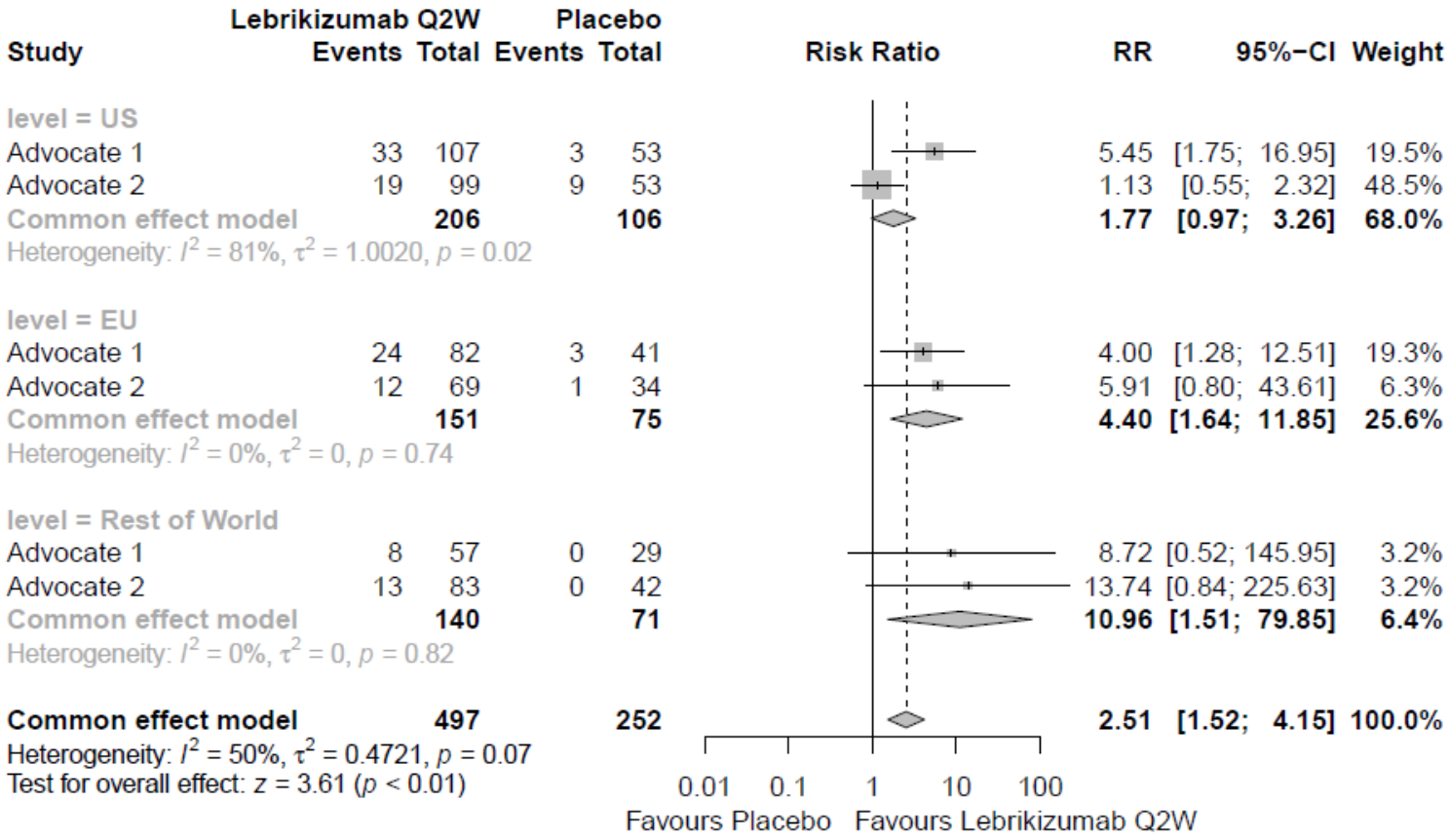

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Baseline IGA 3
Advocate 1 41 148 3 73 8.94 [2.67; 29.99] 21.1%
Advocate 2 32 156 7 84 2.84 [1.19; 6.75] 41.3%
Common effect model 304 157 4.19 [2.07; 8.46] 62.4%
Heterogeneity: I^2 = 56%, τ^2 = 0.3699, p = 0.13
level = Baseline IGA 4
Advocate 1 24 98 3 50 5.08 [1.45; 17.82] 19.7%
Advocate 2 12 95 3 48 2.17 [0.58; 8.09] 17.9%
Common effect model 193 98 3.39 [1.37; 8.40] 37.6%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.36
Common effect model 497 255 3.87 [2.22; 6.74] 100.0%
Heterogeneity: I^2 = 8%, τ^2 = 0.0213, p = 0.35
Test for overall effect: z = 4.76 (p < 0.01)
0.1
0.5
1
2
10
Favours Placebo
Favours Lebrikizumab Q2W

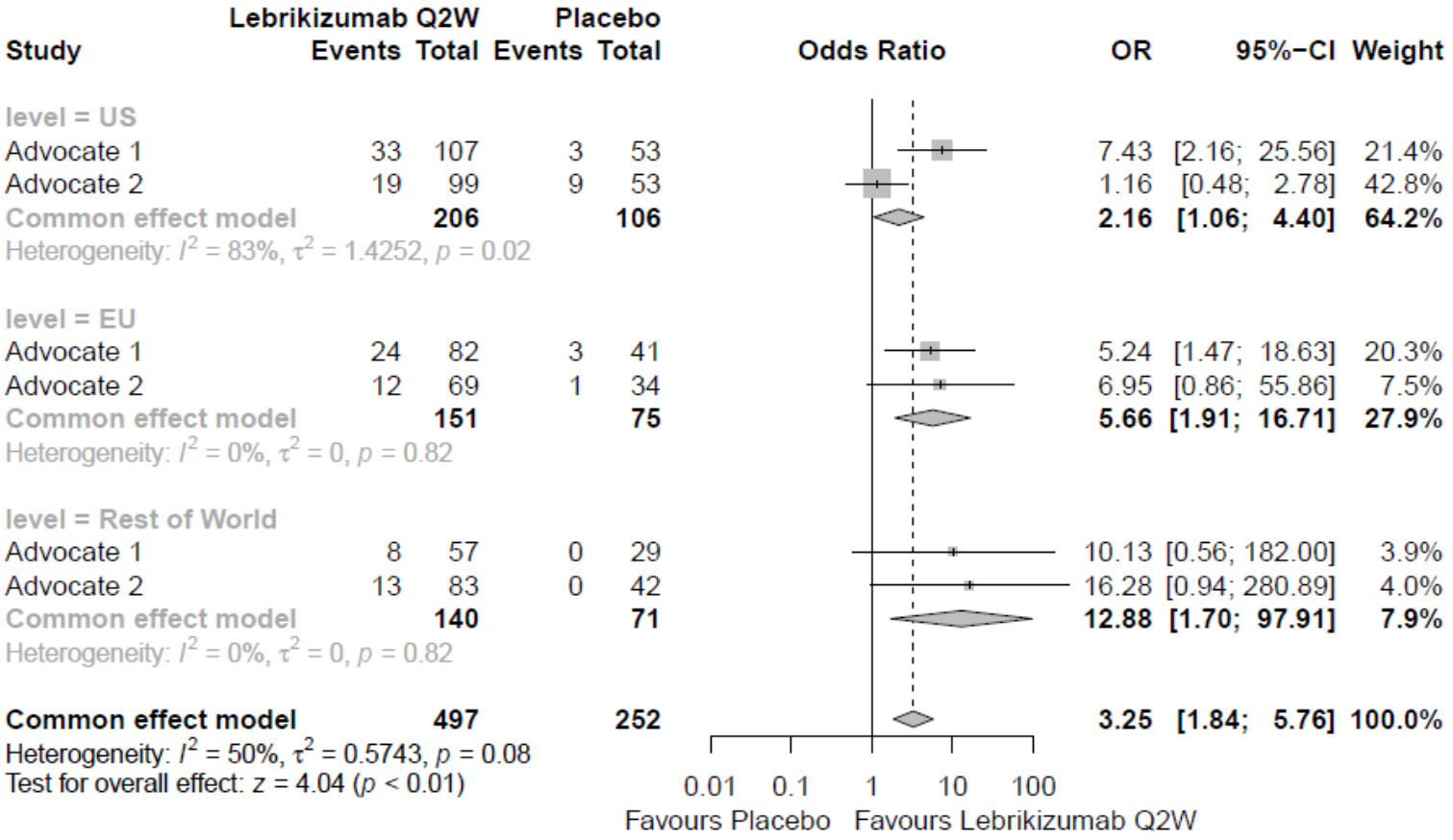

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Baseline IGA 3
Advocate 1 41 148 3 73 0.24 [0.15; 0.32] 29.5%
Advocate 2 32 156 7 84 0.12 [0.04; 0.21] 28.6%
Common effect model 304 157 0.18 [0.12; 0.24] 58.1%
Heterogeneity: I^2 = 70%, τ^2 = 0.0046, p = 0.07
level = Baseline IGA 4
Advocate 1 24 98 3 50 0.18 [0.08; 0.29] 18.5%
Advocate 2 12 95 3 48 0.06 [−0.03; 0.16] 23.4%
Common effect model 193 98 0.12 [0.05; 0.19] 41.9%
Heterogeneity: I^2 = 63%, τ^2 = 0.0046, p = 0.10
Common effect model 497 255 0.15 [0.11; 0.20] 100.0%
Heterogeneity: I^2 = 62%, τ^2 = 0.0036, p = 0.05
Test for overall effect: z = 6.50 (p < 0.01)
−0.3 −0.2 −0.1 0 0.1 0.2 0.3
Favours Placebo
Favours Lebrikizumab Q2W

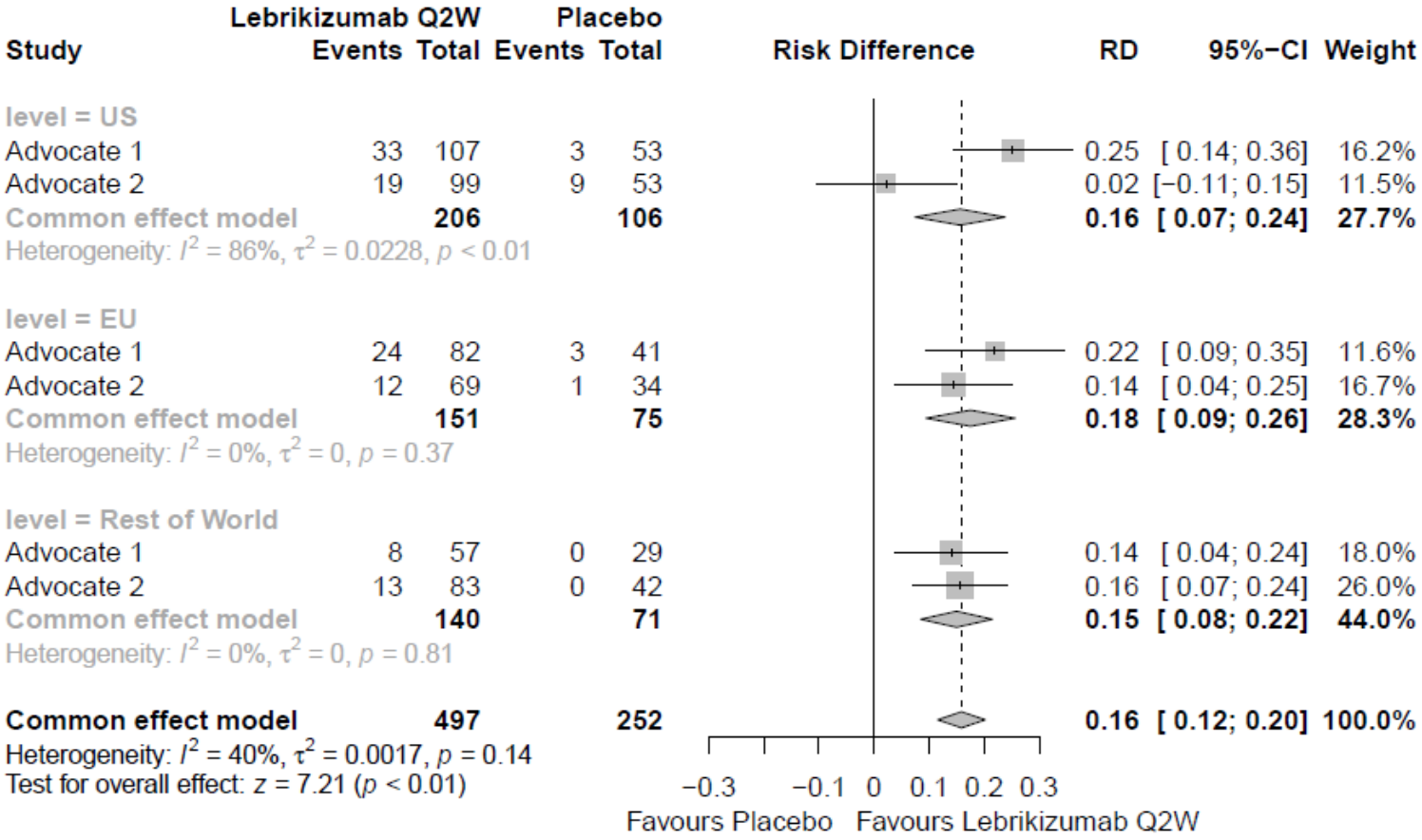
4.5.1.12.2 Ethnie



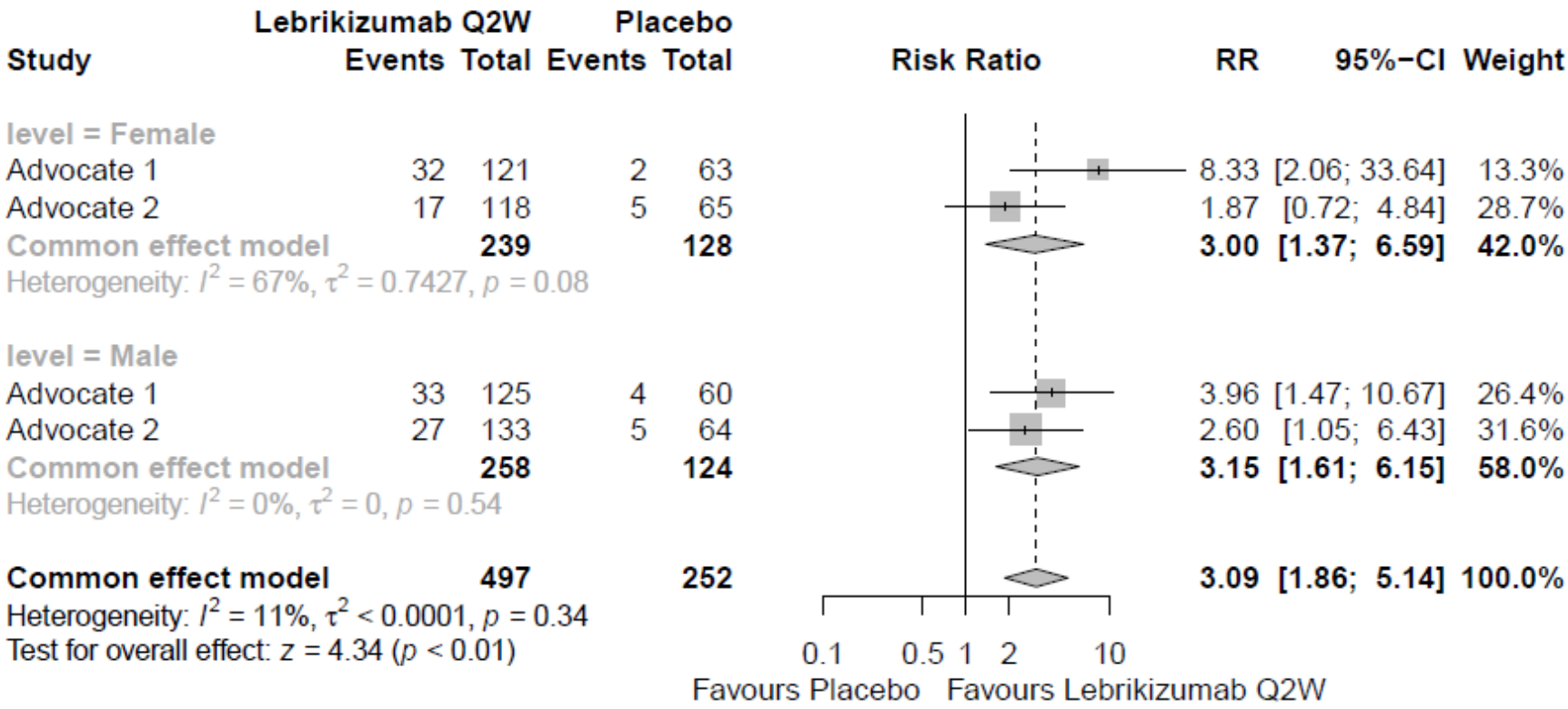
4.5.1.12.3 Region

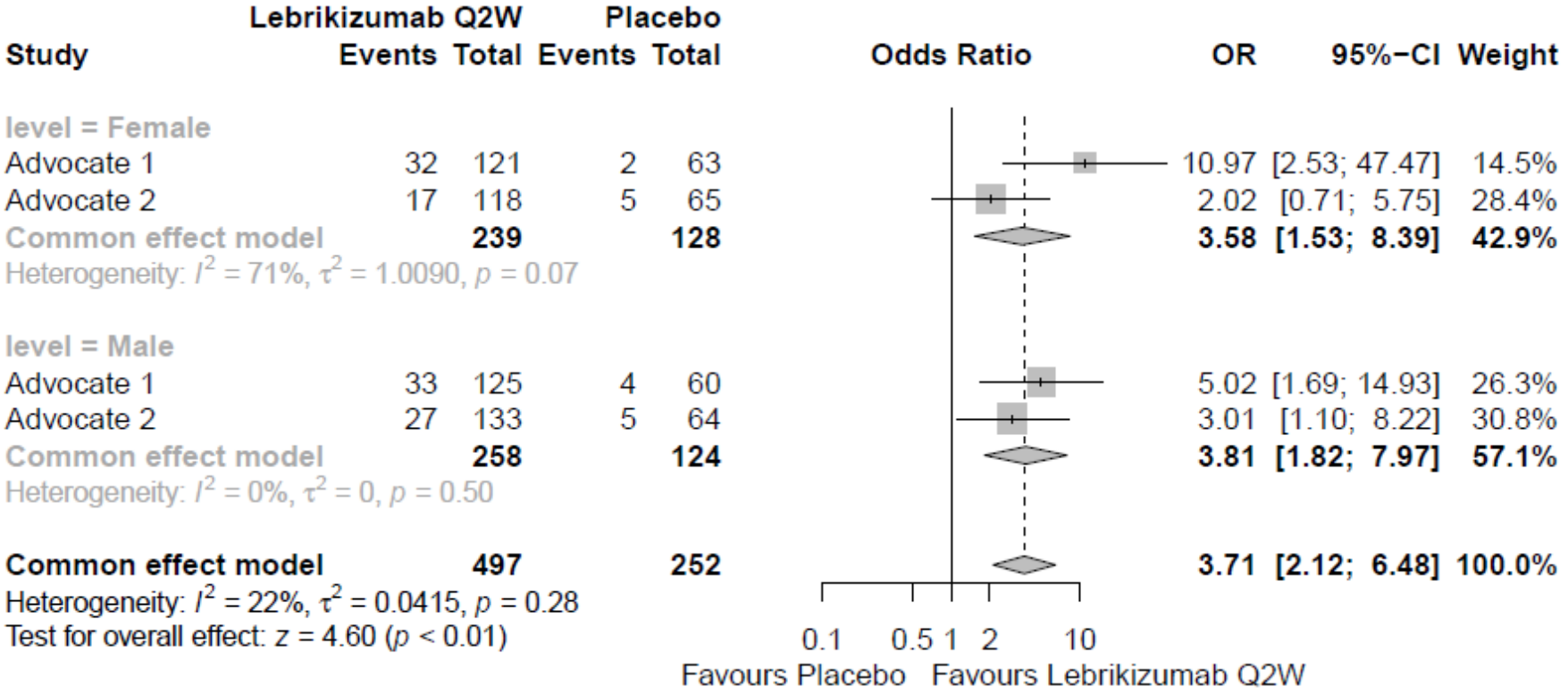


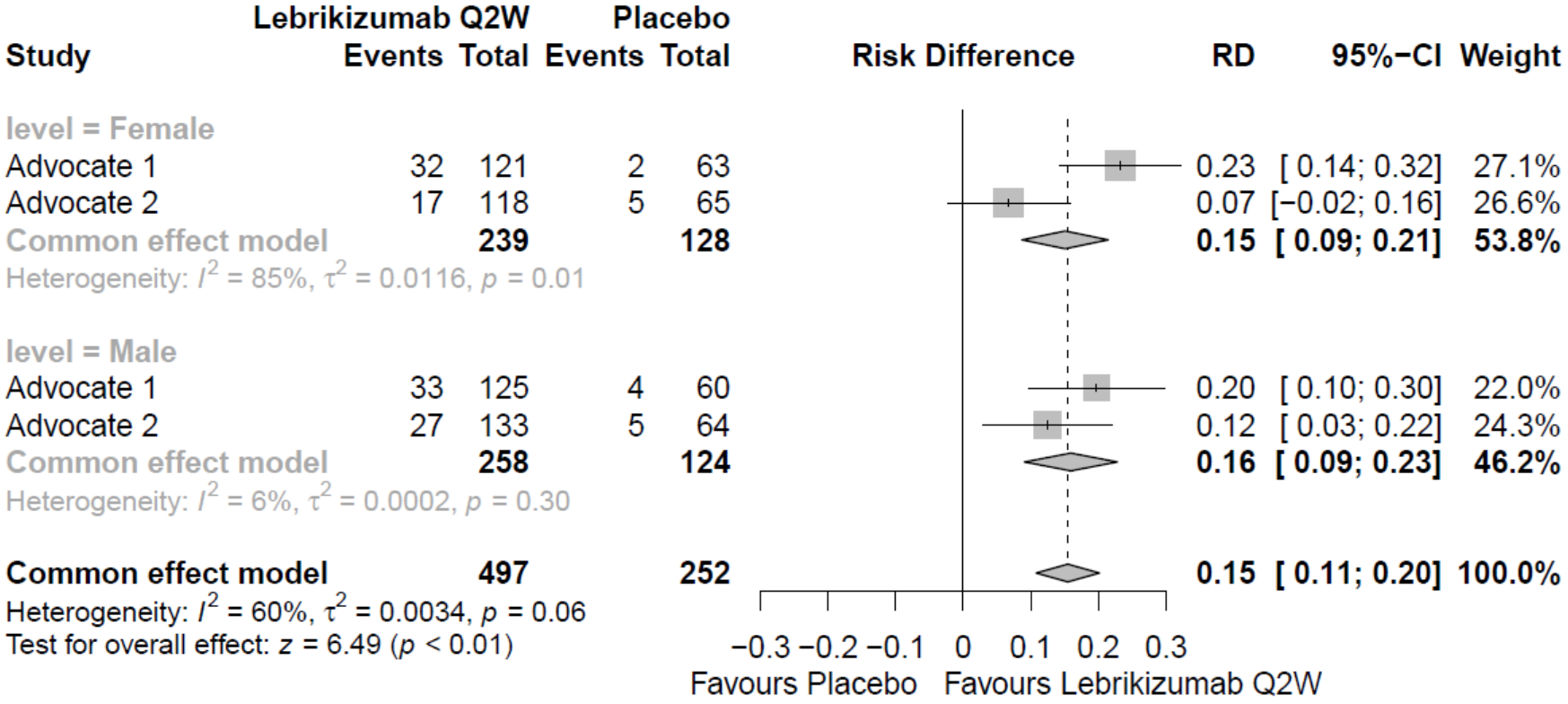

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = US
Advocate 1 33 107 3 53 7.43 [2.16; 25.56] 21.4%
Advocate 2 19 99 9 53 1.16 [0.48; 2.78] 42.8%
Common effect model 206 106 2.16 [1.06; 4.40] 64.2%
Heterogeneity: I^2 = 83%, τ^2 = 1.4252, p = 0.02
level = EU
Advocate 1 24 82 3 41 5.24 [1.47; 18.63] 20.3%
Advocate 2 12 69 1 34 6.95 [0.86; 55.86] 7.5%
Common effect model 151 75 5.66 [1.91; 16.71] 27.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.82
level = Rest of World
Advocate 1 8 57 0 29 10.13 [0.56; 182.00] 3.9%
Advocate 2 13 83 0 42 16.28 [0.94; 280.89] 4.0%
Common effect model 140 71 12.88 [1.70; 97.91] 7.9%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.82
Common effect model 497 252 3.25 [1.84; 5.76] 100.0%
Heterogeneity: I^2 = 50%, τ^2 = 0.5743, p = 0.08
Test for overall effect: z = 4.04 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = US
Advocate 1 33 107 3 53 0.25 [0.14; 0.36] 16.2%
Advocate 2 19 99 9 53 0.02 [−0.11; 0.15] 11.5%
Common effect model 206 106 0.16 [0.07; 0.24] 27.7%
Heterogeneity: I^2 = 86%, τ^2 = 0.0228, p < 0.01
level = EU
Advocate 1 24 82 3 41 0.22 [0.09; 0.35] 11.6%
Advocate 2 12 69 1 34 0.14 [0.04; 0.25] 16.7%
Common effect model 151 75 0.18 [0.09; 0.26] 28.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.37
level = Rest of World
Advocate 1 8 57 0 29 0.14 [0.04; 0.24] 18.0%
Advocate 2 13 83 0 42 0.16 [0.07; 0.24] 26.0%
Common effect model 140 71 0.15 [0.08; 0.22] 44.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.81
Common effect model 497 252 0.16 [0.12; 0.20] 100.0%
Heterogeneity: I^2 = 40%, τ^2 = 0.0017, p = 0.14
Test for overall effect: z = 7.21 (p < 0.01)
−0.3 −0.1 0 0.1 0.2 0.3
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.12.4 Geschlecht

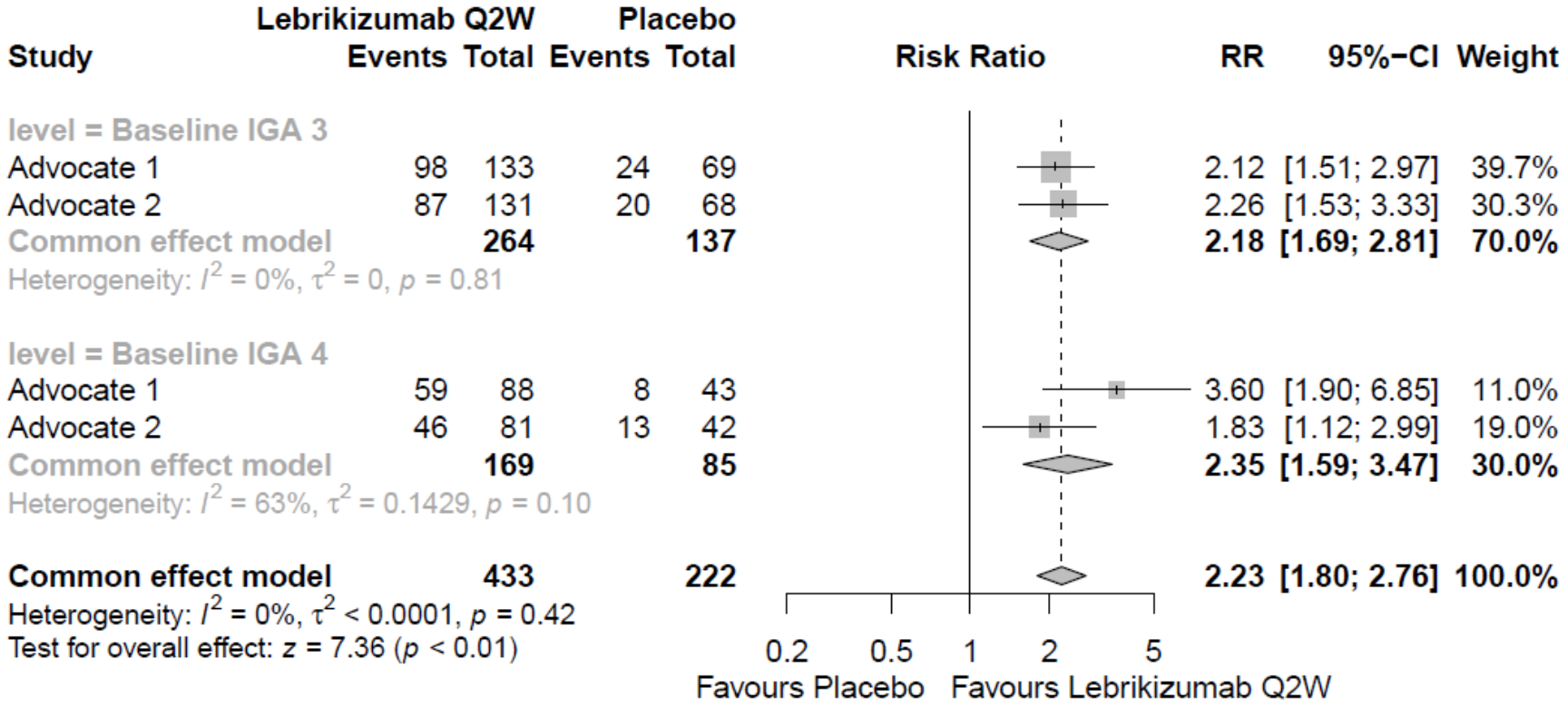


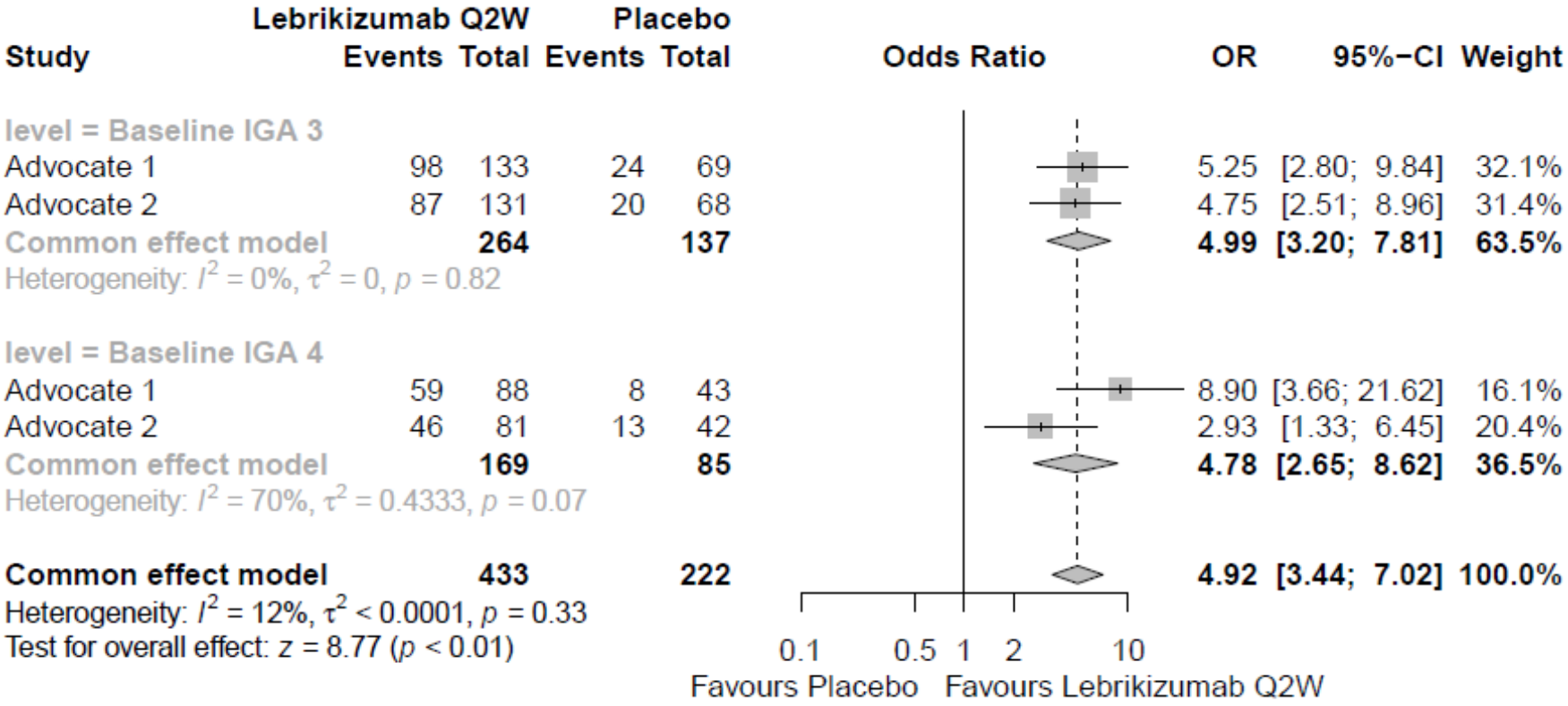

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Female
Advocate 1 32 121 2 63 10.97 [2.53; 47.47] 14.5%
Advocate 2 17 118 5 65 2.02 [0.71; 5.75] 28.4%
Common effect model 239 128 3.58 [1.53; 8.39] 42.9%
Heterogeneity: I^2 = 71%, τ^2 = 1.0090, p = 0.07
level = Male
Advocate 1 33 125 4 60 5.02 [1.69; 14.93] 26.3%
Advocate 2 27 133 5 64 3.01 [1.10; 8.22] 30.8%
Common effect model 258 124 3.81 [1.82; 7.97] 57.1%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.50
Common effect model 497 252 3.71 [2.12; 6.48] 100.0%
Heterogeneity: I^2 = 22%, τ^2 = 0.0415, p = 0.28
Test for overall effect: z = 4.60 (p < 0.01)
0.1 0.5 1 2 10
Favours Placebo
Favours Lebrikizumab Q2W

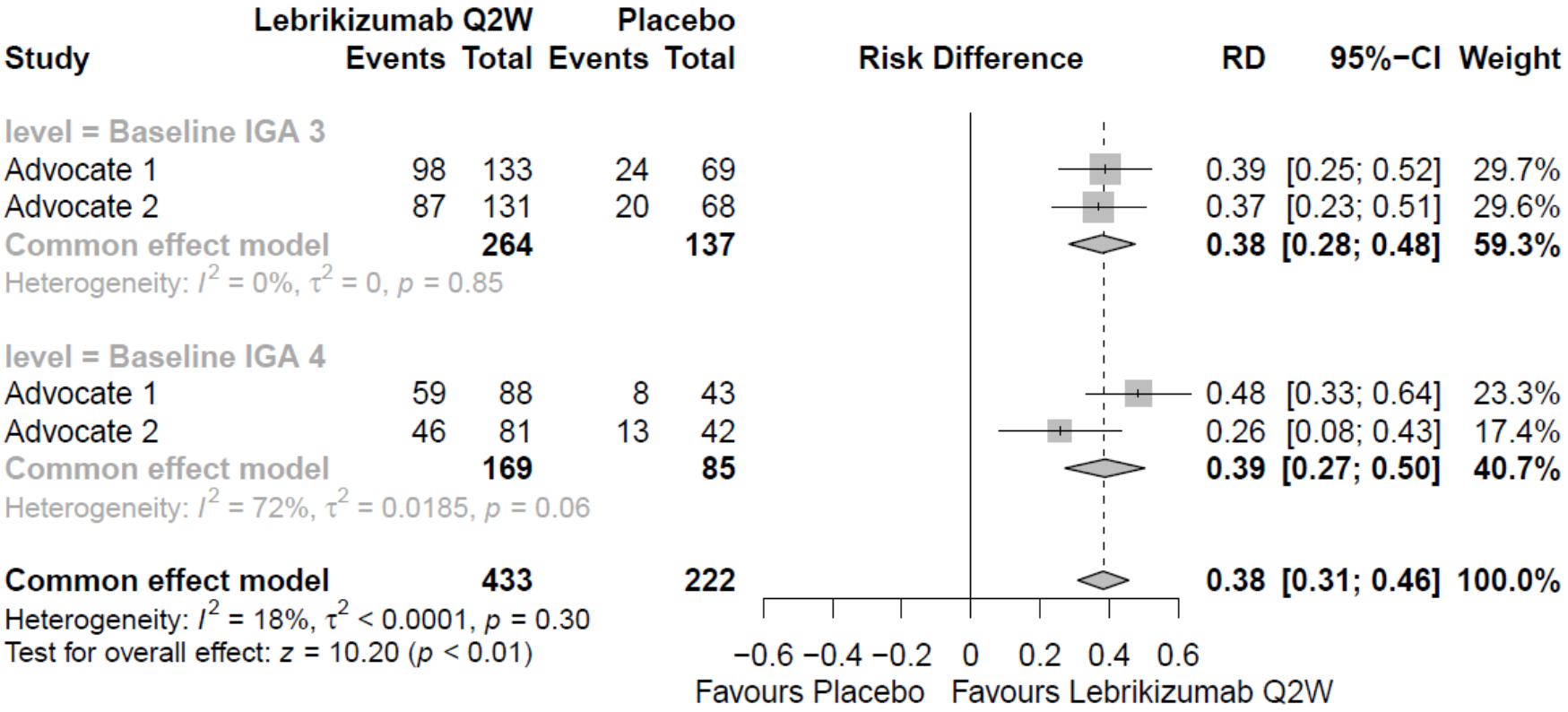

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Female
Advocate 1 32 121 2 63 0.23 [0.14; 0.32] 27.1%
Advocate 2 17 118 5 65 0.07 [−0.02; 0.16] 26.6%
Common effect model 239 128 0.15 [0.09; 0.21] 53.8%
Heterogeneity: I^2 = 85%, τ^2 = 0.0116, p = 0.01
level = Male
Advocate 1 33 125 4 60 0.20 [0.10; 0.30] 22.0%
Advocate 2 27 133 5 64 0.12 [0.03; 0.22] 24.3%
Common effect model 258 124 0.16 [0.09; 0.23] 46.2%
Heterogeneity: I^2 = 6%, τ^2 = 0.0002, p = 0.30
Common effect model 497 252 0.15 [0.11; 0.20] 100.0%
Heterogeneity: I^2 = 60%, τ^2 = 0.0034, p = 0.06
Test for overall effect: z = 6.49 (p < 0.01)
−0.3 −0.2 −0.1 0 0.1 0.2 0.3
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.13 DLQI Verbesserung um 4 Punkte

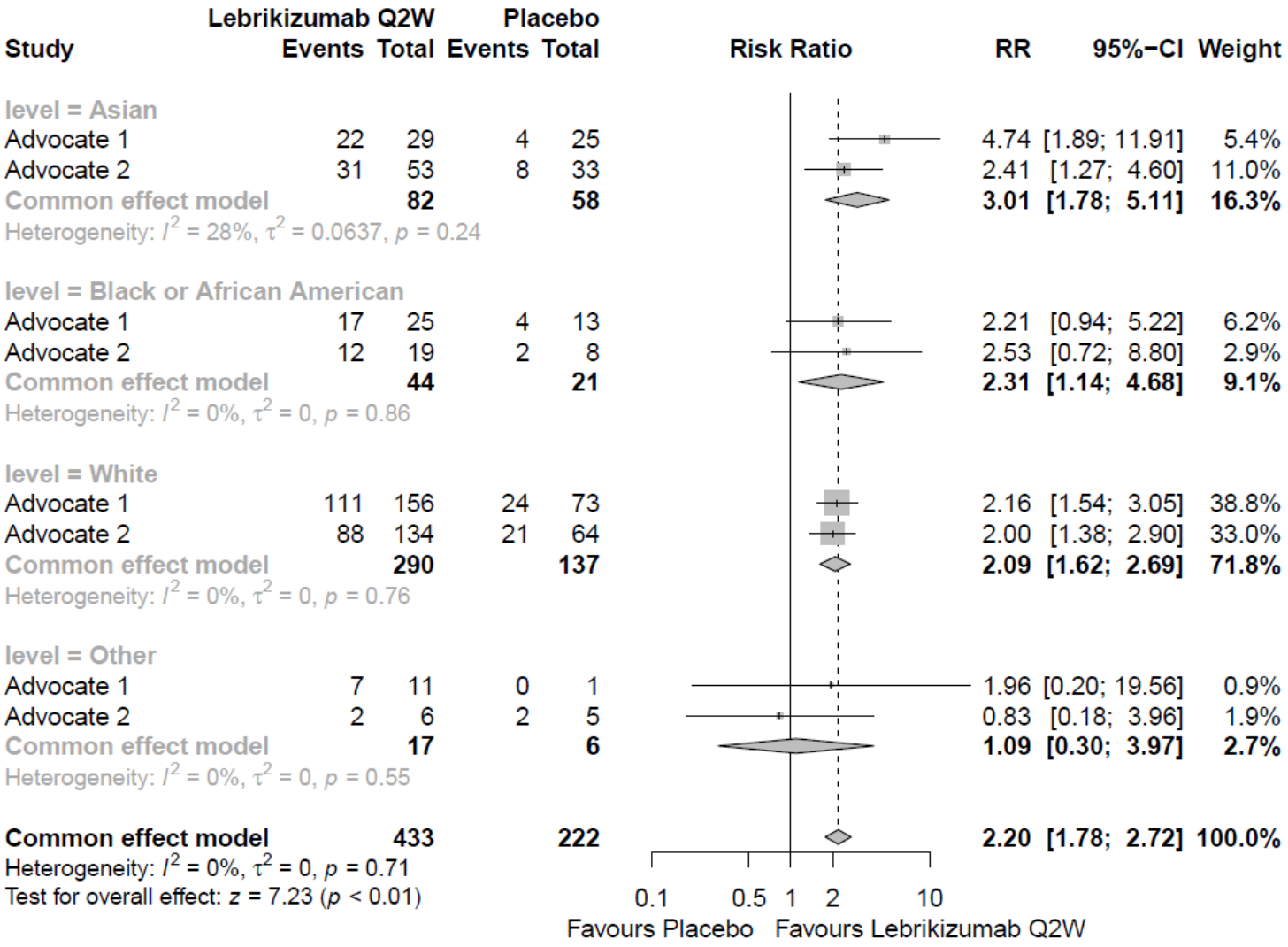
4.5.1.13.1 Krankheitsschwere

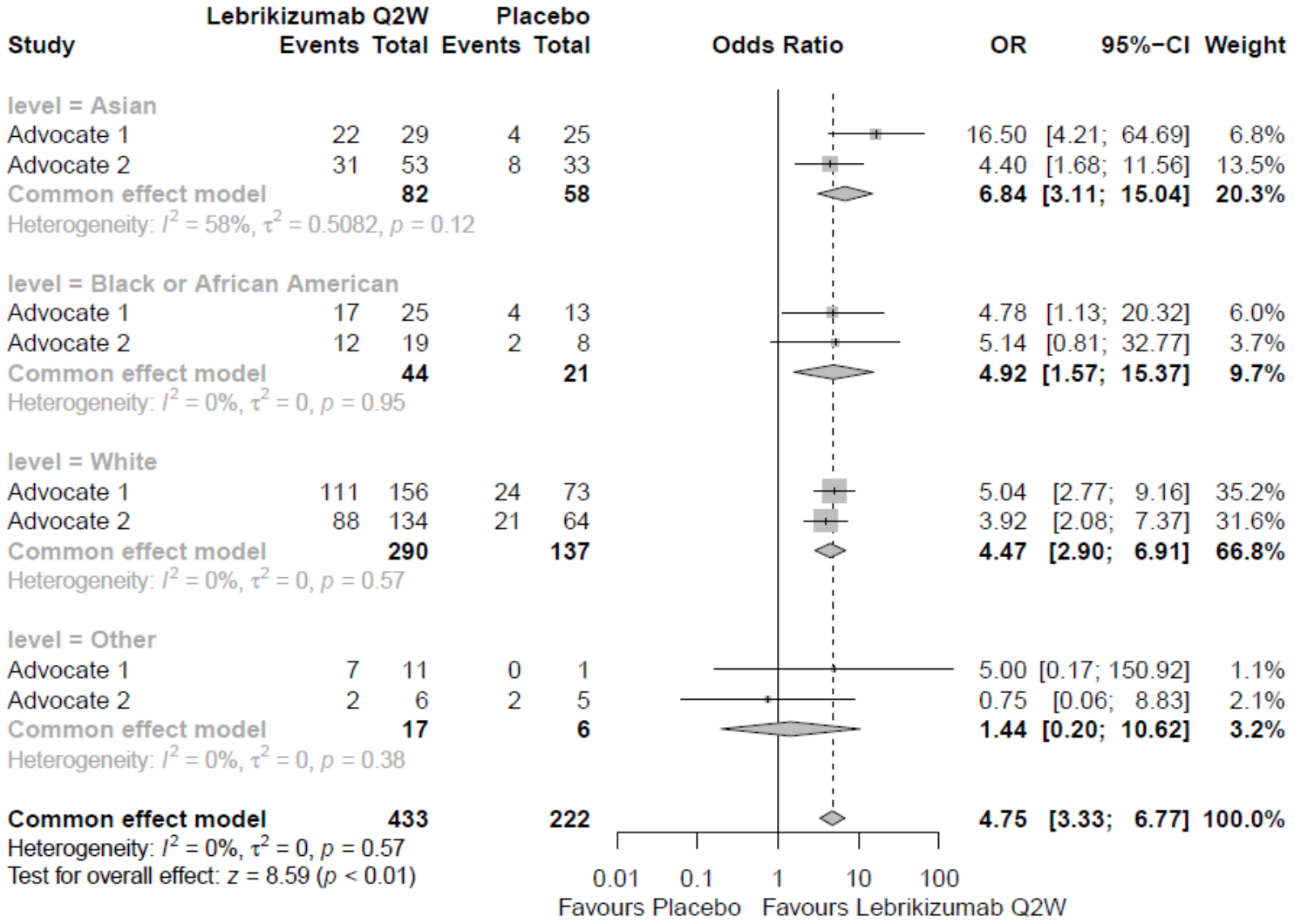


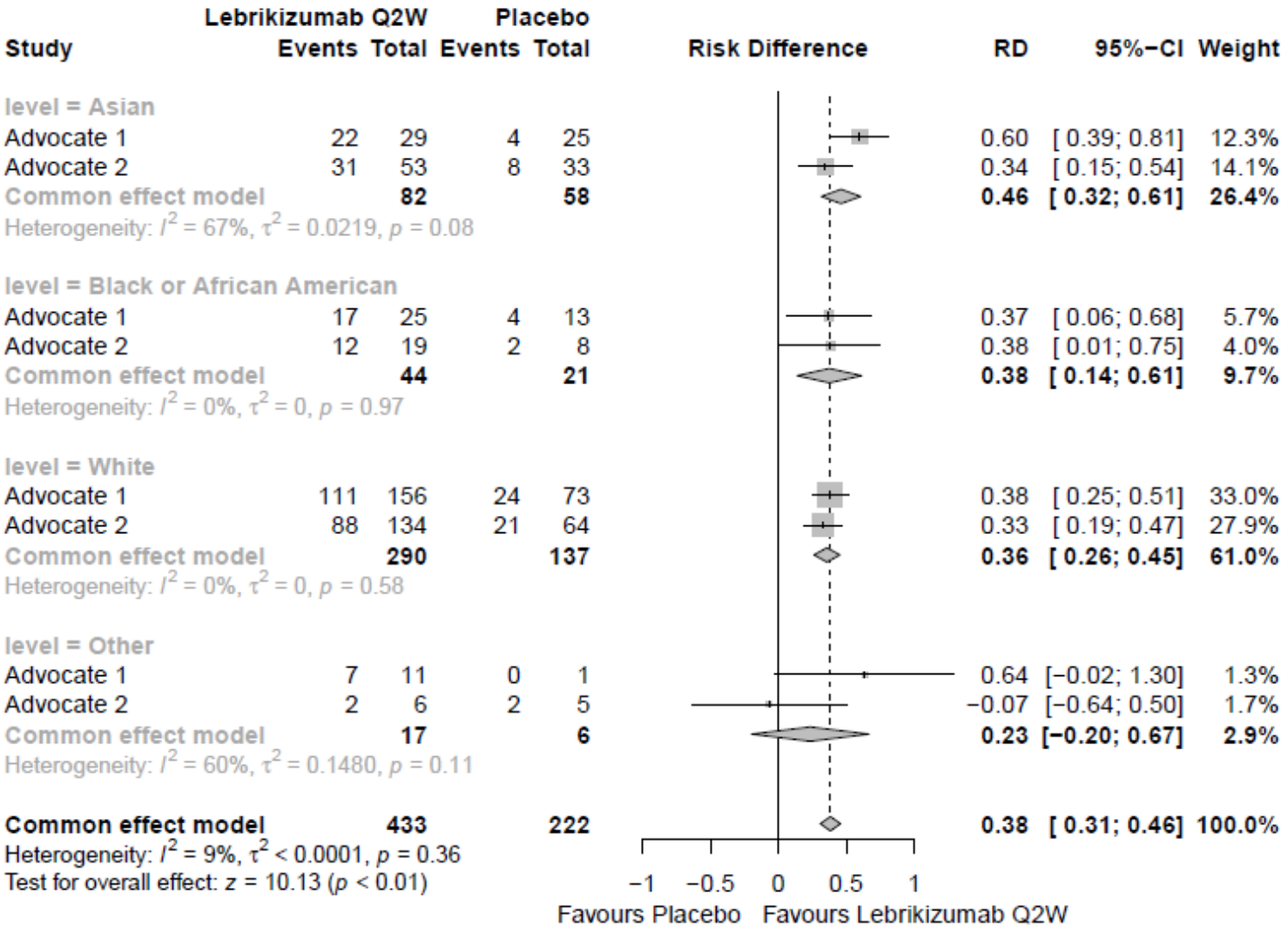

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Baseline IGA 3
Advocate 1 98 133 24 69 5.25 [2.80; 9.84] 32.1%
Advocate 2 87 131 20 68 4.75 [2.51; 8.96] 31.4%
Common effect model 264 137 4.99 [3.20; 7.81] 63.5%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.82
level = Baseline IGA 4
Advocate 1 59 88 8 43 8.90 [3.66; 21.62] 16.1%
Advocate 2 46 81 13 42 2.93 [1.33; 6.45] 20.4%
Common effect model 169 85 4.78 [2.65; 8.62] 36.5%
Heterogeneity: I^2 = 70%, τ^2 = 0.4333, p = 0.07
Common effect model 433 222 4.92 [3.44; 7.02] 100.0%
Heterogeneity: I^2 = 12%, τ^2 < 0.0001, p = 0.33
Test for overall effect: z = 8.77 (p < 0.01)
0.1
0.5
1
2
10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Baseline IGA 3
Advocate 1 98 133 24 69 0.39 [0.25; 0.52] 29.7%
Advocate 2 87 131 20 68 0.37 [0.23; 0.51] 29.6%
Common effect model 264 137 0.38 [0.28; 0.48] 59.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.85
level = Baseline IGA 4
Advocate 1 59 88 8 43 0.48 [0.33; 0.64] 23.3%
Advocate 2 46 81 13 42 0.26 [0.08; 0.43] 17.4%
Common effect model 169 85 0.39 [0.27; 0.50] 40.7%
Heterogeneity: I^2 = 72%, τ^2 = 0.0185, p = 0.06
Common effect model 433 222 0.38 [0.31; 0.46] 100.0%
Heterogeneity: I^2 = 18%, τ^2 < 0.0001, p = 0.30
Test for overall effect: z = 10.20 (p < 0.01)
−0.6 −0.4 −0.2 0 0.2 0.4 0.6
Favours Placebo
Favours Lebrikizumab Q2W

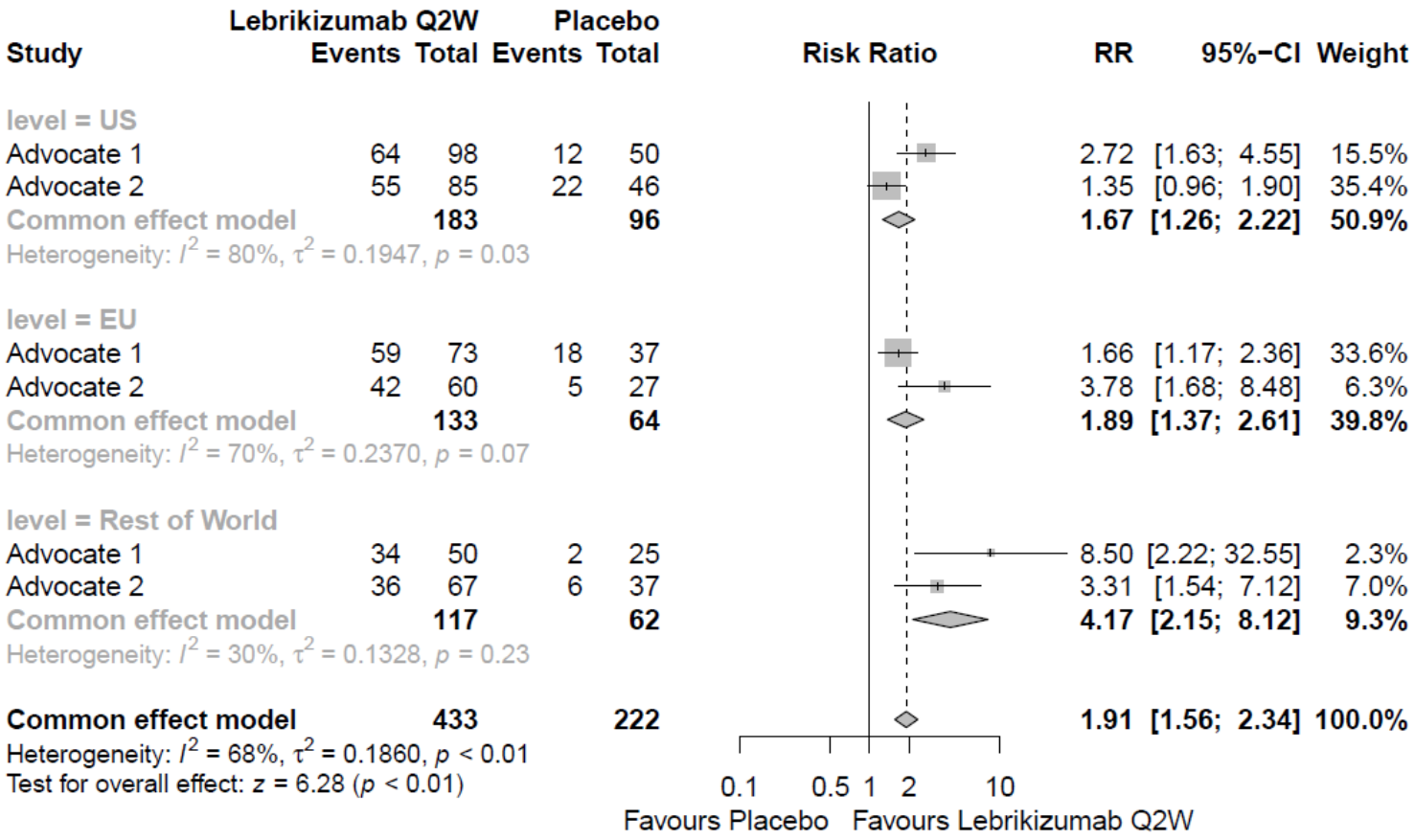
4.5.1.13.2 Ethnie

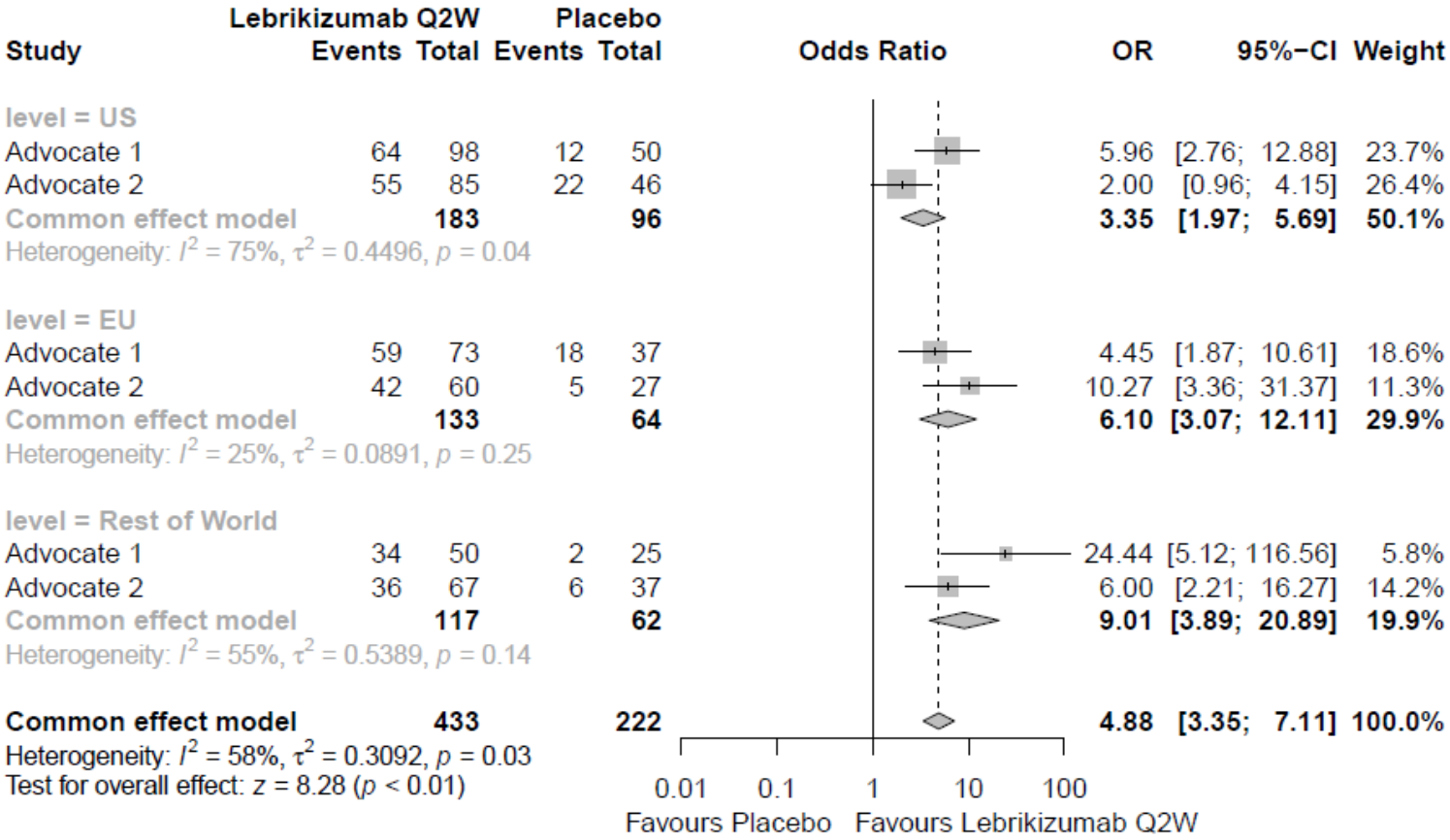


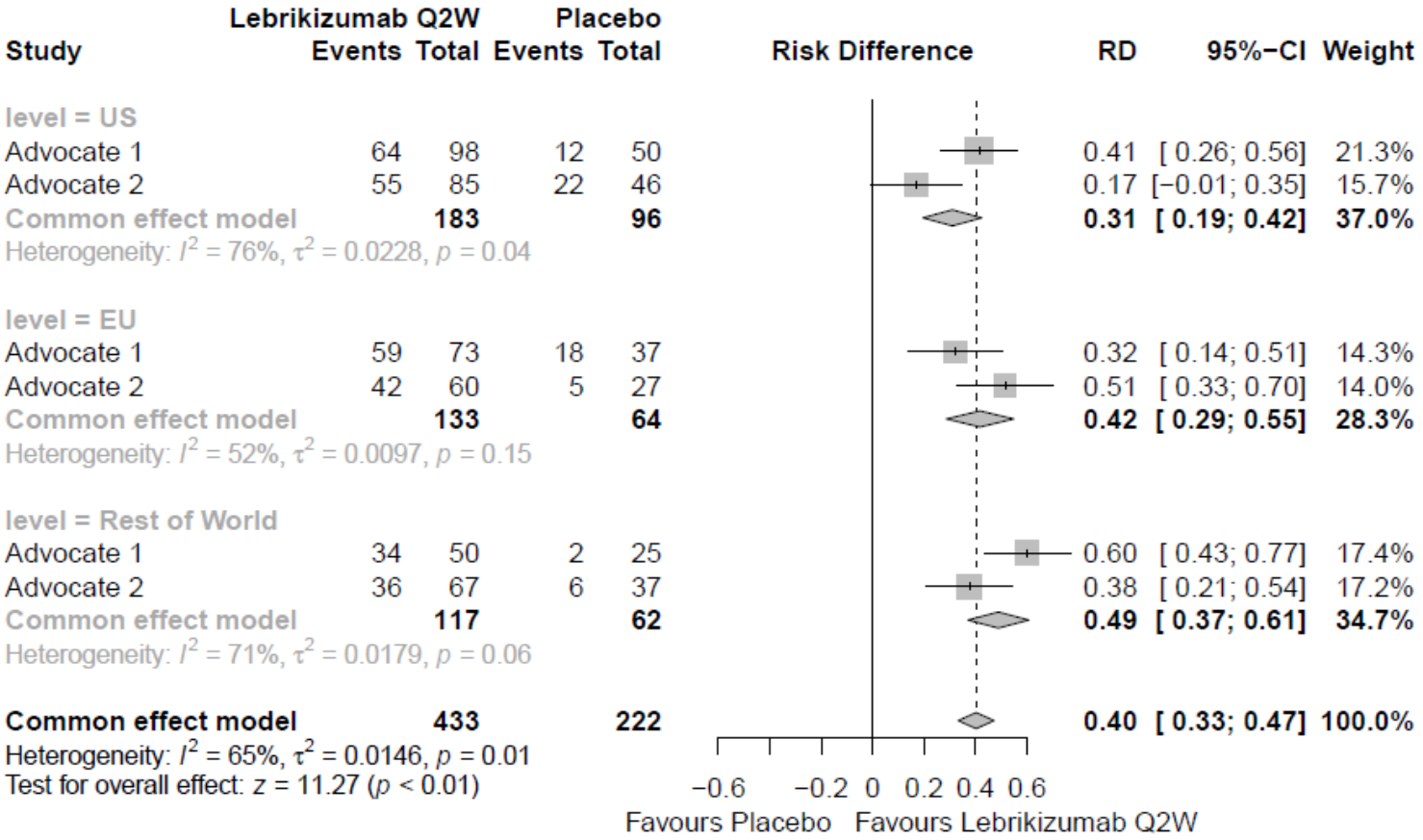

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Asian
Advocate 1 22 29 4 25 16.50 [4.21; 64.69] 6.8%
Advocate 2 31 53 8 33 4.40 [1.68; 11.56] 13.5%
Common effect model 82 58 6.84 [3.11; 15.04] 20.3%
Heterogeneity: I^2 = 58%, τ^2 = 0.5082, p = 0.12
level = Black or African American
Advocate 1 17 25 4 13 4.78 [1.13; 20.32] 6.0%
Advocate 2 12 19 2 8 5.14 [0.81; 32.77] 3.7%
Common effect model 44 21 4.92 [1.57; 15.37] 9.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.95
level = White
Advocate 1 111 156 24 73 5.04 [2.77; 9.16] 35.2%
Advocate 2 88 134 21 64 3.92 [2.08; 7.37] 31.6%
Common effect model 290 137 4.47 [2.90; 6.91] 66.8%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.57
level = Other
Advocate 1 7 11 0 1 5.00 [0.17; 150.92] 1.1%
Advocate 2 2 6 2 5 0.75 [0.06; 8.83] 2.1%
Common effect model 17 6 1.44 [0.20; 10.62] 3.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.38
Common effect model 433 222 4.75 [3.33; 6.77] 100.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.57
Test for overall effect: z = 8.59 (p < 0.01)
0.01 0.1 1 10 100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Asian
Advocate 1 22 29 4 25 0.60 [0.39; 0.81] 12.3%
Advocate 2 31 53 8 33 0.34 [0.15; 0.54] 14.1%
Common effect model 82 58 0.46 [0.32; 0.61] 26.4%
Heterogeneity: I^2 = 67%, τ^2 = 0.0219, p = 0.08
level = Black or African American
Advocate 1 17 25 4 13 0.37 [0.06; 0.68] 5.7%
Advocate 2 12 19 2 8 0.38 [0.01; 0.75] 4.0%
Common effect model 44 21 0.38 [0.14; 0.61] 9.7%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.97
level = White
Advocate 1 111 156 24 73 0.38 [0.25; 0.51] 33.0%
Advocate 2 88 134 21 64 0.33 [0.19; 0.47] 27.9%
Common effect model 290 137 0.36 [0.26; 0.45] 61.0%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.58
level = Other
Advocate 1 7 11 0 1 0.64 [−0.02; 1.30] 1.3%
Advocate 2 2 6 2 5 −0.07 [−0.64; 0.50] 1.7%
Common effect model 17 6 0.23 [−0.20; 0.67] 2.9%
Heterogeneity: I^2 = 60%, τ^2 = 0.1480, p = 0.11
Common effect model 433 222 0.38 [0.31; 0.46] 100.0%
Heterogeneity: I^2 = 9%, τ^2 < 0.0001, p = 0.36
Test for overall effect: z = 10.13 (p < 0.01)
−1 −0.5 0 0.5 1
Favours Placebo
Favours Lebrikizumab Q2W

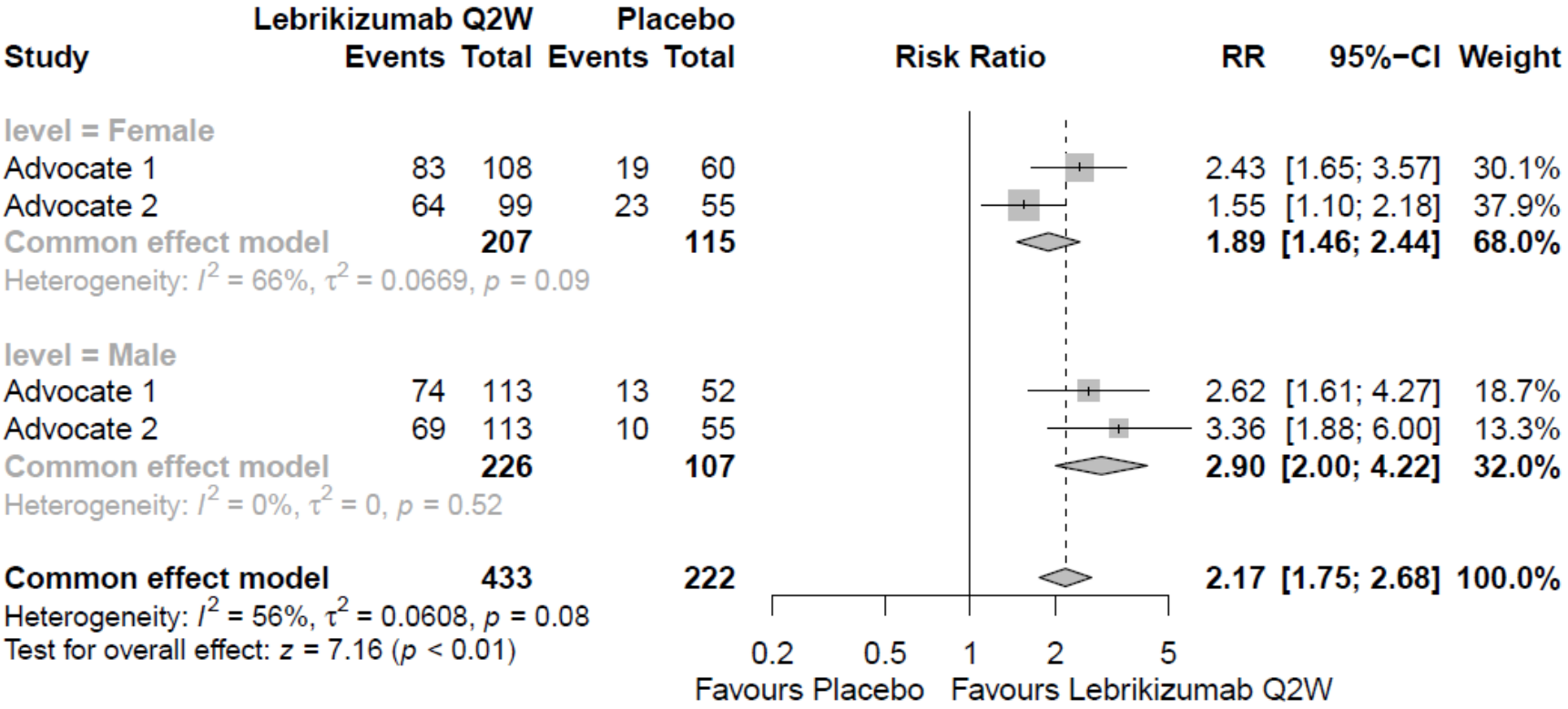
4.5.1.13.3 Region

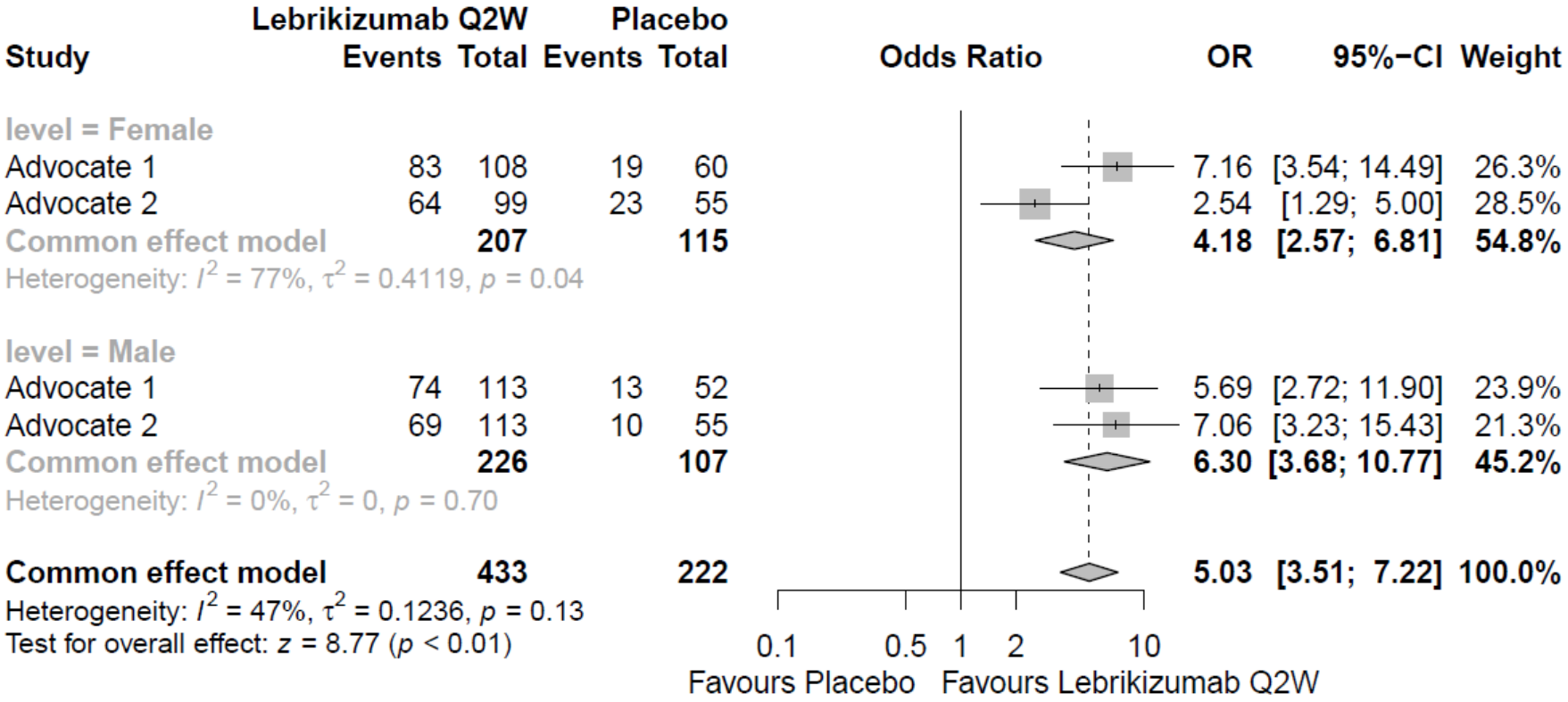


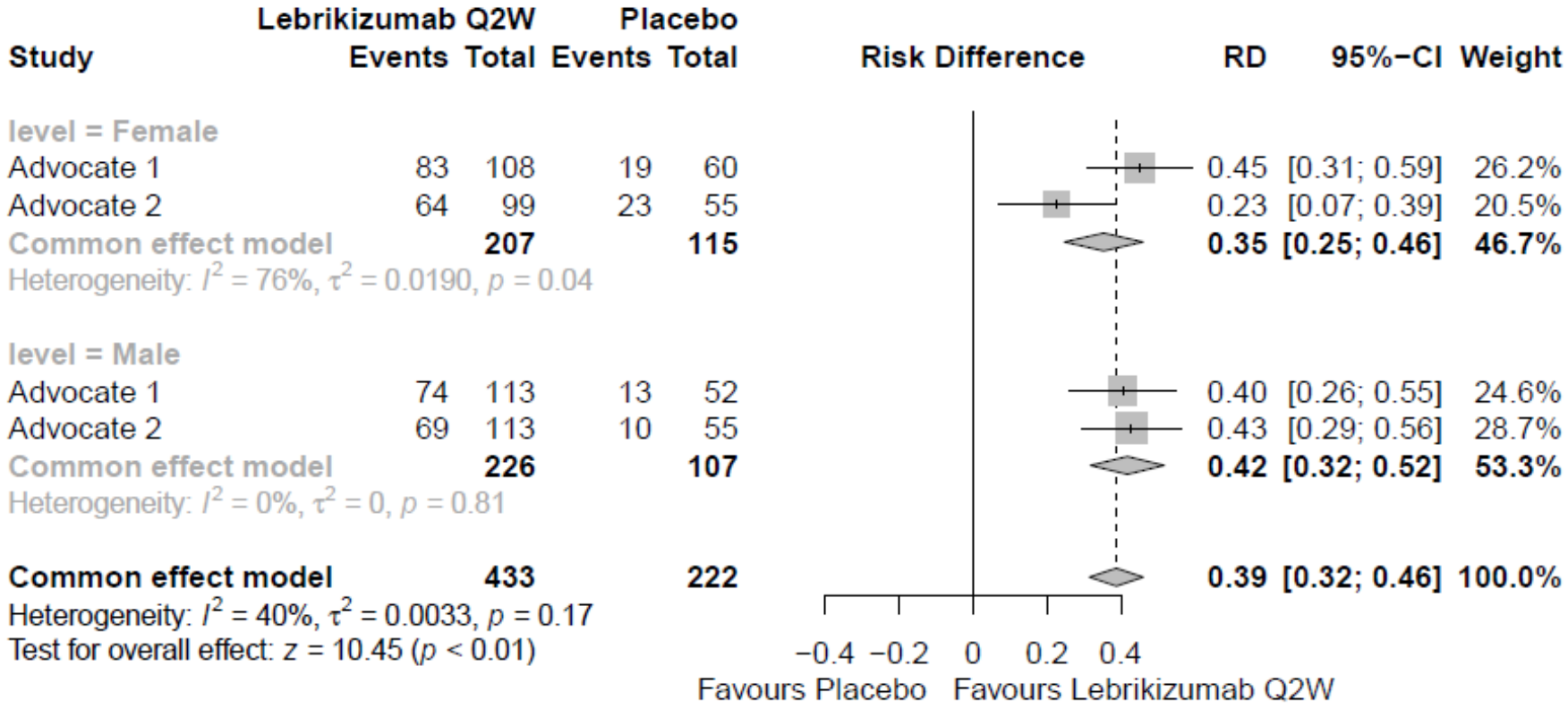

Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = US
Advocate 1 64 98 12 50 5.96 [2.76; 12.88] 23.7%
Advocate 2 55 85 22 46 2.00 [0.96; 4.15] 26.4%
Common effect model 183 96 3.35 [1.97; 5.69] 50.1%
Heterogeneity: I^2 = 75%, τ^2 = 0.4496, p = 0.04
level = EU
Advocate 1 59 73 18 37 4.45 [1.87; 10.61] 18.6%
Advocate 2 42 60 5 27 10.27 [3.36; 31.37] 11.3%
Common effect model 133 64 6.10 [3.07; 12.11] 29.9%
Heterogeneity: I^2 = 25%, τ^2 = 0.0891, p = 0.25
level = Rest of World
Advocate 1 34 50 2 25 24.44 [5.12; 116.56] 5.8%
Advocate 2 36 67 6 37 6.00 [2.21; 16.27] 14.2%
Common effect model 117 62 9.01 [3.89; 20.89] 19.9%
Heterogeneity: I^2 = 55%, τ^2 = 0.5389, p = 0.14
Common effect model 433 222 4.88 [3.35; 7.11] 100.0%
Heterogeneity: I^2 = 58%, τ^2 = 0.3092, p = 0.03
Test for overall effect: z = 8.28 (p < 0.01)
0.01
0.1
1
10
100
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = US
Advocate 1 64 98 12 50 0.41 [0.26; 0.56] 21.3%
Advocate 2 55 85 22 46 0.17 [−0.01; 0.35] 15.7%
Common effect model 183 96 0.31 [0.19; 0.42] 37.0%
Heterogeneity: I^2 = 76%, τ^2 = 0.0228, p = 0.04
level = EU
Advocate 1 59 73 18 37 0.32 [0.14; 0.51] 14.3%
Advocate 2 42 60 5 27 0.51 [0.33; 0.70] 14.0%
Common effect model 133 64 0.42 [0.29; 0.55] 28.3%
Heterogeneity: I^2 = 52%, τ^2 = 0.0097, p = 0.15
level = Rest of World
Advocate 1 34 50 2 25 0.60 [0.43; 0.77] 17.4%
Advocate 2 36 67 6 37 0.38 [0.21; 0.54] 17.2%
Common effect model 117 62 0.49 [0.37; 0.61] 34.7%
Heterogeneity: I^2 = 71%, τ^2 = 0.0179, p = 0.06
Common effect model 433 222 0.40 [0.33; 0.47] 100.0%
Heterogeneity: I^2 = 65%, τ^2 = 0.0146, p = 0.01
Test for overall effect: z = 11.27 (p < 0.01)
−0.6 −0.2 0 0.2 0.4 0.6
Favours Placebo
Favours Lebrikizumab Q2W

4.5.1.13.4 Geschlecht




Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Odds Ratio
OR 95%−CI Weight
level = Female
Advocate 1 83 108 19 60 7.16 [3.54; 14.49] 26.3%
Advocate 2 64 99 23 55 2.54 [1.29; 5.00] 28.5%
Common effect model 207 115 4.18 [2.57; 6.81] 54.8%
Heterogeneity: I^2 = 77%, τ^2 = 0.4119, p = 0.04
level = Male
Advocate 1 74 113 13 52 5.69 [2.72; 11.90] 23.9%
Advocate 2 69 113 10 55 7.06 [3.23; 15.43] 21.3%
Common effect model 226 107 6.30 [3.68; 10.77] 45.2%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.70
Common effect model 433 222 5.03 [3.51; 7.22] 100.0%
Heterogeneity: I^2 = 47%, τ^2 = 0.1236, p = 0.13
Test for overall effect: z = 8.77 (p < 0.01)
0.1
0.5
1
2
10
Favours Placebo
Favours Lebrikizumab Q2W


Lebrikizumab Q2W
Placebo
Study
Events Total Events Total
Risk Difference
RD 95%−CI Weight
level = Female
Advocate 1 83 108 19 60 0.45 [0.31; 0.59] 26.2%
Advocate 2 64 99 23 55 0.23 [0.07; 0.39] 20.5%
Common effect model 207 115 0.35 [0.25; 0.46] 46.7%
Heterogeneity: I^2 = 76%, τ^2 = 0.0190, p = 0.04
level = Male
Advocate 1 74 113 13 52 0.40 [0.26; 0.55] 24.6%
Advocate 2 69 113 10 55 0.43 [0.29; 0.56] 28.7%
Common effect model 226 107 0.42 [0.32; 0.52] 53.3%
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.81
Common effect model 433 222 0.39 [0.32; 0.46] 100.0%
Heterogeneity: I^2 = 40%, τ^2 = 0.0033, p = 0.17
Test for overall effect: z = 10.45 (p < 0.01)
−0.4 −0.2 0 0.2 0.4
Favours Placebo
Favours Lebrikizumab Q2W

4.5.2 Subgruppenanalyse der Meta-Analyse

4.5.2.1 ADvocate 1 + ADvocate 2. Responder analysis of EASI75 by Gender, baseline to Week 16 NRI (mITT)

Gender: Overall

		PBO N=287	LEB250Q2W N=564
EASI75 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	109 (37.98%)	147 (26.06%)
	Responder	45 (15.68%)	301 (53.37%)
	Missing	133 (46.34%)	116 (20.57%)
EASI75 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	242 (84.32%)	263 (46.63%)
	Responder	45 (15.68%)	301 (53.37%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.063 (4.203 , 8.748)
	Relative Risk (95% CI)		3.814 (2.833 , 5.135)
	Common Risk Difference (95% CI)		36.994 (31.096 , 42.893)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.537299

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI75 by Gender, baseline to Week 16 NRI (mITT)

Gender: F

		PBO N=287	LEB250Q2W N=564
EASI75 score (Observed up to ICE), n(%)	Total	148 (51.57%)	277 (49.11%)
	Non-responder	56 (19.51%)	60 (10.64%)
	Responder	25 (8.71%)	164 (29.08%)
	Missing	67 (23.34%)	53 (9.40%)
EASI75 score (NRI) [1] [2], n(%)	Total	148 (51.57%)	277 (49.11%)
	Non-responder	123 (42.86%)	113 (20.04%)
	Responder	25 (8.71%)	164 (29.08%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.785 (4.050 , 11.365)
	Relative Risk (95% CI)		4.073 (2.698 , 6.149)
	Common Risk Difference (95% CI)		41.030 (32.488 , 49.573)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI75 by Gender, baseline to Week 16 NRI (mITT)

Gender: M

		PBO N=287	LEB250Q2W N=564
EASI75 score (Observed up to ICE), n(%)	Total	139 (48.43%)	287 (50.89%)
	Non-responder	53 (18.47%)	87 (15.43%)
	Responder	20 (6.97%)	137 (24.29%)
	Missing	66 (23.00%)	63 (11.17%)
EASI75 score (NRI) [1] [2], n(%)	Total	139 (48.43%)	287 (50.89%)
	Non-responder	119 (41.46%)	150 (26.60%)
	Responder	20 (6.97%)	137 (24.29%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.439 (3.166 , 9.345)
	Relative Risk (95% CI)		3.480 (2.241 , 5.403)
	Common Risk Difference (95% CI)		33.377 (24.973 , 41.780)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.2 **ADvocate 1 + ADvocate 2. Responder analysis of EASI75 by Age Group I, baseline to Week 16 NRI (mITT)**

Age Group I: Overall

		PBO N=287	LEB250Q2W N=564
EASI75 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	109 (37.98%)	147 (26.06%)
	Responder	45 (15.68%)	301 (53.37%)
	Missing	133 (46.34%)	116 (20.57%)
EASI75 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	242 (84.32%)	263 (46.63%)
	Responder	45 (15.68%)	301 (53.37%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.063 (4.203 , 8.748)
	Relative Risk (95% CI)		3.814 (2.833 , 5.135)
	Common Risk Difference (95% CI)		36.994 (31.096 , 42.893)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.691053

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI75 by Age Group I, baseline to Week 16 NRI (mITT)

Age Group I: Adolescents (12<18) years

		PBO N=287	LEB250Q2W N=564
EASI75 score (Observed up to ICE), n(%)	Total	35 (12.20%)	67 (11.88%)
	Non-responder	15 (5.23%)	16 (2.84%)
	Responder	6 (2.09%)	41 (7.27%)
	Missing	14 (4.88%)	10 (1.77%)
EASI75 score (NRI) [1] [2], n(%)	Total	35 (12.20%)	67 (11.88%)
	Non-responder	29 (10.10%)	26 (4.61%)
	Responder	6 (2.09%)	41 (7.27%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.062 (2.102 , 17.481)
	Relative Risk (95% CI)		4.276 (1.795 , 10.184)
	Common Risk Difference (95% CI)		38.492 (20.495 , 56.489)
	CMH p-value		0.000089

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI75 by Age Group I, baseline to Week 16 NRI (mITT)

Age Group I: Adults >= 18 years

		PBO N=287	LEB250Q2W N=564
EASI75 score (Observed up to ICE), n(%)	Total	252 (87.80%)	497 (88.12%)
	Non-responder	94 (32.75%)	131 (23.23%)
	Responder	39 (13.59%)	260 (46.10%)
	Missing	119 (41.46%)	106 (18.79%)
EASI75 score (NRI) [1] [2], n(%)	Total	252 (87.80%)	497 (88.12%)
	Non-responder	213 (74.22%)	237 (42.02%)
	Responder	39 (13.59%)	260 (46.10%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.063 (4.103 , 8.962)
	Relative Risk (95% CI)		3.760 (2.740 , 5.160)
	Common Risk Difference (95% CI)		36.795 (30.555 , 43.036)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.3 **ADvocate 1 + ADvocate 2. Responder analysis of EASI75 by Disease Severity II, baseline to Week 16 NRI (mITT)**

Disease Severity II: Overall

		PBO N=287	LEB250Q2W N=564
EASI75 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	109 (37.98%)	147 (26.06%)
	Responder	45 (15.68%)	301 (53.37%)
	Missing	133 (46.34%)	116 (20.57%)
EASI75 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	242 (84.32%)	263 (46.63%)
	Responder	45 (15.68%)	301 (53.37%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.063 (4.203 , 8.748)
	Relative Risk (95% CI)		3.814 (2.833 , 5.135)
	Common Risk Difference (95% CI)		36.994 (31.096 , 42.893)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.353589

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI75 by Disease Severity II, baseline to Week 16 NRI (mITT)

Disease Severity II: IGA = 3

		PBO N=287	LEB250Q2W N=564
EASI75 score (Observed up to ICE), n(%)	Total	178 (62.02%)	345 (61.17%)
	Non-responder	71 (24.74%)	90 (15.96%)
	Responder	33 (11.50%)	191 (33.87%)
	Missing	74 (25.78%)	64 (11.35%)
EASI75 score (NRI) [1] [2], n(%)	Total	178 (62.02%)	345 (61.17%)
	Non-responder	145 (50.52%)	154 (27.30%)
	Responder	33 (11.50%)	191 (33.87%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.306 (3.414 , 8.247)
	Relative Risk (95% CI)		3.408 (2.403 , 4.834)
	Common Risk Difference (95% CI)		36.382 (28.575 , 44.188)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI75 by Disease Severity II, baseline to Week 16 NRI (mITT)

Disease Severity II: IGA = 4

		PBO N=287	LEB250Q2W N=564
EASI75 score (Observed up to ICE), n(%)	Total	109 (37.98%)	219 (38.83%)
	Non-responder	38 (13.24%)	57 (10.11%)
	Responder	12 (4.18%)	110 (19.50%)
	Missing	59 (20.56%)	52 (9.22%)
EASI75 score (NRI) [1] [2], n(%)	Total	109 (37.98%)	219 (38.83%)
	Non-responder	97 (33.80%)	109 (19.33%)
	Responder	12 (4.18%)	110 (19.50%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		7.960 (4.102 , 15.448)
	Relative Risk (95% CI)		4.809 (2.744 , 8.429)
	Common Risk Difference (95% CI)		37.985 (29.110 , 46.860)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.4 **ADvocate 1 + ADvocate 2. Responder analysis of EASI75 by Region, baseline to Week 16 NRI (mITT)**

Region: Overall

		PBO N=287	LEB250Q2W N=564
EASI75 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	109 (37.98%)	147 (26.06%)
	Responder	45 (15.68%)	301 (53.37%)
	Missing	133 (46.34%)	116 (20.57%)
EASI75 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	242 (84.32%)	263 (46.63%)
	Responder	45 (15.68%)	301 (53.37%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.063 (4.203 , 8.748)
	Relative Risk (95% CI)		3.814 (2.833 , 5.135)
	Common Risk Difference (95% CI)		36.994 (31.096 , 42.893)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.015293

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI75 by Region, baseline to Week 16 NRI (mITT)

Region: Europe

		PBO N=287	LEB250Q2W N=564
EASI75 score (Observed up to ICE), n(%)	Total	84 (29.27%)	168 (29.79%)
	Non-responder	37 (12.89%)	46 (8.16%)
	Responder	15 (5.23%)	104 (18.44%)
	Missing	32 (11.15%)	18 (3.19%)
EASI75 score (NRI) [1] [2], n(%)	Total	84 (29.27%)	168 (29.79%)
	Non-responder	69 (24.04%)	64 (11.35%)
	Responder	15 (5.23%)	104 (18.44%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		7.060 (3.683 , 13.534)
	Relative Risk (95% CI)		4.100 (2.483 , 6.768)
	Common Risk Difference (95% CI)		43.746 (32.614 , 54.879)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI75 by Region, baseline to Week 16 NRI (mITT)

Region: US

		PBO N=287	LEB250Q2W N=564
EASI75 score (Observed up to ICE), n(%)	Total	122 (42.51%)	235 (41.67%)
	Non-responder	43 (14.98%)	63 (11.17%)
	Responder	27 (9.41%)	121 (21.45%)
	Missing	52 (18.12%)	51 (9.04%)
EASI75 score (NRI) [1] [2], n(%)	Total	122 (42.51%)	235 (41.67%)
	Non-responder	95 (33.10%)	114 (20.21%)
	Responder	27 (9.41%)	121 (21.45%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.608 (2.189 , 5.947)
	Relative Risk (95% CI)		2.523 (1.715 , 3.713)
	Common Risk Difference (95% CI)		28.691 (18.861 , 38.522)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI75 by Region, baseline to Week 16 NRI (mITT)

Region: Rest of the World

		PBO N=287	LEB250Q2W N=564
EASI75 score (Observed up to ICE), n(%)	Total	81 (28.22%)	161 (28.55%)
	Non-responder	29 (10.10%)	38 (6.74%)
	Responder	3 (1.05%)	76 (13.48%)
	Missing	49 (17.07%)	47 (8.33%)
EASI75 score (NRI) [1] [2], n(%)	Total	81 (28.22%)	161 (28.55%)
	Non-responder	78 (27.18%)	85 (15.07%)
	Responder	3 (1.05%)	76 (13.48%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		23.457 (7.079 , 77.725)
	Relative Risk (95% CI)		12.617 (4.148 , 38.383)
	Common Risk Difference (95% CI)		42.344 (33.559 , 51.128)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.5 **ADvocate 1 + ADvocate 2. Responder analysis of EASI75 by Race, baseline to Week 16 NRI (mITT)**

Race: Overall

		PBO N=287	LEB250Q2W N=564
EASI75 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	109 (37.98%)	147 (26.06%)
	Responder	45 (15.68%)	301 (53.37%)
	Missing	133 (46.34%)	116 (20.57%)
EASI75 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	242 (84.32%)	263 (46.63%)
	Responder	45 (15.68%)	301 (53.37%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.063 (4.203 , 8.748)
	Relative Risk (95% CI)		3.814 (2.833 , 5.135)
	Common Risk Difference (95% CI)		36.994 (31.096 , 42.893)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.778330

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI75 by Race, baseline to Week 16 NRI (mITT)

Race: ASIAN

		PBO N=287	LEB250Q2W N=564
EASI75 score (Observed up to ICE), n(%)	Total	75 (26.13%)	117 (20.74%)
	Non-responder	26 (9.06%)	33 (5.85%)
	Responder	6 (2.09%)	53 (9.40%)
	Missing	43 (14.98%)	31 (5.50%)
EASI75 score (NRI) [1] [2], n(%)	Total	75 (26.13%)	117 (20.74%)
	Non-responder	69 (24.04%)	64 (11.35%)
	Responder	6 (2.09%)	53 (9.40%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		11.519 (4.165 , 31.861)
	Relative Risk (95% CI)		5.677 (2.468 , 13.060)
	Common Risk Difference (95% CI)		37.080 (26.254 , 47.906)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI75 by Race, baseline to Week 16 NRI (mITT)

Race: BLACK OR AFRICAN AMERICAN

		PBO N=287	LEB250Q2W N=564
EASI75 score (Observed up to ICE), n(%)	Total	26 (9.06%)	58 (10.28%)
	Non-responder	8 (2.79%)	19 (3.37%)
	Responder	4 (1.39%)	29 (5.14%)
	Missing	14 (4.88%)	10 (1.77%)
EASI75 score (NRI) [1] [2], n(%)	Total	26 (9.06%)	58 (10.28%)
	Non-responder	22 (7.67%)	29 (5.14%)
	Responder	4 (1.39%)	29 (5.14%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.391 (1.341 , 14.380)
	Relative Risk (95% CI)		2.912 (1.153 , 7.351)
	Common Risk Difference (95% CI)		31.321 (10.542 , 52.101)
	CMH p-value		0.010830

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI75 by Race, baseline to Week 16 NRI (mITT)

Race: WHITE

		PBO N=287	LEB250Q2W N=564
EASI75 score (Observed up to ICE), n(%)	Total	178 (62.02%)	364 (64.54%)
	Non-responder	71 (24.74%)	90 (15.96%)
	Responder	34 (11.85%)	208 (36.88%)
	Missing	73 (25.44%)	66 (11.70%)
EASI75 score (NRI) [1] [2], n(%)	Total	178 (62.02%)	364 (64.54%)
	Non-responder	144 (50.17%)	156 (27.66%)
	Responder	34 (11.85%)	208 (36.88%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.517 (3.567 , 8.533)
	Relative Risk (95% CI)		3.451 (2.460 , 4.840)
	Common Risk Difference (95% CI)		38.109 (30.274 , 45.945)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI75 by Race, baseline to Week 16 NRI (mITT)

Race: OTHER

		PBO N=287	LEB250Q2W N=564
EASI75 score (Observed up to ICE), n(%)	Total	8 (2.79%)	25 (4.43%)
	Non-responder	4 (1.39%)	5 (0.89%)
	Responder	1 (0.35%)	11 (1.95%)
	Missing	3 (1.05%)	9 (1.60%)
EASI75 score (NRI) [1] [2], n(%)	Total	8 (2.79%)	25 (4.43%)
	Non-responder	7 (2.44%)	14 (2.48%)
	Responder	1 (0.35%)	11 (1.95%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.143 (0.322 , 82.037)
	Relative Risk (95% CI)		2.381 (0.464 , 12.226)
	Common Risk Difference (95% CI)		27.445 (-11.89 , 66.777)
	CMH p-value		0.244382

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.6 **ADvocate 1 + ADvocate 2. Responder analysis of IGA score 0/1 and reduction >= 2 points by Gender, baseline to Week 16 NRI (mITT)**

Gender: Overall

		PBO N=287	LEB250Q2W N=564
IGA-Score 0/1 and reduction >=2 points score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	124 (43.21%)	244 (43.26%)
	Responder	30 (10.45%)	204 (36.17%)
	Missing	133 (46.34%)	116 (20.57%)
IGA-Score 0/1 and reduction >=2 points score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	257 (89.55%)	360 (63.83%)
	Responder	30 (10.45%)	204 (36.17%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.961 (3.229 , 7.622)
	Relative Risk (95% CI)		3.405 (2.377 , 4.879)
	Common Risk Difference (95% CI)		25.096 (19.843 , 30.349)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.296288

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of IGA score 0/1 and reduction >= 2 points by Gender, baseline to Week 16 NRI (mITT)

Gender: F

		PBO N=287	LEB250Q2W N=564
IGA-Score 0/1 and reduction >=2 points score (Observed up to ICE), n(%)	Total	148 (51.57%)	277 (49.11%)
	Non-responder	65 (22.65%)	105 (18.62%)
	Responder	16 (5.57%)	119 (21.10%)
	Missing	67 (23.34%)	53 (9.40%)
IGA-Score 0/1 and reduction >=2 points score (NRI) [1] [2], n(%)	Total	148 (51.57%)	277 (49.11%)
	Non-responder	132 (45.99%)	158 (28.01%)
	Responder	16 (5.57%)	119 (21.10%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.389 (3.470 , 11.762)
	Relative Risk (95% CI)		4.022 (2.430 , 6.656)
	Common Risk Difference (95% CI)		30.795 (23.111 , 38.478)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of IGA score 0/1 and reduction >= 2 points by Gender, baseline to Week 16 NRI (mITT)

Gender: M

		PBO N=287	LEB250Q2W N=564
IGA-Score 0/1 and reduction >=2 points score (Observed up to ICE), n(%)	Total	139 (48.43%)	287 (50.89%)
	Non-responder	59 (20.56%)	139 (24.65%)
	Responder	14 (4.88%)	85 (15.07%)
	Missing	66 (23.00%)	63 (11.17%)
IGA-Score 0/1 and reduction >=2 points score (NRI) [1] [2], n(%)	Total	139 (48.43%)	287 (50.89%)
	Non-responder	125 (43.55%)	202 (35.82%)
	Responder	14 (4.88%)	85 (15.07%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.883 (2.072 , 7.276)
	Relative Risk (95% CI)		2.786 (1.663 , 4.668)
	Common Risk Difference (95% CI)		19.579 (12.176 , 26.982)
	CMH p-value		0.000007

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.7 **ADvocate 1 + ADvocate 2. Responder analysis of IGA score 0/1 and reduction >= 2 points by Age Group I, baseline to Week 16 NRI (mITT)**

Age Group I: Overall

		PBO N=287	LEB250Q2W N=564
IGA-Score 0/1 and reduction >=2 points score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	124 (43.21%)	244 (43.26%)
	Responder	30 (10.45%)	204 (36.17%)
	Missing	133 (46.34%)	116 (20.57%)
IGA-Score 0/1 and reduction >=2 points score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	257 (89.55%)	360 (63.83%)
	Responder	30 (10.45%)	204 (36.17%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.961 (3.229 , 7.622)
	Relative Risk (95% CI)		3.405 (2.377 , 4.879)
	Common Risk Difference (95% CI)		25.096 (19.843 , 30.349)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.921429

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of IGA score 0/1 and reduction >= 2 points by Age Group I, baseline to Week 16 NRI (mITT)

Age Group I: Adolescents (12<18) years

		PBO N=287	LEB250Q2W N=564
IGA-Score 0/1 and reduction >=2 points score (Observed up to ICE), n(%)	Total	35 (12.20%)	67 (11.88%)
	Non-responder	16 (5.57%)	26 (4.61%)
	Responder	5 (1.74%)	31 (5.50%)
	Missing	14 (4.88%)	10 (1.77%)
IGA-Score 0/1 and reduction >=2 points score (NRI) [1] [2], n(%)	Total	35 (12.20%)	67 (11.88%)
	Non-responder	30 (10.45%)	36 (6.38%)
	Responder	5 (1.74%)	31 (5.50%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.986 (1.486 , 16.736)
	Relative Risk (95% CI)		3.590 (1.339 , 9.622)
	Common Risk Difference (95% CI)		27.314 (10.905 , 43.723)
	CMH p-value		0.003152

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of IGA score 0/1 and reduction >= 2 points by Age Group I, baseline to Week 16 NRI (mITT)

Age Group I: Adults >= 18 years

		PBO N=287	LEB250Q2W N=564
IGA-Score 0/1 and reduction >=2 points score (Observed up to ICE), n(%)	Total	252 (87.80%)	497 (88.12%)
	Non-responder	108 (37.63%)	218 (38.65%)
	Responder	25 (8.71%)	173 (30.67%)
	Missing	119 (41.46%)	106 (18.79%)
IGA-Score 0/1 and reduction >=2 points score (NRI) [1] [2], n(%)	Total	252 (87.80%)	497 (88.12%)
	Non-responder	227 (79.09%)	324 (57.45%)
	Responder	25 (8.71%)	173 (30.67%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.957 (3.131 , 7.847)
	Relative Risk (95% CI)		3.381 (2.298 , 4.973)
	Common Risk Difference (95% CI)		24.801 (19.262 , 30.341)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.8 **ADvocate 1 + ADvocate 2. Responder analysis of IGA score 0/1 and reduction >= 2 points by Disease Severity II, baseline to Week 16 NRI (mITT)**

Disease Severity II: Overall

		PBO N=287	LEB250Q2W N=564
IGA-Score 0/1 and reduction >=2 points score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	124 (43.21%)	244 (43.26%)
	Responder	30 (10.45%)	204 (36.17%)
	Missing	133 (46.34%)	116 (20.57%)
IGA-Score 0/1 and reduction >=2 points score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	257 (89.55%)	360 (63.83%)
	Responder	30 (10.45%)	204 (36.17%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.961 (3.229 , 7.622)
	Relative Risk (95% CI)		3.405 (2.377 , 4.879)
	Common Risk Difference (95% CI)		25.096 (19.843 , 30.349)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.918594

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of IGA score 0/1 and reduction >= 2 points by Disease Severity II, baseline to Week 16 NRI (mITT)

Disease Severity II: IGA = 3

		PBO N=287	LEB250Q2W N=564
IGA-Score 0/1 and reduction >=2 points score (Observed up to ICE), n(%)	Total	178 (62.02%)	345 (61.17%)
	Non-responder	82 (28.57%)	142 (25.18%)
	Responder	22 (7.67%)	139 (24.65%)
	Missing	74 (25.78%)	64 (11.35%)
IGA-Score 0/1 and reduction >=2 points score (NRI) [1] [2], n(%)	Total	178 (62.02%)	345 (61.17%)
	Non-responder	156 (54.36%)	206 (36.52%)
	Responder	22 (7.67%)	139 (24.65%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.946 (2.954 , 8.282)
	Relative Risk (95% CI)		3.353 (2.183 , 5.148)
	Common Risk Difference (95% CI)		27.437 (20.446 , 34.428)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of IGA score 0/1 and reduction >= 2 points by Disease Severity II, baseline to Week 16 NRI (mITT)

Disease Severity II: IGA = 4

		PBO N=287	LEB250Q2W N=564
IGA-Score 0/1 and reduction >=2 points score (Observed up to ICE), n(%)	Total	109 (37.98%)	219 (38.83%)
	Non-responder	42 (14.63%)	102 (18.09%)
	Responder	8 (2.79%)	65 (11.52%)
	Missing	59 (20.56%)	52 (9.22%)
IGA-Score 0/1 and reduction >=2 points score (NRI) [1] [2], n(%)	Total	109 (37.98%)	219 (38.83%)
	Non-responder	101 (35.19%)	154 (27.30%)
	Responder	8 (2.79%)	65 (11.52%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.991 (2.298 , 10.837)
	Relative Risk (95% CI)		3.523 (1.823 , 6.807)
	Common Risk Difference (95% CI)		21.307 (13.486 , 29.128)
	CMH p-value		0.000008

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.9 **ADvocate 1 + ADvocate 2. Responder analysis of IGA score 0/1 and reduction >= 2 points by Region, baseline to Week 16 NRI (mITT)**

Region: Overall

		PBO N=287	LEB250Q2W N=564
IGA-Score 0/1 and reduction >=2 points score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	124 (43.21%)	244 (43.26%)
	Responder	30 (10.45%)	204 (36.17%)
	Missing	133 (46.34%)	116 (20.57%)
IGA-Score 0/1 and reduction >=2 points score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	257 (89.55%)	360 (63.83%)
	Responder	30 (10.45%)	204 (36.17%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.961 (3.229 , 7.622)
	Relative Risk (95% CI)		3.405 (2.377 , 4.879)
	Common Risk Difference (95% CI)		25.096 (19.843 , 30.349)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.065565

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of IGA score 0/1 and reduction >= 2 points by Region, baseline to Week 16 NRI (mITT)

Region: Europe

		PBO N=287	LEB250Q2W N=564
IGA-Score 0/1 and reduction >=2 points score (Observed up to ICE), n(%)	Total	84 (29.27%)	168 (29.79%)
	Non-responder	42 (14.63%)	72 (12.77%)
	Responder	10 (3.48%)	78 (13.83%)
	Missing	32 (11.15%)	18 (3.19%)
IGA-Score 0/1 and reduction >=2 points score (NRI) [1] [2], n(%)	Total	84 (29.27%)	168 (29.79%)
	Non-responder	74 (25.78%)	90 (15.96%)
	Responder	10 (3.48%)	78 (13.83%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.276 (2.982 , 13.210)
	Relative Risk (95% CI)		4.013 (2.175 , 7.405)
	Common Risk Difference (95% CI)		34.140 (23.867 , 44.412)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of IGA score 0/1 and reduction >= 2 points by Region, baseline to Week 16 NRI (mITT)

Region: US

		PBO N=287	LEB250Q2W N=564
IGA-Score 0/1 and reduction >=2 points score (Observed up to ICE), n(%)	Total	122 (42.51%)	235 (41.67%)
	Non-responder	52 (18.12%)	104 (18.44%)
	Responder	18 (6.27%)	80 (14.18%)
	Missing	52 (18.12%)	51 (9.04%)
IGA-Score 0/1 and reduction >=2 points score (NRI) [1] [2], n(%)	Total	122 (42.51%)	235 (41.67%)
	Non-responder	104 (36.24%)	155 (27.48%)
	Responder	18 (6.27%)	80 (14.18%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		2.995 (1.666 , 5.382)
	Relative Risk (95% CI)		2.250 (1.410 , 3.591)
	Common Risk Difference (95% CI)		18.520 (9.921 , 27.119)
	CMH p-value		0.000138

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of IGA score 0/1 and reduction >= 2 points by Region, baseline to Week 16 NRI (mITT)

Region: Rest of the World

		PBO N=287	LEB250Q2W N=564
IGA-Score 0/1 and reduction >=2 points score (Observed up to ICE), n(%)	Total	81 (28.22%)	161 (28.55%)
	Non-responder	30 (10.45%)	68 (12.06%)
	Responder	2 (0.70%)	46 (8.16%)
	Missing	49 (17.07%)	47 (8.33%)
IGA-Score 0/1 and reduction >=2 points score (NRI) [1] [2], n(%)	Total	81 (28.22%)	161 (28.55%)
	Non-responder	79 (27.53%)	115 (20.39%)
	Responder	2 (0.70%)	46 (8.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		15.176 (3.631 , 63.430)
	Relative Risk (95% CI)		9.621 (2.546 , 36.354)
	Common Risk Difference (95% CI)		25.481 (17.699 , 33.263)
	CMH p-value		0.000002

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.10 **ADvocate 1 + ADvocate 2. Responder analysis of IGA score 0/1 and reduction >= 2 points by Race, baseline to Week 16 NRI (mITT)**

Race: Overall

		PBO N=287	LEB250Q2W N=564
IGA-Score 0/1 and reduction >=2 points score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	124 (43.21%)	244 (43.26%)
	Responder	30 (10.45%)	204 (36.17%)
	Missing	133 (46.34%)	116 (20.57%)
IGA-Score 0/1 and reduction >=2 points score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	257 (89.55%)	360 (63.83%)
	Responder	30 (10.45%)	204 (36.17%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.961 (3.229 , 7.622)
	Relative Risk (95% CI)		3.405 (2.377 , 4.879)
	Common Risk Difference (95% CI)		25.096 (19.843 , 30.349)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.672477

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of IGA score 0/1 and reduction >= 2 points by Race, baseline to Week 16 NRI (mITT)

Race: ASIAN

		PBO N=287	LEB250Q2W N=564
IGA-Score 0/1 and reduction >=2 points score (Observed up to ICE), n(%)	Total	75 (26.13%)	117 (20.74%)
	Non-responder	29 (10.10%)	57 (10.11%)
	Responder	3 (1.05%)	29 (5.14%)
	Missing	43 (14.98%)	31 (5.50%)
IGA-Score 0/1 and reduction >=2 points score (NRI) [1] [2], n(%)	Total	75 (26.13%)	117 (20.74%)
	Non-responder	72 (25.09%)	88 (15.60%)
	Responder	3 (1.05%)	29 (5.14%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		8.824 (2.343 , 33.224)
	Relative Risk (95% CI)		4.912 (1.614 , 14.946)
	Common Risk Difference (95% CI)		20.219 (11.282 , 29.157)
	CMH p-value		0.000220

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of IGA score 0/1 and reduction >= 2 points by Race, baseline to Week 16 NRI (mITT)

Race: BLACK OR AFRICAN AMERICAN

		PBO N=287	LEB250Q2W N=564
IGA-Score 0/1 and reduction >=2 points score (Observed up to ICE), n(%)	Total	26 (9.06%)	58 (10.28%)
	Non-responder	9 (3.14%)	30 (5.32%)
	Responder	3 (1.05%)	18 (3.19%)
	Missing	14 (4.88%)	10 (1.77%)
IGA-Score 0/1 and reduction >=2 points score (NRI) [1] [2], n(%)	Total	26 (9.06%)	58 (10.28%)
	Non-responder	23 (8.01%)	40 (7.09%)
	Responder	3 (1.05%)	18 (3.19%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		2.630 (0.660 , 10.482)
	Relative Risk (95% CI)		1.990 (0.695 , 5.698)
	Common Risk Difference (95% CI)		14.144 (-3.697 , 31.985)
	CMH p-value		0.167270

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of IGA score 0/1 and reduction >= 2 points by Race, baseline to Week 16 NRI (mITT)

Race: WHITE

		PBO N=287	LEB250Q2W N=564
IGA-Score 0/1 and reduction >=2 points score (Observed up to ICE), n(%)	Total	178 (62.02%)	364 (64.54%)
	Non-responder	82 (28.57%)	149 (26.42%)
	Responder	23 (8.01%)	149 (26.42%)
	Missing	73 (25.44%)	66 (11.70%)
IGA-Score 0/1 and reduction >=2 points score (NRI) [1] [2], n(%)	Total	178 (62.02%)	364 (64.54%)
	Non-responder	155 (54.01%)	215 (38.12%)
	Responder	23 (8.01%)	149 (26.42%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.844 (2.922 , 8.029)
	Relative Risk (95% CI)		3.276 (2.172 , 4.943)
	Common Risk Difference (95% CI)		28.116 (21.034 , 35.199)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of IGA score 0/1 and reduction >= 2 points by Race, baseline to Week 16 NRI (mITT)

Race: OTHER

		PBO N=287	LEB250Q2W N=564
IGA-Score 0/1 and reduction >=2 points score (Observed up to ICE), n(%)	Total	8 (2.79%)	25 (4.43%)
	Non-responder	4 (1.39%)	8 (1.42%)
	Responder	1 (0.35%)	8 (1.42%)
	Missing	3 (1.05%)	9 (1.60%)
IGA-Score 0/1 and reduction >=2 points score (NRI) [1] [2], n(%)	Total	8 (2.79%)	25 (4.43%)
	Non-responder	7 (2.44%)	17 (3.01%)
	Responder	1 (0.35%)	8 (1.42%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		2.571 (0.104 , 63.535)
	Relative Risk (95% CI)		1.524 (0.295 , 7.871)
	Common Risk Difference (95% CI)		10.410 (-22.47 , 43.293)
	CMH p-value		0.599582

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.11 **ADvocate 1 + ADvocate 2. Responder analysis of EASI90 score by Gender, baseline to Week 16 NRI (mITT)**

Gender: Overall

		PBO N=287	LEB250Q2W N=564
EASI90 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	130 (45.30%)	261 (46.28%)
	Responder	24 (8.36%)	187 (33.16%)
	Missing	133 (46.34%)	116 (20.57%)
EASI90 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	263 (91.64%)	377 (66.84%)
	Responder	24 (8.36%)	187 (33.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.385 (3.399 , 8.531)
	Relative Risk (95% CI)		3.700 (2.485 , 5.510)
	Common Risk Difference (95% CI)		24.200 (19.175 , 29.226)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.865137

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI90 score by Gender, baseline to Week 16 NRI (mITT)

Gender: F

		PBO N=287	LEB250Q2W N=564
EASI90 score (Observed up to ICE), n(%)	Total	148 (51.57%)	277 (49.11%)
	Non-responder	67 (23.34%)	120 (21.28%)
	Responder	14 (4.88%)	104 (18.44%)
	Missing	67 (23.34%)	53 (9.40%)
EASI90 score (NRI) [1] [2], n(%)	Total	148 (51.57%)	277 (49.11%)
	Non-responder	134 (46.69%)	173 (30.67%)
	Responder	14 (4.88%)	104 (18.44%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.691 (3.060 , 10.581)
	Relative Risk (95% CI)		3.758 (2.227 , 6.342)
	Common Risk Difference (95% CI)		27.176 (19.680 , 34.673)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI90 score by Gender, baseline to Week 16 NRI (mITT)

Gender: M

		PBO N=287	LEB250Q2W N=564
EASI90 score (Observed up to ICE), n(%)	Total	139 (48.43%)	287 (50.89%)
	Non-responder	63 (21.95%)	141 (25.00%)
	Responder	10 (3.48%)	83 (14.72%)
	Missing	66 (23.00%)	63 (11.17%)
EASI90 score (NRI) [1] [2], n(%)	Total	139 (48.43%)	287 (50.89%)
	Non-responder	129 (44.95%)	204 (36.17%)
	Responder	10 (3.48%)	83 (14.72%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.627 (2.334 , 9.173)
	Relative Risk (95% CI)		3.464 (1.872 , 6.410)
	Common Risk Difference (95% CI)		20.972 (13.788 , 28.156)
	CMH p-value		0.000002

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.12 **ADvocate 1 + ADvocate 2. Responder analysis of EASI90 score by Age Group I, baseline to Week 16 NRI (mITT)**

Age Group I: Overall

		PBO N=287	LEB250Q2W N=564
EASI90 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	130 (45.30%)	261 (46.28%)
	Responder	24 (8.36%)	187 (33.16%)
	Missing	133 (46.34%)	116 (20.57%)
EASI90 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	263 (91.64%)	377 (66.84%)
	Responder	24 (8.36%)	187 (33.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.385 (3.399 , 8.531)
	Relative Risk (95% CI)		3.700 (2.485 , 5.510)
	Common Risk Difference (95% CI)		24.200 (19.175 , 29.226)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.865681

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI90 score by Age Group I, baseline to Week 16 NRI (mITT)

Age Group I: Adolescents (12<18) years

		PBO N=287	LEB250Q2W N=564
EASI90 score (Observed up to ICE), n(%)	Total	35 (12.20%)	67 (11.88%)
	Non-responder	17 (5.92%)	30 (5.32%)
	Responder	4 (1.39%)	27 (4.79%)
	Missing	14 (4.88%)	10 (1.77%)
EASI90 score (NRI) [1] [2], n(%)	Total	35 (12.20%)	67 (11.88%)
	Non-responder	31 (10.80%)	40 (7.09%)
	Responder	4 (1.39%)	27 (4.79%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.139 (1.438 , 18.365)
	Relative Risk (95% CI)		3.760 (1.241 , 11.389)
	Common Risk Difference (95% CI)		24.375 (8.927 , 39.822)
	CMH p-value		0.006362

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI90 score by Age Group I, baseline to Week 16 NRI (mITT)

Age Group I: Adults >= 18 years

		PBO N=287	LEB250Q2W N=564
EASI90 score (Observed up to ICE), n(%)	Total	252 (87.80%)	497 (88.12%)
	Non-responder	113 (39.37%)	231 (40.96%)
	Responder	20 (6.97%)	160 (28.37%)
	Missing	119 (41.46%)	106 (18.79%)
EASI90 score (NRI) [1] [2], n(%)	Total	252 (87.80%)	497 (88.12%)
	Non-responder	232 (80.84%)	337 (59.75%)
	Responder	20 (6.97%)	160 (28.37%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.420 (3.309 , 8.876)
	Relative Risk (95% CI)		3.693 (2.411 , 5.656)
	Common Risk Difference (95% CI)		24.177 (18.866 , 29.488)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.13 **ADvocate 1 + ADvocate 2. Responder analysis of EASI90 score by Disease Severity II, baseline to Week 16 NRI (mITT)**

Disease Severity II: Overall

		PBO N=287	LEB250Q2W N=564
EASI90 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	130 (45.30%)	261 (46.28%)
	Responder	24 (8.36%)	187 (33.16%)
	Missing	133 (46.34%)	116 (20.57%)
EASI90 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	263 (91.64%)	377 (66.84%)
	Responder	24 (8.36%)	187 (33.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.385 (3.399 , 8.531)
	Relative Risk (95% CI)		3.700 (2.485 , 5.510)
	Common Risk Difference (95% CI)		24.200 (19.175 , 29.226)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.144549

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI90 score by Disease Severity II, baseline to Week 16 NRI (mITT)

Disease Severity II: IGA = 3

		PBO N=287	LEB250Q2W N=564
EASI90 score (Observed up to ICE), n(%)	Total	178 (62.02%)	345 (61.17%)
	Non-responder	85 (29.62%)	165 (29.26%)
	Responder	19 (6.62%)	116 (20.57%)
	Missing	74 (25.78%)	64 (11.35%)
EASI90 score (NRI) [1] [2], n(%)	Total	178 (62.02%)	345 (61.17%)
	Non-responder	159 (55.40%)	229 (40.60%)
	Responder	19 (6.62%)	116 (20.57%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.245 (2.482 , 7.261)
	Relative Risk (95% CI)		3.008 (1.913 , 4.731)
	Common Risk Difference (95% CI)		22.422 (15.725 , 29.120)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI90 score by Disease Severity II, baseline to Week 16 NRI (mITT)

Disease Severity II: IGA = 4

		PBO N=287	LEB250Q2W N=564
EASI90 score (Observed up to ICE), n(%)	Total	109 (37.98%)	219 (38.83%)
	Non-responder	45 (15.68%)	96 (17.02%)
	Responder	5 (1.74%)	71 (12.59%)
	Missing	59 (20.56%)	52 (9.22%)
EASI90 score (NRI) [1] [2], n(%)	Total	109 (37.98%)	219 (38.83%)
	Non-responder	104 (36.24%)	148 (26.24%)
	Responder	5 (1.74%)	71 (12.59%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		9.283 (3.686 , 23.379)
	Relative Risk (95% CI)		6.014 (2.614 , 13.839)
	Common Risk Difference (95% CI)		27.077 (19.656 , 34.497)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.14 **ADvocate 1 + ADvocate 2. Responder analysis of EASI90 score by Region, baseline to Week 16 NRI (mITT)**

Region: Overall

		PBO N=287	LEB250Q2W N=564
EASI90 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	130 (45.30%)	261 (46.28%)
	Responder	24 (8.36%)	187 (33.16%)
	Missing	133 (46.34%)	116 (20.57%)
EASI90 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	263 (91.64%)	377 (66.84%)
	Responder	24 (8.36%)	187 (33.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.385 (3.399 , 8.531)
	Relative Risk (95% CI)		3.700 (2.485 , 5.510)
	Common Risk Difference (95% CI)		24.200 (19.175 , 29.226)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.090994

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI90 score by Region, baseline to Week 16 NRI (mITT)

Region: Europe

		PBO N=287	LEB250Q2W N=564
EASI90 score (Observed up to ICE), n(%)	Total	84 (29.27%)	168 (29.79%)
	Non-responder	46 (16.03%)	86 (15.25%)
	Responder	6 (2.09%)	64 (11.35%)
	Missing	32 (11.15%)	18 (3.19%)
EASI90 score (NRI) [1] [2], n(%)	Total	84 (29.27%)	168 (29.79%)
	Non-responder	78 (27.18%)	104 (18.44%)
	Responder	6 (2.09%)	64 (11.35%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		7.635 (3.161 , 18.445)
	Relative Risk (95% CI)		4.927 (2.278 , 10.654)
	Common Risk Difference (95% CI)		30.967 (21.666 , 40.267)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI90 score by Region, baseline to Week 16 NRI (mITT)

Region: US

		PBO N=287	LEB250Q2W N=564
EASI90 score (Observed up to ICE), n(%)	Total	122 (42.51%)	235 (41.67%)
	Non-responder	54 (18.82%)	106 (18.79%)
	Responder	16 (5.57%)	78 (13.83%)
	Missing	52 (18.12%)	51 (9.04%)
EASI90 score (NRI) [1] [2], n(%)	Total	122 (42.51%)	235 (41.67%)
	Non-responder	106 (36.93%)	157 (27.84%)
	Responder	16 (5.57%)	78 (13.83%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.251 (1.777 , 5.948)
	Relative Risk (95% CI)		2.404 (1.472 , 3.927)
	Common Risk Difference (95% CI)		19.159 (10.754 , 27.564)
	CMH p-value		0.000073

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI90 score by Region, baseline to Week 16 NRI (mITT)

Region: Rest of the World

		PBO N=287	LEB250Q2W N=564
EASI90 score (Observed up to ICE), n(%)	Total	81 (28.22%)	161 (28.55%)
	Non-responder	30 (10.45%)	69 (12.23%)
	Responder	2 (0.70%)	45 (7.98%)
	Missing	49 (17.07%)	47 (8.33%)
EASI90 score (NRI) [1] [2], n(%)	Total	81 (28.22%)	161 (28.55%)
	Non-responder	79 (27.53%)	116 (20.57%)
	Responder	2 (0.70%)	45 (7.98%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		13.685 (3.347 , 55.947)
	Relative Risk (95% CI)		8.950 (2.382 , 33.634)
	Common Risk Difference (95% CI)		24.669 (16.882 , 32.456)
	CMH p-value		0.000004

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.15 **ADvocate 1 + ADvocate 2. Responder analysis of EASI90 score by Race, baseline to Week 16 NRI (mITT)**

Race: Overall

		PBO N=287	LEB250Q2W N=564
EASI90 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	130 (45.30%)	261 (46.28%)
	Responder	24 (8.36%)	187 (33.16%)
	Missing	133 (46.34%)	116 (20.57%)
EASI90 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	263 (91.64%)	377 (66.84%)
	Responder	24 (8.36%)	187 (33.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.385 (3.399 , 8.531)
	Relative Risk (95% CI)		3.700 (2.485 , 5.510)
	Common Risk Difference (95% CI)		24.200 (19.175 , 29.226)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.615717

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI90 score by Race, baseline to Week 16 NRI (mITT)

Race: ASIAN

		PBO N=287	LEB250Q2W N=564
EASI90 score (Observed up to ICE), n(%)	Total	75 (26.13%)	117 (20.74%)
	Non-responder	29 (10.10%)	55 (9.75%)
	Responder	3 (1.05%)	31 (5.50%)
	Missing	43 (14.98%)	31 (5.50%)
EASI90 score (NRI) [1] [2], n(%)	Total	75 (26.13%)	117 (20.74%)
	Non-responder	72 (25.09%)	86 (15.25%)
	Responder	3 (1.05%)	31 (5.50%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		10.294 (2.686 , 39.454)
	Relative Risk (95% CI)		5.471 (1.751 , 17.092)
	Common Risk Difference (95% CI)		22.262 (13.159 , 31.365)
	CMH p-value		0.000091

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI90 score by Race, baseline to Week 16 NRI (mITT)

Race: BLACK OR AFRICAN AMERICAN

		PBO N=287	LEB250Q2W N=564
EASI90 score (Observed up to ICE), n(%)	Total	26 (9.06%)	58 (10.28%)
	Non-responder	9 (3.14%)	33 (5.85%)
	Responder	3 (1.05%)	15 (2.66%)
	Missing	14 (4.88%)	10 (1.77%)
EASI90 score (NRI) [1] [2], n(%)	Total	26 (9.06%)	58 (10.28%)
	Non-responder	23 (8.01%)	43 (7.62%)
	Responder	3 (1.05%)	15 (2.66%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		1.981 (0.485 , 8.092)
	Relative Risk (95% CI)		1.612 (0.570 , 4.559)
	Common Risk Difference (95% CI)		9.116 (-8.069 , 26.301)
	CMH p-value		0.343210

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI90 score by Race, baseline to Week 16 NRI (mITT)

Race: WHITE

		PBO N=287	LEB250Q2W N=564
EASI90 score (Observed up to ICE), n(%)	Total	178 (62.02%)	364 (64.54%)
	Non-responder	87 (30.31%)	165 (29.26%)
	Responder	18 (6.27%)	133 (23.58%)
	Missing	73 (25.44%)	66 (11.70%)
EASI90 score (NRI) [1] [2], n(%)	Total	178 (62.02%)	364 (64.54%)
	Non-responder	160 (55.75%)	231 (40.96%)
	Responder	18 (6.27%)	133 (23.58%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.101 (2.963 , 8.784)
	Relative Risk (95% CI)		3.478 (2.200 , 5.500)
	Common Risk Difference (95% CI)		26.280 (19.551 , 33.009)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of EASI90 score by Race, baseline to Week 16 NRI (mITT)

Race: OTHER

		PBO N=287	LEB250Q2W N=564
EASI90 score (Observed up to ICE), n(%)	Total	8 (2.79%)	25 (4.43%)
	Non-responder	5 (1.74%)	8 (1.42%)
	Responder	0 (0.00%)	8 (1.42%)
	Missing	3 (1.05%)	9 (1.60%)
EASI90 score (NRI) [1] [2], n(%)	Total	8 (2.79%)	25 (4.43%)
	Non-responder	8 (2.79%)	17 (3.01%)
	Responder	0 (0.00%)	8 (1.42%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		20.820 (-6.881 , 48.521)
	CMH p-value		0.243615

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.16 **ADvocate 1 + ADvocate 2. Responder analysis of SCORAD75 score by Gender, baseline to Week 16 NRI (mITT)**

Gender: Overall

		PBO N=287	LEB250Q2W N=564
SCORAD75 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	136 (47.39%)	308 (54.61%)
	Responder	10 (3.48%)	122 (21.63%)
	Missing	141 (49.13%)	134 (23.76%)
SCORAD75 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	277 (96.52%)	442 (78.37%)
	Responder	10 (3.48%)	122 (21.63%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		7.638 (3.912 , 14.910)
	Relative Risk (95% CI)		5.162 (2.806 , 9.495)
	Common Risk Difference (95% CI)		17.882 (13.882 , 21.882)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.263815

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD75 score by Gender, baseline to Week 16 NRI (mITT)

Gender: F

		PBO N=287	LEB250Q2W N=564
SCORAD75 score (Observed up to ICE), n(%)	Total	148 (51.57%)	277 (49.11%)
	Non-responder	70 (24.39%)	143 (25.35%)
	Responder	8 (2.79%)	69 (12.23%)
	Missing	70 (24.39%)	65 (11.52%)
SCORAD75 score (NRI) [1] [2], n(%)	Total	148 (51.57%)	277 (49.11%)
	Non-responder	140 (48.78%)	208 (36.88%)
	Responder	8 (2.79%)	69 (12.23%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.916 (2.733 , 12.802)
	Relative Risk (95% CI)		3.947 (2.028 , 7.682)
	Common Risk Difference (95% CI)		19.953 (13.546 , 26.360)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD75 score by Gender, baseline to Week 16 NRI (mITT)

Gender: M

		PBO N=287	LEB250Q2W N=564
SCORAD75 score (Observed up to ICE), n(%)	Total	139 (48.43%)	287 (50.89%)
	Non-responder	66 (23.00%)	165 (29.26%)
	Responder	2 (0.70%)	53 (9.40%)
	Missing	71 (24.74%)	69 (12.23%)
SCORAD75 score (NRI) [1] [2], n(%)	Total	139 (48.43%)	287 (50.89%)
	Non-responder	137 (47.74%)	234 (41.49%)
	Responder	2 (0.70%)	53 (9.40%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		15.543 (3.588 , 67.341)
	Relative Risk (95% CI)		9.877 (2.521 , 38.692)
	Common Risk Difference (95% CI)		16.893 (11.798 , 21.988)
	CMH p-value		0.000002

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.17 **ADvocate 1 + ADvocate 2. Responder analysis of SCORAD75 score by Age Group I, baseline to Week 16 NRI (mITT)**

Age Group I: Overall

		PBO N=287	LEB250Q2W N=564
SCORAD75 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	136 (47.39%)	308 (54.61%)
	Responder	10 (3.48%)	122 (21.63%)
	Missing	141 (49.13%)	134 (23.76%)
SCORAD75 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	277 (96.52%)	442 (78.37%)
	Responder	10 (3.48%)	122 (21.63%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		7.638 (3.912 , 14.910)
	Relative Risk (95% CI)		5.162 (2.806 , 9.495)
	Common Risk Difference (95% CI)		17.882 (13.882 , 21.882)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.340285

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD75 score by Age Group I, baseline to Week 16 NRI (mITT)

Age Group I: Adolescents (12<18) years

		PBO N=287	LEB250Q2W N=564
SCORAD75 score (Observed up to ICE), n(%)	Total	35 (12.20%)	67 (11.88%)
	Non-responder	19 (6.62%)	41 (7.27%)
	Responder	2 (0.70%)	14 (2.48%)
	Missing	14 (4.88%)	12 (2.13%)
SCORAD75 score (NRI) [1] [2], n(%)	Total	35 (12.20%)	67 (11.88%)
	Non-responder	33 (11.50%)	53 (9.40%)
	Responder	2 (0.70%)	14 (2.48%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.574 (0.782 , 16.335)
	Relative Risk (95% CI)		2.746 (0.763 , 9.887)
	Common Risk Difference (95% CI)		13.109 (0.308 , 25.910)
	CMH p-value		0.084712

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD75 score by Age Group I, baseline to Week 16 NRI (mITT)

Age Group I: Adults >= 18 years

		PBO N=287	LEB250Q2W N=564
SCORAD75 score (Observed up to ICE), n(%)	Total	252 (87.80%)	497 (88.12%)
	Non-responder	117 (40.77%)	267 (47.34%)
	Responder	8 (2.79%)	108 (19.15%)
	Missing	127 (44.25%)	122 (21.63%)
SCORAD75 score (NRI) [1] [2], n(%)	Total	252 (87.80%)	497 (88.12%)
	Non-responder	244 (85.02%)	389 (68.97%)
	Responder	8 (2.79%)	108 (19.15%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		8.793 (4.166 , 18.560)
	Relative Risk (95% CI)		5.783 (2.908 , 11.501)
	Common Risk Difference (95% CI)		18.515 (14.323 , 22.708)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.18 **ADvocate 1 + ADvocate 2. Responder analysis of SCORAD75 score by Disease Severity II, baseline to Week 16 NRI (mITT)**

Disease Severity II: Overall

		PBO N=287	LEB250Q2W N=564
SCORAD75 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	136 (47.39%)	308 (54.61%)
	Responder	10 (3.48%)	122 (21.63%)
	Missing	141 (49.13%)	134 (23.76%)
SCORAD75 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	277 (96.52%)	442 (78.37%)
	Responder	10 (3.48%)	122 (21.63%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		7.638 (3.912 , 14.910)
	Relative Risk (95% CI)		5.162 (2.806 , 9.495)
	Common Risk Difference (95% CI)		17.882 (13.882 , 21.882)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.783795

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD75 score by Disease Severity II, baseline to Week 16 NRI (mITT)

Disease Severity II: IGA = 3

		PBO N=287	LEB250Q2W N=564
SCORAD75 score (Observed up to ICE), n(%)	Total	178 (62.02%)	345 (61.17%)
	Non-responder	94 (32.75%)	189 (33.51%)
	Responder	6 (2.09%)	76 (13.48%)
	Missing	78 (27.18%)	80 (14.18%)
SCORAD75 score (NRI) [1] [2], n(%)	Total	178 (62.02%)	345 (61.17%)
	Non-responder	172 (59.93%)	269 (47.70%)
	Responder	6 (2.09%)	76 (13.48%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		8.205 (3.446 , 19.534)
	Relative Risk (95% CI)		5.498 (2.480 , 12.189)
	Common Risk Difference (95% CI)		18.540 (13.437 , 23.643)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD75 score by Disease Severity II, baseline to Week 16 NRI (mITT)

Disease Severity II: IGA = 4

		PBO N=287	LEB250Q2W N=564
SCORAD75 score (Observed up to ICE), n(%)	Total	109 (37.98%)	219 (38.83%)
	Non-responder	42 (14.63%)	119 (21.10%)
	Responder	4 (1.39%)	46 (8.16%)
	Missing	63 (21.95%)	54 (9.57%)
SCORAD75 score (NRI) [1] [2], n(%)	Total	109 (37.98%)	219 (38.83%)
	Non-responder	105 (36.59%)	173 (30.67%)
	Responder	4 (1.39%)	46 (8.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.820 (2.383 , 19.522)
	Relative Risk (95% CI)		4.672 (1.814 , 12.032)
	Common Risk Difference (95% CI)		16.818 (10.376 , 23.259)
	CMH p-value		0.000061

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.19 **ADvocate 1 + ADvocate 2. Responder analysis of SCORAD75 score by Region, baseline to Week 16 NRI (mITT)**

Region: Overall

		PBO N=287	LEB250Q2W N=564
SCORAD75 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	136 (47.39%)	308 (54.61%)
	Responder	10 (3.48%)	122 (21.63%)
	Missing	141 (49.13%)	134 (23.76%)
SCORAD75 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	277 (96.52%)	442 (78.37%)
	Responder	10 (3.48%)	122 (21.63%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		7.638 (3.912 , 14.910)
	Relative Risk (95% CI)		5.162 (2.806 , 9.495)
	Common Risk Difference (95% CI)		17.882 (13.882 , 21.882)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.431190

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD75 score by Region, baseline to Week 16 NRI (mITT)

Region: Europe

		PBO N=287	LEB250Q2W N=564
SCORAD75 score (Observed up to ICE), n(%)	Total	84 (29.27%)	168 (29.79%)
	Non-responder	46 (16.03%)	100 (17.73%)
	Responder	3 (1.05%)	42 (7.45%)
	Missing	35 (12.20%)	26 (4.61%)
SCORAD75 score (NRI) [1] [2], n(%)	Total	84 (29.27%)	168 (29.79%)
	Non-responder	81 (28.22%)	126 (22.34%)
	Responder	3 (1.05%)	42 (7.45%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		8.605 (2.584 , 28.655)
	Relative Risk (95% CI)		5.819 (1.940 , 17.456)
	Common Risk Difference (95% CI)		21.444 (13.699 , 29.189)
	CMH p-value		0.000034

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD75 score by Region, baseline to Week 16 NRI (mITT)

Region: US

		PBO N=287	LEB250Q2W N=564
SCORAD75 score (Observed up to ICE), n(%)	Total	122 (42.51%)	235 (41.67%)
	Non-responder	59 (20.56%)	120 (21.28%)
	Responder	7 (2.44%)	56 (9.93%)
	Missing	56 (19.51%)	59 (10.46%)
SCORAD75 score (NRI) [1] [2], n(%)	Total	122 (42.51%)	235 (41.67%)
	Non-responder	115 (40.07%)	179 (31.74%)
	Responder	7 (2.44%)	56 (9.93%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.033 (2.216 , 11.432)
	Relative Risk (95% CI)		3.517 (1.718 , 7.198)
	Common Risk Difference (95% CI)		17.793 (10.939 , 24.647)
	CMH p-value		0.000030

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD75 score by Region, baseline to Week 16 NRI (mITT)

Region: Rest of the World

		PBO N=287	LEB250Q2W N=564
SCORAD75 score (Observed up to ICE), n(%)	Total	81 (28.22%)	161 (28.55%)
	Non-responder	31 (10.80%)	88 (15.60%)
	Responder	0 (0.00%)	24 (4.26%)
	Missing	50 (17.42%)	49 (8.69%)
SCORAD75 score (NRI) [1] [2], n(%)	Total	81 (28.22%)	161 (28.55%)
	Non-responder	81 (28.22%)	137 (24.29%)
	Responder	0 (0.00%)	24 (4.26%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		14.303 (8.848 , 19.758)
	CMH p-value		0.000385

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.20 **ADvocate 1 + ADvocate 2. Responder analysis of SCORAD75 score by Race, baseline to Week 16 NRI (mITT)**

Race: Overall

		PBO N=287	LEB250Q2W N=564
SCORAD75 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	136 (47.39%)	308 (54.61%)
	Responder	10 (3.48%)	122 (21.63%)
	Missing	141 (49.13%)	134 (23.76%)
SCORAD75 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	277 (96.52%)	442 (78.37%)
	Responder	10 (3.48%)	122 (21.63%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		7.638 (3.912 , 14.910)
	Relative Risk (95% CI)		5.162 (2.806 , 9.495)
	Common Risk Difference (95% CI)		17.882 (13.882 , 21.882)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.518151

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD75 score by Race, baseline to Week 16 NRI (mITT)

Race: ASIAN

		PBO N=287	LEB250Q2W N=564
SCORAD75 score (Observed up to ICE), n(%)	Total	75 (26.13%)	117 (20.74%)
	Non-responder	31 (10.80%)	71 (12.59%)
	Responder	1 (0.35%)	14 (2.48%)
	Missing	43 (14.98%)	32 (5.67%)
SCORAD75 score (NRI) [1] [2], n(%)	Total	75 (26.13%)	117 (20.74%)
	Non-responder	74 (25.78%)	103 (18.26%)
	Responder	1 (0.35%)	14 (2.48%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		10.721 (1.095 , 105.02)
	Relative Risk (95% CI)		7.076 (0.759 , 65.937)
	Common Risk Difference (95% CI)		9.192 (3.031 , 15.352)
	CMH p-value		0.017198

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD75 score by Race, baseline to Week 16 NRI (mITT)

Race: BLACK OR AFRICAN AMERICAN

		PBO N=287	LEB250Q2W N=564
SCORAD75 score (Observed up to ICE), n(%)	Total	26 (9.06%)	58 (10.28%)
	Non-responder	9 (3.14%)	36 (6.38%)
	Responder	2 (0.70%)	10 (1.77%)
	Missing	15 (5.23%)	12 (2.13%)
SCORAD75 score (NRI) [1] [2], n(%)	Total	26 (9.06%)	58 (10.28%)
	Non-responder	24 (8.36%)	48 (8.51%)
	Responder	2 (0.70%)	10 (1.77%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		2.764 (0.499 , 15.300)
	Relative Risk (95% CI)		1.990 (0.557 , 7.113)
	Common Risk Difference (95% CI)		9.906 (-4.646 , 24.457)
	CMH p-value		0.247040

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD75 score by Race, baseline to Week 16 NRI (mITT)

Race: WHITE

		PBO N=287	LEB250Q2W N=564
SCORAD75 score (Observed up to ICE), n(%)	Total	178 (62.02%)	364 (64.54%)
	Non-responder	92 (32.06%)	191 (33.87%)
	Responder	7 (2.44%)	93 (16.49%)
	Missing	79 (27.53%)	80 (14.18%)
SCORAD75 score (NRI) [1] [2], n(%)	Total	178 (62.02%)	364 (64.54%)
	Non-responder	171 (59.58%)	271 (48.05%)
	Responder	7 (2.44%)	93 (16.49%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		8.039 (3.623 , 17.836)
	Relative Risk (95% CI)		5.357 (2.612 , 10.988)
	Common Risk Difference (95% CI)		21.245 (15.824 , 26.666)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD75 score by Race, baseline to Week 16 NRI (mITT)

Race: OTHER

		PBO N=287	LEB250Q2W N=564
SCORAD75 score (Observed up to ICE), n(%)	Total	8 (2.79%)	25 (4.43%)
	Non-responder	4 (1.39%)	10 (1.77%)
	Responder	0 (0.00%)	5 (0.89%)
	Missing	4 (1.39%)	10 (1.77%)
SCORAD75 score (NRI) [1] [2], n(%)	Total	8 (2.79%)	25 (4.43%)
	Non-responder	8 (2.79%)	20 (3.55%)
	Responder	0 (0.00%)	5 (0.89%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		17.035 (-8.208 , 42.277)
	CMH p-value		0.292171

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.21 **ADvocate 1 + ADvocate 2. Responder analysis of SCORAD90 score by Gender, baseline to Week 16 NRI (mITT)**

Gender: Overall

		PBO N=287	LEB250Q2W N=564
SCORAD90 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	145 (50.52%)	384 (68.09%)
	Responder	1 (0.35%)	46 (8.16%)
	Missing	141 (49.13%)	134 (23.76%)
SCORAD90 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	286 (99.65%)	518 (91.84%)
	Responder	1 (0.35%)	46 (8.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		25.406 (3.480 , 185.50)
	Relative Risk (95% CI)		16.657 (2.416 , 114.85)
	Common Risk Difference (95% CI)		7.757 (5.394 , 10.121)
	CMH p-value		0.000003
	Treatment by subgroup interaction test p-value [7]		0.491373

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD90 score by Gender, baseline to Week 16 NRI (mITT)

Gender: F

		PBO N=287	LEB250Q2W N=564
SCORAD90 score (Observed up to ICE), n(%)	Total	148 (51.57%)	277 (49.11%)
	Non-responder	77 (26.83%)	190 (33.69%)
	Responder	1 (0.35%)	22 (3.90%)
	Missing	70 (24.39%)	65 (11.52%)
SCORAD90 score (NRI) [1] [2], n(%)	Total	148 (51.57%)	277 (49.11%)
	Non-responder	147 (51.22%)	255 (45.21%)
	Responder	1 (0.35%)	22 (3.90%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		12.864 (1.697 , 97.548)
	Relative Risk (95% CI)		7.968 (1.258 , 50.476)
	Common Risk Difference (95% CI)		7.228 (3.722 , 10.735)
	CMH p-value		0.002018

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD90 score by Gender, baseline to Week 16 NRI (mITT)

Gender: M

		PBO N=287	LEB250Q2W N=564
SCORAD90 score (Observed up to ICE), n(%)	Total	139 (48.43%)	287 (50.89%)
	Non-responder	68 (23.69%)	194 (34.40%)
	Responder	0 (0.00%)	24 (4.26%)
	Missing	71 (24.74%)	69 (12.23%)
SCORAD90 score (NRI) [1] [2], n(%)	Total	139 (48.43%)	287 (50.89%)
	Non-responder	139 (48.43%)	263 (46.63%)
	Responder	0 (0.00%)	24 (4.26%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		8.370 (5.019 , 11.721)
	CMH p-value		0.000585

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.22 **ADvocate 1 + ADvocate 2. Responder analysis of SCORAD90 score by Age Group I, baseline to Week 16 NRI (mITT)**

Age Group I: Overall

		PBO N=287	LEB250Q2W N=564
SCORAD90 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	145 (50.52%)	384 (68.09%)
	Responder	1 (0.35%)	46 (8.16%)
	Missing	141 (49.13%)	134 (23.76%)
SCORAD90 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	286 (99.65%)	518 (91.84%)
	Responder	1 (0.35%)	46 (8.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		25.406 (3.480 , 185.50)
	Relative Risk (95% CI)		16.657 (2.416 , 114.85)
	Common Risk Difference (95% CI)		7.757 (5.394 , 10.121)
	CMH p-value		0.000003
	Treatment by subgroup interaction test p-value [7]		0.411909

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD90 score by Age Group I, baseline to Week 16 NRI (mITT)

Age Group I: Adolescents (12<18) years

		PBO N=287	LEB250Q2W N=564
SCORAD90 score (Observed up to ICE), n(%)	Total	35 (12.20%)	67 (11.88%)
	Non-responder	21 (7.32%)	52 (9.22%)
	Responder	0 (0.00%)	3 (0.53%)
	Missing	14 (4.88%)	12 (2.13%)
SCORAD90 score (NRI) [1] [2], n(%)	Total	35 (12.20%)	67 (11.88%)
	Non-responder	35 (12.20%)	64 (11.35%)
	Responder	0 (0.00%)	3 (0.53%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		4.332 (-0.727 , 9.392)
	CMH p-value		0.234115

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD90 score by Age Group I, baseline to Week 16 NRI (mITT)

Age Group I: Adults >= 18 years

		PBO N=287	LEB250Q2W N=564
SCORAD90 score (Observed up to ICE), n(%)	Total	252 (87.80%)	497 (88.12%)
	Non-responder	124 (43.21%)	332 (58.87%)
	Responder	1 (0.35%)	43 (7.62%)
	Missing	127 (44.25%)	122 (21.63%)
SCORAD90 score (NRI) [1] [2], n(%)	Total	252 (87.80%)	497 (88.12%)
	Non-responder	251 (87.46%)	454 (80.50%)
	Responder	1 (0.35%)	43 (7.62%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		23.809 (3.240 , 174.94)
	Relative Risk (95% CI)		15.632 (2.254 , 108.40)
	Common Risk Difference (95% CI)		8.212 (5.626 , 10.797)
	CMH p-value		0.000007

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.23 **ADvocate 1 + ADvocate 2. Responder analysis of SCORAD90 score by Disease Severity II, baseline to Week 16 NRI (mITT)**

Disease Severity II: Overall

		PBO N=287	LEB250Q2W N=564
SCORAD90 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	145 (50.52%)	384 (68.09%)
	Responder	1 (0.35%)	46 (8.16%)
	Missing	141 (49.13%)	134 (23.76%)
SCORAD90 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	286 (99.65%)	518 (91.84%)
	Responder	1 (0.35%)	46 (8.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		25.406 (3.480 , 185.50)
	Relative Risk (95% CI)		16.657 (2.416 , 114.85)
	Common Risk Difference (95% CI)		7.757 (5.394 , 10.121)
	CMH p-value		0.000003
	Treatment by subgroup interaction test p-value [7]		0.649831

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD90 score by Disease Severity II, baseline to Week 16 NRI (mITT)

Disease Severity II: IGA = 3

		PBO N=287	LEB250Q2W N=564
SCORAD90 score (Observed up to ICE), n(%)	Total	178 (62.02%)	345 (61.17%)
	Non-responder	99 (34.49%)	238 (42.20%)
	Responder	1 (0.35%)	27 (4.79%)
	Missing	78 (27.18%)	80 (14.18%)
SCORAD90 score (NRI) [1] [2], n(%)	Total	178 (62.02%)	345 (61.17%)
	Non-responder	177 (61.67%)	318 (56.38%)
	Responder	1 (0.35%)	27 (4.79%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		14.930 (1.991 , 111.98)
	Relative Risk (95% CI)		9.936 (1.441 , 68.501)
	Common Risk Difference (95% CI)		7.164 (4.133 , 10.195)
	CMH p-value		0.000602

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD90 score by Disease Severity II, baseline to Week 16 NRI (mITT)

Disease Severity II: IGA = 4

		PBO N=287	LEB250Q2W N=564
SCORAD90 score (Observed up to ICE), n(%)	Total	109 (37.98%)	219 (38.83%)
	Non-responder	46 (16.03%)	146 (25.89%)
	Responder	0 (0.00%)	19 (3.37%)
	Missing	63 (21.95%)	54 (9.57%)
SCORAD90 score (NRI) [1] [2], n(%)	Total	109 (37.98%)	219 (38.83%)
	Non-responder	109 (37.98%)	200 (35.46%)
	Responder	0 (0.00%)	19 (3.37%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		8.717 (4.953 , 12.481)
	CMH p-value		0.001586

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.24 **ADvocate 1 + ADvocate 2. Responder analysis of SCORAD90 score by Region, baseline to Week 16 NRI (mITT)**

Region: Overall

		PBO N=287	LEB250Q2W N=564
SCORAD90 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	145 (50.52%)	384 (68.09%)
	Responder	1 (0.35%)	46 (8.16%)
	Missing	141 (49.13%)	134 (23.76%)
SCORAD90 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	286 (99.65%)	518 (91.84%)
	Responder	1 (0.35%)	46 (8.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		25.406 (3.480 , 185.50)
	Relative Risk (95% CI)		16.657 (2.416 , 114.85)
	Common Risk Difference (95% CI)		7.757 (5.394 , 10.121)
	CMH p-value		0.000003
	Treatment by subgroup interaction test p-value [7]		0.834813

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD90 score by Region, baseline to Week 16 NRI (mITT)

Region: Europe

		PBO N=287	LEB250Q2W N=564
SCORAD90 score (Observed up to ICE), n(%)	Total	84 (29.27%)	168 (29.79%)
	Non-responder	49 (17.07%)	125 (22.16%)
	Responder	0 (0.00%)	17 (3.01%)
	Missing	35 (12.20%)	26 (4.61%)
SCORAD90 score (NRI) [1] [2], n(%)	Total	84 (29.27%)	168 (29.79%)
	Non-responder	84 (29.27%)	151 (26.77%)
	Responder	0 (0.00%)	17 (3.01%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		10.052 (5.483 , 14.620)
	CMH p-value		0.002892

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD90 score by Region, baseline to Week 16 NRI (mITT)

Region: US

		PBO N=287	LEB250Q2W N=564
SCORAD90 score (Observed up to ICE), n(%)	Total	122 (42.51%)	235 (41.67%)
	Non-responder	65 (22.65%)	157 (27.84%)
	Responder	1 (0.35%)	19 (3.37%)
	Missing	56 (19.51%)	59 (10.46%)
SCORAD90 score (NRI) [1] [2], n(%)	Total	122 (42.51%)	235 (41.67%)
	Non-responder	121 (42.16%)	216 (38.30%)
	Responder	1 (0.35%)	19 (3.37%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		10.504 (1.392 , 79.257)
	Relative Risk (95% CI)		7.097 (1.060 , 47.491)
	Common Risk Difference (95% CI)		7.156 (3.326 , 10.986)
	CMH p-value		0.005557

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD90 score by Region, baseline to Week 16 NRI (mITT)

Region: Rest of the World

		PBO N=287	LEB250Q2W N=564
SCORAD90 score (Observed up to ICE), n(%)	Total	81 (28.22%)	161 (28.55%)
	Non-responder	31 (10.80%)	102 (18.09%)
	Responder	0 (0.00%)	10 (1.77%)
	Missing	50 (17.42%)	49 (8.69%)
SCORAD90 score (NRI) [1] [2], n(%)	Total	81 (28.22%)	161 (28.55%)
	Non-responder	81 (28.22%)	151 (26.77%)
	Responder	0 (0.00%)	10 (1.77%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		6.264 (2.498 , 10.030)
	CMH p-value		0.022155

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.25 **ADvocate 1 + ADvocate 2. Responder analysis of SCORAD90 score by Race, baseline to Week 16 NRI (mITT)**

Race: Overall

		PBO N=287	LEB250Q2W N=564
SCORAD90 score (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	145 (50.52%)	384 (68.09%)
	Responder	1 (0.35%)	46 (8.16%)
	Missing	141 (49.13%)	134 (23.76%)
SCORAD90 score (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non-responder	286 (99.65%)	518 (91.84%)
	Responder	1 (0.35%)	46 (8.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		25.406 (3.480 , 185.50)
	Relative Risk (95% CI)		16.657 (2.416 , 114.85)
	Common Risk Difference (95% CI)		7.757 (5.394 , 10.121)
	CMH p-value		0.000003
	Treatment by subgroup interaction test p-value [7]		0.288537

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD90 score by Race, baseline to Week 16 NRI (mITT)

Race: ASIAN

		PBO N=287	LEB250Q2W N=564
SCORAD90 score (Observed up to ICE), n(%)	Total	75 (26.13%)	117 (20.74%)
	Non-responder	31 (10.80%)	81 (14.36%)
	Responder	1 (0.35%)	4 (0.71%)
	Missing	43 (14.98%)	32 (5.67%)
SCORAD90 score (NRI) [1] [2], n(%)	Total	75 (26.13%)	117 (20.74%)
	Non-responder	74 (25.78%)	113 (20.04%)
	Responder	1 (0.35%)	4 (0.71%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		1.678 (0.180 , 15.676)
	Relative Risk (95% CI)		1.493 (0.232 , 9.624)
	Common Risk Difference (95% CI)		1.026 (-3.069 , 5.120)
	CMH p-value		0.636035

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD90 score by Race, baseline to Week 16 NRI (mITT)

Race: BLACK OR AFRICAN AMERICAN

		PBO N=287	LEB250Q2W N=564
SCORAD90 score (Observed up to ICE), n(%)	Total	26 (9.06%)	58 (10.28%)
	Non-responder	11 (3.83%)	42 (7.45%)
	Responder	0 (0.00%)	4 (0.71%)
	Missing	15 (5.23%)	12 (2.13%)
SCORAD90 score (NRI) [1] [2], n(%)	Total	26 (9.06%)	58 (10.28%)
	Non-responder	26 (9.06%)	54 (9.57%)
	Responder	0 (0.00%)	4 (0.71%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		4.926 (-1.353 , 11.205)
	CMH p-value		0.236518

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD90 score by Race, baseline to Week 16 NRI (mITT)

Race: WHITE

		PBO N=287	LEB250Q2W N=564
SCORAD90 score (Observed up to ICE), n(%)	Total	178 (62.02%)	364 (64.54%)
	Non-responder	99 (34.49%)	247 (43.79%)
	Responder	0 (0.00%)	37 (6.56%)
	Missing	79 (27.53%)	80 (14.18%)
SCORAD90 score (NRI) [1] [2], n(%)	Total	178 (62.02%)	364 (64.54%)
	Non-responder	178 (62.02%)	327 (57.98%)
	Responder	0 (0.00%)	37 (6.56%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		9.866 (6.726 , 13.006)
	CMH p-value		0.000023

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of SCORAD90 score by Race, baseline to Week 16 NRI (mITT)

Race: OTHER

		PBO N=287	LEB250Q2W N=564
SCORAD90 score (Observed up to ICE), n(%)	Total	8 (2.79%)	25 (4.43%)
	Non-responder	4 (1.39%)	14 (2.48%)
	Responder	0 (0.00%)	1 (0.18%)
	Missing	4 (1.39%)	10 (1.77%)
SCORAD90 score (NRI) [1] [2], n(%)	Total	8 (2.79%)	25 (4.43%)
	Non-responder	8 (2.79%)	24 (4.26%)
	Responder	0 (0.00%)	1 (0.18%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		13.249 (-9.176 , 35.674)
	CMH p-value		0.317311

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.26 **ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Gender from baseline at Week 16, NRi (mITT, patients with baseline >= 4)**

Gender: Overall

		PBO N=264	LEB250Q2W N=516
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	264 (100.00%)	516 (100.00%)
	Non-responder	108 (40.91%)	193 (37.40%)
	Responder	28 (10.61%)	208 (40.31%)
	Missing	128 (48.48%)	115 (22.29%)
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	264 (100.00%)	516 (100.00%)
	Non-responder	236 (89.39%)	308 (59.69%)
	Responder	28 (10.61%)	208 (40.31%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.722 (3.705 , 8.837)
	Relative Risk (95% CI)		3.768 (2.605 , 5.452)
	Common Risk Difference (95% CI)		29.539 (23.901 , 35.176)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.393476

	PBO N=264	LEB250Q2W N=516

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Gender from baseline at Week 16, NRi (mITT, patients with baseline >= 4)

Gender: F

		PBO N=264	LEB250Q2W N=516
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	133 (50.38%)	250 (48.45%)
	Non-responder	54 (20.45%)	91 (17.64%)
	Responder	17 (6.44%)	104 (20.16%)
	Missing	62 (23.48%)	55 (10.66%)
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	133 (50.38%)	250 (48.45%)
	Non-responder	116 (43.94%)	146 (28.29%)
	Responder	17 (6.44%)	104 (20.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.645 (2.638 , 8.181)
	Relative Risk (95% CI)		3.163 (1.978 , 5.056)
	Common Risk Difference (95% CI)		28.998 (20.312 , 37.683)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Gender from baseline at Week 16, NRi (mITT, patients with baseline >= 4)

Gender: M

		PBO N=264	LEB250Q2W N=516
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	131 (49.62%)	266 (51.55%)
	Non-responder	54 (20.45%)	102 (19.77%)
	Responder	11 (4.17%)	104 (20.16%)
	Missing	66 (25.00%)	60 (11.63%)
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	131 (49.62%)	266 (51.55%)
	Non-responder	120 (45.45%)	162 (31.40%)
	Responder	11 (4.17%)	104 (20.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		7.970 (3.942 , 16.116)
	Relative Risk (95% CI)		4.835 (2.647 , 8.830)
	Common Risk Difference (95% CI)		32.227 (24.555 , 39.900)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.27 **ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Age Group I from baseline at Week 16, NRi (mITT, patients with baseline >= 4)**

Age Group I: Overall

		PBO N=264	LEB250Q2W N=516
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	264 (100.00%)	516 (100.00%)
	Non-responder	108 (40.91%)	193 (37.40%)
	Responder	28 (10.61%)	208 (40.31%)
	Missing	128 (48.48%)	115 (22.29%)
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	264 (100.00%)	516 (100.00%)
	Non-responder	236 (89.39%)	308 (59.69%)
	Responder	28 (10.61%)	208 (40.31%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.722 (3.705 , 8.837)
	Relative Risk (95% CI)		3.768 (2.605 , 5.452)
	Common Risk Difference (95% CI)		29.539 (23.901 , 35.176)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.914061

	PBO N=264	LEB250Q2W N=516

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Age Group I from baseline at Week 16, NRi (mITT, patients with baseline >= 4)

Age Group I: Adolescents (12<18) years

		PBO N=264	LEB250Q2W N=516
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	30 (11.36%)	56 (10.85%)
	Non-responder	14 (5.30%)	21 (4.07%)
	Responder	3 (1.14%)	24 (4.65%)
	Missing	13 (4.92%)	11 (2.13%)
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	30 (11.36%)	56 (10.85%)
	Non-responder	27 (10.23%)	32 (6.20%)
	Responder	3 (1.14%)	24 (4.65%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.403 (1.606 , 25.528)
	Relative Risk (95% CI)		4.859 (1.289 , 18.317)
	Common Risk Difference (95% CI)		31.342 (13.939 , 48.746)
	CMH p-value		0.003982

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Age Group I from baseline at Week 16, NRi (mITT, patients with baseline >= 4)

Age Group I: Adults >= 18 years

		PBO N=264	LEB250Q2W N=516
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	234 (88.64%)	460 (89.15%)
	Non-responder	94 (35.61%)	172 (33.33%)
	Responder	25 (9.47%)	184 (35.66%)
	Missing	115 (43.56%)	104 (20.16%)
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	234 (88.64%)	460 (89.15%)
	Non-responder	209 (79.17%)	276 (53.49%)
	Responder	25 (9.47%)	184 (35.66%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.647 (3.572 , 8.929)
	Relative Risk (95% CI)		3.672 (2.501 , 5.393)
	Common Risk Difference (95% CI)		29.323 (23.364 , 35.283)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.28 **ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Disease Severity II from baseline at Week 16, NRi (mITT, patients with baseline >= 4)**

Disease Severity II: Overall

		PBO N=264	LEB250Q2W N=516
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	264 (100.00%)	516 (100.00%)
	Non-responder	108 (40.91%)	193 (37.40%)
	Responder	28 (10.61%)	208 (40.31%)
	Missing	128 (48.48%)	115 (22.29%)
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	264 (100.00%)	516 (100.00%)
	Non-responder	236 (89.39%)	308 (59.69%)
	Responder	28 (10.61%)	208 (40.31%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.722 (3.705 , 8.837)
	Relative Risk (95% CI)		3.768 (2.605 , 5.452)
	Common Risk Difference (95% CI)		29.539 (23.901 , 35.176)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.167626

	PBO N=264	LEB250Q2W N=516

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Disease Severity II from baseline at Week 16, NRi (mITT, patients with baseline >= 4)

Disease Severity II: IGA = 3

		PBO N=264	LEB250Q2W N=516
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	160 (60.61%)	306 (59.30%)
	Non-responder	71 (26.89%)	125 (24.22%)
	Responder	20 (7.58%)	119 (23.06%)
	Missing	69 (26.14%)	62 (12.02%)
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	160 (60.61%)	306 (59.30%)
	Non-responder	140 (53.03%)	187 (36.24%)
	Responder	20 (7.58%)	119 (23.06%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.398 (2.614 , 7.400)
	Relative Risk (95% CI)		3.041 (1.976 , 4.681)
	Common Risk Difference (95% CI)		26.499 (18.936 , 34.062)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Disease Severity II from baseline at Week 16, NRi (mITT, patients with baseline >= 4)

Disease Severity II: IGA = 4

		PBO N=264	LEB250Q2W N=516
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	104 (39.39%)	210 (40.70%)
	Non-responder	37 (14.02%)	68 (13.18%)
	Responder	8 (3.03%)	89 (17.25%)
	Missing	59 (22.35%)	53 (10.27%)
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	104 (39.39%)	210 (40.70%)
	Non-responder	96 (36.36%)	121 (23.45%)
	Responder	8 (3.03%)	89 (17.25%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		9.703 (4.324 , 21.772)
	Relative Risk (95% CI)		5.758 (2.818 , 11.768)
	Common Risk Difference (95% CI)		34.135 (25.851 , 42.419)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.29 **ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Region from baseline at Week 16, NRi (mITT, patients with baseline >= 4)**

Region: Overall

		PBO N=264	LEB250Q2W N=516
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	264 (100.00%)	516 (100.00%)
	Non-responder	108 (40.91%)	193 (37.40%)
	Responder	28 (10.61%)	208 (40.31%)
	Missing	128 (48.48%)	115 (22.29%)
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	264 (100.00%)	516 (100.00%)
	Non-responder	236 (89.39%)	308 (59.69%)
	Responder	28 (10.61%)	208 (40.31%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.722 (3.705 , 8.837)
	Relative Risk (95% CI)		3.768 (2.605 , 5.452)
	Common Risk Difference (95% CI)		29.539 (23.901 , 35.176)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.047319

	PBO N=264	LEB250Q2W N=516

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Region from baseline at Week 16, NRi (mITT, patients with baseline >= 4)

Region: Europe

		PBO N=264	LEB250Q2W N=516
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	76 (28.79%)	151 (29.26%)
	Non-responder	38 (14.39%)	68 (13.18%)
	Responder	9 (3.41%)	67 (12.98%)
	Missing	29 (10.98%)	16 (3.10%)
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	76 (28.79%)	151 (29.26%)
	Non-responder	67 (25.38%)	84 (16.28%)
	Responder	9 (3.41%)	67 (12.98%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.925 (2.742 , 12.800)
	Relative Risk (95% CI)		3.741 (1.971 , 7.103)
	Common Risk Difference (95% CI)		32.279 (21.515 , 43.043)
	CMH p-value		0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Region from baseline at Week 16, NRi (mITT, patients with baseline >= 4)

Region: US

		PBO N=264	LEB250Q2W N=516
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	110 (41.67%)	211 (40.89%)
	Non-responder	41 (15.53%)	77 (14.92%)
	Responder	17 (6.44%)	81 (15.70%)
	Missing	52 (19.70%)	53 (10.27%)
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	110 (41.67%)	211 (40.89%)
	Non-responder	93 (35.23%)	130 (25.19%)
	Responder	17 (6.44%)	81 (15.70%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.379 (1.874 , 6.093)
	Relative Risk (95% CI)		2.452 (1.527 , 3.936)
	Common Risk Difference (95% CI)		22.825 (13.349 , 32.301)
	CMH p-value		0.000028

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Region from baseline at Week 16, NRi (mITT, patients with baseline >= 4)

Region: Rest of the World

		PBO N=264	LEB250Q2W N=516
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	78 (29.55%)	154 (29.84%)
	Non-responder	29 (10.98%)	48 (9.30%)
	Responder	2 (0.76%)	60 (11.63%)
	Missing	47 (17.80%)	46 (8.91%)
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	78 (29.55%)	154 (29.84%)
	Non-responder	76 (28.79%)	94 (18.22%)
	Responder	2 (0.76%)	60 (11.63%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		28.911 (6.340 , 131.83)
	Relative Risk (95% CI)		15.340 (3.705 , 63.504)
	Common Risk Difference (95% CI)		36.233 (27.836 , 44.631)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.30 **ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Race from baseline at Week 16, NRi (mITT, patients with baseline >= 4)**

Race: Overall

		PBO N=264	LEB250Q2W N=516
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	264 (100.00%)	516 (100.00%)
	Non-responder	108 (40.91%)	193 (37.40%)
	Responder	28 (10.61%)	208 (40.31%)
	Missing	128 (48.48%)	115 (22.29%)
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	264 (100.00%)	516 (100.00%)
	Non-responder	236 (89.39%)	308 (59.69%)
	Responder	28 (10.61%)	208 (40.31%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.722 (3.705 , 8.837)
	Relative Risk (95% CI)		3.768 (2.605 , 5.452)
	Common Risk Difference (95% CI)		29.539 (23.901 , 35.176)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.458385

	PBO N=264	LEB250Q2W N=516

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Race from baseline at Week 16, NRi (mITT, patients with baseline >= 4)

Race: ASIAN

		PBO N=264	LEB250Q2W N=516
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	74 (28.03%)	110 (21.32%)
	Non-responder	27 (10.23%)	41 (7.95%)
	Responder	3 (1.14%)	40 (7.75%)
	Missing	44 (16.67%)	29 (5.62%)
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	74 (28.03%)	110 (21.32%)
	Non-responder	71 (26.89%)	70 (13.57%)
	Responder	3 (1.14%)	40 (7.75%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		14.971 (4.127 , 54.313)
	Relative Risk (95% CI)		7.217 (2.380 , 21.888)
	Common Risk Difference (95% CI)		32.269 (22.148 , 42.390)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Race from baseline at Week 16, NRi (mITT, patients with baseline >= 4)

Race: BLACK OR AFRICAN AMERICAN

		PBO N=264	LEB250Q2W N=516
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	26 (9.85%)	49 (9.50%)
	Non-responder	10 (3.79%)	20 (3.88%)
	Responder	2 (0.76%)	19 (3.68%)
	Missing	14 (5.30%)	10 (1.94%)
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	26 (9.85%)	49 (9.50%)
	Non-responder	24 (9.09%)	30 (5.81%)
	Responder	2 (0.76%)	19 (3.68%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.657 (1.097 , 19.777)
	Relative Risk (95% CI)		3.582 (0.958 , 13.396)
	Common Risk Difference (95% CI)		26.149 (6.386 , 45.911)
	CMH p-value		0.017739

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Race from baseline at Week 16, NRi (mITT, patients with baseline >= 4)

Race: WHITE

		PBO N=264	LEB250Q2W N=516
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	157 (59.47%)	332 (64.34%)
	Non-responder	68 (25.76%)	125 (24.22%)
	Responder	23 (8.71%)	142 (27.52%)
	Missing	66 (25.00%)	65 (12.60%)
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	157 (59.47%)	332 (64.34%)
	Non-responder	134 (50.76%)	190 (36.82%)
	Responder	23 (8.71%)	142 (27.52%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.472 (2.691 , 7.430)
	Relative Risk (95% CI)		3.005 (2.001 , 4.513)
	Common Risk Difference (95% CI)		28.335 (20.575 , 36.096)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Race from baseline at Week 16, NRi (mITT, patients with baseline >= 4)

Race: OTHER

		PBO N=264	LEB250Q2W N=516
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	7 (2.65%)	25 (4.84%)
	Non-responder	3 (1.14%)	7 (1.36%)
	Responder	0 (0.00%)	7 (1.36%)
	Missing	4 (1.52%)	11 (2.13%)
Pruritus NRS, Baseline >= 4 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	7 (2.65%)	25 (4.84%)
	Non-responder	7 (2.65%)	18 (3.49%)
	Responder	0 (0.00%)	7 (1.36%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		27.142 (-2.932 , 57.216)
	CMH p-value		0.174642

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.31 **ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Gender from baseline at Week 16, NRi (mITT, patients with baseline >= 5)**

Gender: Overall

		PBO N=245	LEB250Q2W N=478
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	245 (100.00%)	478 (100.00%)
	Non-responder	96 (39.18%)	167 (34.94%)
	Responder	27 (11.02%)	204 (42.68%)
	Missing	122 (49.80%)	107 (22.38%)
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	245 (100.00%)	478 (100.00%)
	Non-responder	218 (88.98%)	274 (57.32%)
	Responder	27 (11.02%)	204 (42.68%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.001 (3.843 , 9.371)
	Relative Risk (95% CI)		3.898 (2.671 , 5.690)
	Common Risk Difference (95% CI)		31.321 (25.385 , 37.258)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.750149

	PBO N=245	LEB250Q2W N=478

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Gender from baseline at Week 16, NRi (mITT, patients with baseline >= 5)

Gender: F

		PBO N=245	LEB250Q2W N=478
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	127 (51.84%)	223 (46.65%)
	Non-responder	51 (20.82%)	75 (15.69%)
	Responder	16 (6.53%)	101 (21.13%)
	Missing	60 (24.49%)	47 (9.83%)
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	127 (51.84%)	223 (46.65%)
	Non-responder	111 (45.31%)	122 (25.52%)
	Responder	16 (6.53%)	101 (21.13%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.306 (2.960 , 9.511)
	Relative Risk (95% CI)		3.437 (2.123 , 5.562)
	Common Risk Difference (95% CI)		32.680 (23.495 , 41.864)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Gender from baseline at Week 16, NRi (mITT, patients with baseline >= 5)

Gender: M

		PBO N=245	LEB250Q2W N=478
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	118 (48.16%)	255 (53.35%)
	Non-responder	45 (18.37%)	92 (19.25%)
	Responder	11 (4.49%)	103 (21.55%)
	Missing	62 (25.31%)	60 (12.55%)
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	118 (48.16%)	255 (53.35%)
	Non-responder	107 (43.67%)	152 (31.80%)
	Responder	11 (4.49%)	103 (21.55%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		7.323 (3.603 , 14.885)
	Relative Risk (95% CI)		4.589 (2.504 , 8.410)
	Common Risk Difference (95% CI)		31.988 (23.866 , 40.111)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.32 **ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Age Group I from baseline at Week 16, NRi (mITT, patients with baseline >= 5)**

Age Group I: Overall

		PBO N=245	LEB250Q2W N=478
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	245 (100.00%)	478 (100.00%)
	Non-responder	96 (39.18%)	167 (34.94%)
	Responder	27 (11.02%)	204 (42.68%)
	Missing	122 (49.80%)	107 (22.38%)
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	245 (100.00%)	478 (100.00%)
	Non-responder	218 (88.98%)	274 (57.32%)
	Responder	27 (11.02%)	204 (42.68%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.001 (3.843 , 9.371)
	Relative Risk (95% CI)		3.898 (2.671 , 5.690)
	Common Risk Difference (95% CI)		31.321 (25.385 , 37.258)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.903321

	PBO N=245	LEB250Q2W N=478

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Age Group I from baseline at Week 16, NRi (mITT, patients with baseline >= 5)

Age Group I: Adolescents (12<18) years

		PBO N=245	LEB250Q2W N=478
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	28 (11.43%)	52 (10.88%)
	Non-responder	13 (5.31%)	18 (3.77%)
	Responder	3 (1.22%)	24 (5.02%)
	Missing	12 (4.90%)	10 (2.09%)
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	28 (11.43%)	52 (10.88%)
	Non-responder	25 (10.20%)	28 (5.86%)
	Responder	3 (1.22%)	24 (5.02%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.391 (1.612 , 25.338)
	Relative Risk (95% CI)		4.851 (1.298 , 18.122)
	Common Risk Difference (95% CI)		34.063 (15.253 , 52.874)
	CMH p-value		0.003903

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Age Group I from baseline at Week 16, NRi (mITT, patients with baseline >= 5)

Age Group I: Adults >= 18 years

		PBO N=245	LEB250Q2W N=478
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	217 (88.57%)	426 (89.12%)
	Non-responder	83 (33.88%)	149 (31.17%)
	Responder	24 (9.80%)	180 (37.66%)
	Missing	110 (44.90%)	97 (20.29%)
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	217 (88.57%)	426 (89.12%)
	Non-responder	193 (78.78%)	246 (51.46%)
	Responder	24 (9.80%)	180 (37.66%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.955 (3.718 , 9.538)
	Relative Risk (95% CI)		3.808 (2.567 , 5.650)
	Common Risk Difference (95% CI)		30.997 (24.742 , 37.252)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.33 **ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Disease Severity II from baseline at Week 16, NRi (mITT, patients with baseline >= 5)**

Disease Severity II: Overall

		PBO N=245	LEB250Q2W N=478
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	245 (100.00%)	478 (100.00%)
	Non-responder	96 (39.18%)	167 (34.94%)
	Responder	27 (11.02%)	204 (42.68%)
	Missing	122 (49.80%)	107 (22.38%)
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	245 (100.00%)	478 (100.00%)
	Non-responder	218 (88.98%)	274 (57.32%)
	Responder	27 (11.02%)	204 (42.68%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.001 (3.843 , 9.371)
	Relative Risk (95% CI)		3.898 (2.671 , 5.690)
	Common Risk Difference (95% CI)		31.321 (25.385 , 37.258)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.152427

	PBO N=245	LEB250Q2W N=478

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Disease Severity II from baseline at Week 16, NRi (mITT, patients with baseline >= 5)

Disease Severity II: IGA = 3

		PBO N=245	LEB250Q2W N=478
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	142 (57.96%)	279 (58.37%)
	Non-responder	60 (24.49%)	108 (22.59%)
	Responder	19 (7.76%)	116 (24.27%)
	Missing	63 (25.71%)	55 (11.51%)
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	142 (57.96%)	279 (58.37%)
	Non-responder	123 (50.20%)	163 (34.10%)
	Responder	19 (7.76%)	116 (24.27%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.494 (2.625 , 7.694)
	Relative Risk (95% CI)		3.096 (1.985 , 4.828)
	Common Risk Difference (95% CI)		28.049 (19.917 , 36.182)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Disease Severity II from baseline at Week 16, NRi (mITT, patients with baseline >= 5)

Disease Severity II: IGA = 4

		PBO N=245	LEB250Q2W N=478
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	103 (42.04%)	199 (41.63%)
	Non-responder	36 (14.69%)	59 (12.34%)
	Responder	8 (3.27%)	88 (18.41%)
	Missing	59 (24.08%)	52 (10.88%)
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	103 (42.04%)	199 (41.63%)
	Non-responder	95 (38.78%)	111 (23.22%)
	Responder	8 (3.27%)	88 (18.41%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		10.434 (4.613 , 23.596)
	Relative Risk (95% CI)		5.972 (2.912 , 12.247)
	Common Risk Difference (95% CI)		35.880 (27.371 , 44.389)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.34 **ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Region from baseline at Week 16, NRi (mITT, patients with baseline >= 5)**

Region: Overall

		PBO N=245	LEB250Q2W N=478
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	245 (100.00%)	478 (100.00%)
	Non-responder	96 (39.18%)	167 (34.94%)
	Responder	27 (11.02%)	204 (42.68%)
	Missing	122 (49.80%)	107 (22.38%)
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	245 (100.00%)	478 (100.00%)
	Non-responder	218 (88.98%)	274 (57.32%)
	Responder	27 (11.02%)	204 (42.68%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.001 (3.843 , 9.371)
	Relative Risk (95% CI)		3.898 (2.671 , 5.690)
	Common Risk Difference (95% CI)		31.321 (25.385 , 37.258)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.061993

	PBO N=245	LEB250Q2W N=478

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Region from baseline at Week 16, NRi (mITT, patients with baseline >= 5)

Region: Europe

		PBO N=245	LEB250Q2W N=478
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	66 (26.94%)	145 (30.33%)
	Non-responder	33 (13.47%)	63 (13.18%)
	Responder	8 (3.27%)	66 (13.81%)
	Missing	25 (10.20%)	16 (3.35%)
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	66 (26.94%)	145 (30.33%)
	Non-responder	58 (23.67%)	79 (16.53%)
	Responder	8 (3.27%)	66 (13.81%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.028 (2.676 , 13.581)
	Relative Risk (95% CI)		3.931 (1.975 , 7.826)
	Common Risk Difference (95% CI)		33.157 (21.848 , 44.467)
	CMH p-value		0.000004

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Region from baseline at Week 16, NRi (mITT, patients with baseline >= 5)

Region: US

		PBO N=245	LEB250Q2W N=478
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	105 (42.86%)	189 (39.54%)
	Non-responder	36 (14.69%)	63 (13.18%)
	Responder	17 (6.94%)	79 (16.53%)
	Missing	52 (21.22%)	47 (9.83%)
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	105 (42.86%)	189 (39.54%)
	Non-responder	88 (35.92%)	110 (23.01%)
	Responder	17 (6.94%)	79 (16.53%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.684 (2.031 , 6.684)
	Relative Risk (95% CI)		2.571 (1.602 , 4.124)
	Common Risk Difference (95% CI)		25.673 (15.639 , 35.706)
	CMH p-value		0.000008

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Region from baseline at Week 16, NRi (mITT, patients with baseline >= 5)
Region: Rest of the World

		PBO N=245	LEB250Q2W N=478
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	74 (30.20%)	144 (30.13%)
	Non-responder	27 (11.02%)	41 (8.58%)
	Responder	2 (0.82%)	59 (12.34%)
	Missing	45 (18.37%)	44 (9.21%)
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	74 (30.20%)	144 (30.13%)
	Non-responder	72 (29.39%)	85 (17.78%)
	Responder	2 (0.82%)	59 (12.34%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		28.606 (6.246 , 131.01)
	Relative Risk (95% CI)		15.294 (3.659 , 63.921)
	Common Risk Difference (95% CI)		37.460 (28.618 , 46.301)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.35 **ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Race from baseline at Week 16, NRi (mITT, patients with baseline >= 5)**

Race: Overall

		PBO N=245	LEB250Q2W N=478
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	245 (100.00%)	478 (100.00%)
	Non-responder	96 (39.18%)	167 (34.94%)
	Responder	27 (11.02%)	204 (42.68%)
	Missing	122 (49.80%)	107 (22.38%)
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	245 (100.00%)	478 (100.00%)
	Non-responder	218 (88.98%)	274 (57.32%)
	Responder	27 (11.02%)	204 (42.68%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.001 (3.843 , 9.371)
	Relative Risk (95% CI)		3.898 (2.671 , 5.690)
	Common Risk Difference (95% CI)		31.321 (25.385 , 37.258)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.346903

	PBO N=245	LEB250Q2W N=478

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Race from baseline at Week 16, NRi (mITT, patients with baseline >= 5)

Race: ASIAN

		PBO N=245	LEB250Q2W N=478
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	72 (29.39%)	99 (20.71%)
	Non-responder	26 (10.61%)	32 (6.69%)
	Responder	3 (1.22%)	40 (8.37%)
	Missing	43 (17.55%)	27 (5.65%)
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	72 (29.39%)	99 (20.71%)
	Non-responder	69 (28.16%)	59 (12.34%)
	Responder	3 (1.22%)	40 (8.37%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		18.624 (4.909 , 70.665)
	Relative Risk (95% CI)		7.832 (2.562 , 23.943)
	Common Risk Difference (95% CI)		35.924 (25.248 , 46.599)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Race from baseline at Week 16, NRi (mITT, patients with baseline >= 5)

Race: BLACK OR AFRICAN AMERICAN

		PBO N=245	LEB250Q2W N=478
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	24 (9.80%)	46 (9.62%)
	Non-responder	8 (3.27%)	17 (3.56%)
	Responder	2 (0.82%)	19 (3.97%)
	Missing	14 (5.71%)	10 (2.09%)
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	24 (9.80%)	46 (9.62%)
	Non-responder	22 (8.98%)	27 (5.65%)
	Responder	2 (0.82%)	19 (3.97%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.544 (1.019 , 20.266)
	Relative Risk (95% CI)		3.362 (0.856 , 13.200)
	Common Risk Difference (95% CI)		26.071 (4.938 , 47.205)
	CMH p-value		0.027886

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Race from baseline at Week 16, NRi (mITT, patients with baseline >= 5)

Race: WHITE

		PBO N=245	LEB250Q2W N=478
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	142 (57.96%)	311 (65.06%)
	Non-responder	59 (24.08%)	113 (23.64%)
	Responder	22 (8.98%)	138 (28.87%)
	Missing	61 (24.90%)	60 (12.55%)
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	142 (57.96%)	311 (65.06%)
	Non-responder	120 (48.98%)	173 (36.19%)
	Responder	22 (8.98%)	138 (28.87%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.513 (2.674 , 7.618)
	Relative Risk (95% CI)		3.044 (2.002 , 4.631)
	Common Risk Difference (95% CI)		29.219 (21.054 , 37.383)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Pruritus NRS, reduction >= 4 points by Race from baseline at Week 16, NRi (mITT, patients with baseline >= 5)

Race: OTHER

		PBO N=245	LEB250Q2W N=478
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (Observed up to ICE), n(%)	Total	7 (2.86%)	22 (4.60%)
	Non-responder	3 (1.22%)	5 (1.05%)
	Responder	0 (0.00%)	7 (1.46%)
	Missing	4 (1.63%)	10 (2.09%)
Pruritus NRS, Baseline >= 5 points and reduction >= 4 points (NRI) [1] [2], n(%)	Total	7 (2.86%)	22 (4.60%)
	Non-responder	7 (2.86%)	15 (3.14%)
	Responder	0 (0.00%)	7 (1.46%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		29.268 (-2.755 , 61.291)
	CMH p-value		0.165518

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.36 **ADvocate 1 + ADvocate 2. Responder analysis of Sleep-Loss-Score, reduction >= 2 points by Gender from baseline at Week 16, NRi (mITT, patients with baseline >= 2)**

Gender: Overall

		PBO N=188	LEB250Q2W N=356
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (Observed up to ICE), n(%)	Total	188 (100.00%)	356 (100.00%)
	Non-responder	81 (43.09%)	160 (44.94%)
	Responder	10 (5.32%)	117 (32.87%)
	Missing	97 (51.60%)	79 (22.19%)
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (NRI) [1] [2], n(%)	Total	188 (100.00%)	356 (100.00%)
	Non-responder	178 (94.68%)	239 (67.13%)
	Responder	10 (5.32%)	117 (32.87%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		8.156 (4.150 , 16.031)
	Relative Risk (95% CI)		5.204 (2.864 , 9.455)
	Common Risk Difference (95% CI)		26.854 (20.900 , 32.809)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.510182

	PBO N=188	LEB250Q2W N=356

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Sleep-Loss-Score, reduction >= 2 points by Gender from baseline at Week 16, NRi (mITT, patients with baseline >= 2)

Gender: F

		PBO N=188	LEB250Q2W N=356
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (Observed up to ICE), n(%)	Total	101 (53.72%)	162 (45.51%)
	Non-responder	48 (25.53%)	68 (19.10%)
	Responder	5 (2.66%)	59 (16.57%)
	Missing	48 (25.53%)	35 (9.83%)
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (NRI) [1] [2], n(%)	Total	101 (53.72%)	162 (45.51%)
	Non-responder	96 (51.06%)	103 (28.93%)
	Responder	5 (2.66%)	59 (16.57%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		10.066 (3.712 , 27.292)
	Relative Risk (95% CI)		6.039 (2.545 , 14.330)
	Common Risk Difference (95% CI)		30.793 (21.870 , 39.715)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Sleep-Loss-Score, reduction >= 2 points by Gender from baseline at Week 16, NRi (mITT, patients with baseline >= 2)

Gender: M

		PBO N=188	LEB250Q2W N=356
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (Observed up to ICE), n(%)	Total	87 (46.28%)	194 (54.49%)
	Non-responder	33 (17.55%)	92 (25.84%)
	Responder	5 (2.66%)	58 (16.29%)
	Missing	49 (26.06%)	44 (12.36%)
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (NRI) [1] [2], n(%)	Total	87 (46.28%)	194 (54.49%)
	Non-responder	82 (43.62%)	136 (38.20%)
	Responder	5 (2.66%)	58 (16.29%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.399 (2.452 , 16.703)
	Relative Risk (95% CI)		4.418 (1.891 , 10.321)
	Common Risk Difference (95% CI)		23.377 (14.770 , 31.984)
	CMH p-value		0.000031

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.37 **ADvocate 1 + ADvocate 2. Responder analysis of Sleep-Loss-Score, reduction >= 2 points by Age Group I from baseline at Week 16, NRi (mITT, patients with baseline >= 2)**

Age Group I: Overall

		PBO N=188	LEB250Q2W N=356
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (Observed up to ICE), n(%)	Total	188 (100.00%)	356 (100.00%)
	Non-responder	81 (43.09%)	160 (44.94%)
	Responder	10 (5.32%)	117 (32.87%)
	Missing	97 (51.60%)	79 (22.19%)
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (NRI) [1] [2], n(%)	Total	188 (100.00%)	356 (100.00%)
	Non-responder	178 (94.68%)	239 (67.13%)
	Responder	10 (5.32%)	117 (32.87%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		8.156 (4.150 , 16.031)
	Relative Risk (95% CI)		5.204 (2.864 , 9.455)
	Common Risk Difference (95% CI)		26.854 (20.900 , 32.809)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.449282

	PBO N=188	LEB250Q2W N=356

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Sleep-Loss-Score, reduction >= 2 points by Age Group I from baseline at Week 16, NRi (mITT, patients with baseline >= 2)

Age Group I: Adolescents (12<18) years

		PBO N=188	LEB250Q2W N=356
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (Observed up to ICE), n(%)	Total	19 (10.11%)	26 (7.30%)
	Non-responder	9 (4.79%)	15 (4.21%)
	Responder	1 (0.53%)	6 (1.69%)
	Missing	9 (4.79%)	5 (1.40%)
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (NRI) [1] [2], n(%)	Total	19 (10.11%)	26 (7.30%)
	Non-responder	18 (9.57%)	20 (5.62%)
	Responder	1 (0.53%)	6 (1.69%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.881 (0.581 , 41.027)
	Relative Risk (95% CI)		3.587 (0.548 , 23.484)
	Common Risk Difference (95% CI)		20.738 (-1.240 , 42.716)
	CMH p-value		0.104186

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Sleep-Loss-Score, reduction >= 2 points by Age Group I from baseline at Week 16, NRi (mITT, patients with baseline >= 2)

Age Group I: Adults >= 18 years

		PBO N=188	LEB250Q2W N=356
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (Observed up to ICE), n(%)	Total	169 (89.89%)	330 (92.70%)
	Non-responder	72 (38.30%)	145 (40.73%)
	Responder	9 (4.79%)	111 (31.18%)
	Missing	88 (46.81%)	74 (20.79%)
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (NRI) [1] [2], n(%)	Total	169 (89.89%)	330 (92.70%)
	Non-responder	160 (85.11%)	219 (61.52%)
	Responder	9 (4.79%)	111 (31.18%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		8.566 (4.211 , 17.426)
	Relative Risk (95% CI)		5.380 (2.867 , 10.095)
	Common Risk Difference (95% CI)		27.373 (21.195 , 33.551)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.38 **ADvocate 1 + ADvocate 2. Responder analysis of Sleep-Loss-Score, reduction >= 2 points by Disease Severity II from baseline at Week 16, NRi (mITT, patients with baseline >= 2)**

Disease Severity II: Overall

		PBO N=188	LEB250Q2W N=356
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (Observed up to ICE), n(%)	Total	188 (100.00%)	356 (100.00%)
	Non-responder	81 (43.09%)	160 (44.94%)
	Responder	10 (5.32%)	117 (32.87%)
	Missing	97 (51.60%)	79 (22.19%)
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (NRI) [1] [2], n(%)	Total	188 (100.00%)	356 (100.00%)
	Non-responder	178 (94.68%)	239 (67.13%)
	Responder	10 (5.32%)	117 (32.87%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		8.156 (4.150 , 16.031)
	Relative Risk (95% CI)		5.204 (2.864 , 9.455)
	Common Risk Difference (95% CI)		26.854 (20.900 , 32.809)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.607452

	PBO N=188	LEB250Q2W N=356

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Sleep-Loss-Score, reduction >= 2 points by Disease Severity II from baseline at Week 16, NRi (mITT, patients with baseline >= 2)

Disease Severity II: IGA = 3

		PBO N=188	LEB250Q2W N=356
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (Observed up to ICE), n(%)	Total	109 (57.98%)	194 (54.49%)
	Non-responder	50 (26.60%)	100 (28.09%)
	Responder	6 (3.19%)	58 (16.29%)
	Missing	53 (28.19%)	36 (10.11%)
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (NRI) [1] [2], n(%)	Total	109 (57.98%)	194 (54.49%)
	Non-responder	103 (54.79%)	136 (38.20%)
	Responder	6 (3.19%)	58 (16.29%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.563 (2.728 , 15.786)
	Relative Risk (95% CI)		4.295 (2.009 , 9.183)
	Common Risk Difference (95% CI)		23.382 (15.425 , 31.339)
	CMH p-value		0.000002

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Sleep-Loss-Score, reduction >= 2 points by Disease Severity II from baseline at Week 16, NRi (mITT, patients with baseline >= 2)

Disease Severity II: IGA = 4

		PBO N=188	LEB250Q2W N=356
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (Observed up to ICE), n(%)	Total	79 (42.02%)	162 (45.51%)
	Non-responder	31 (16.49%)	60 (16.85%)
	Responder	4 (2.13%)	59 (16.57%)
	Missing	44 (23.40%)	43 (12.08%)
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (NRI) [1] [2], n(%)	Total	79 (42.02%)	162 (45.51%)
	Non-responder	75 (39.89%)	103 (28.93%)
	Responder	4 (2.13%)	59 (16.57%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		10.889 (3.769 , 31.458)
	Relative Risk (95% CI)		6.730 (2.553 , 17.741)
	Common Risk Difference (95% CI)		31.345 (22.474 , 40.215)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.39 **ADvocate 1 + ADvocate 2. Responder analysis of Sleep-Loss-Score, reduction >= 2 points by Region from baseline at Week 16, NRi (mITT, patients with baseline >= 2)**

Region: Overall

		PBO N=188	LEB250Q2W N=356
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (Observed up to ICE), n(%)	Total	188 (100.00%)	356 (100.00%)
	Non-responder	81 (43.09%)	160 (44.94%)
	Responder	10 (5.32%)	117 (32.87%)
	Missing	97 (51.60%)	79 (22.19%)
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (NRI) [1] [2], n(%)	Total	188 (100.00%)	356 (100.00%)
	Non-responder	178 (94.68%)	239 (67.13%)
	Responder	10 (5.32%)	117 (32.87%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		8.156 (4.150 , 16.031)
	Relative Risk (95% CI)		5.204 (2.864 , 9.455)
	Common Risk Difference (95% CI)		26.854 (20.900 , 32.809)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.814565

	PBO N=188	LEB250Q2W N=356

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Sleep-Loss-Score, reduction >= 2 points by Region from baseline at Week 16, NRi (mITT, patients with baseline >= 2)

Region: Europe

		PBO N=188	LEB250Q2W N=356
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (Observed up to ICE), n(%)	Total	52 (27.66%)	97 (27.25%)
	Non-responder	29 (15.43%)	51 (14.33%)
	Responder	2 (1.06%)	34 (9.55%)
	Missing	21 (11.17%)	12 (3.37%)
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (NRI) [1] [2], n(%)	Total	52 (27.66%)	97 (27.25%)
	Non-responder	50 (26.60%)	63 (17.70%)
	Responder	2 (1.06%)	34 (9.55%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		13.477 (3.059 , 59.374)
	Relative Risk (95% CI)		8.224 (2.019 , 33.494)
	Common Risk Difference (95% CI)		31.241 (20.157 , 42.326)
	CMH p-value		0.000032

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Sleep-Loss-Score, reduction >= 2 points by Region from baseline at Week 16, NRi (mITT, patients with baseline >= 2)

Region: US

		PBO N=188	LEB250Q2W N=356
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (Observed up to ICE), n(%)	Total	82 (43.62%)	157 (44.10%)
	Non-responder	35 (18.62%)	70 (19.66%)
	Responder	5 (2.66%)	50 (14.04%)
	Missing	42 (22.34%)	37 (10.39%)
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (NRI) [1] [2], n(%)	Total	82 (43.62%)	157 (44.10%)
	Non-responder	77 (40.96%)	107 (30.06%)
	Responder	5 (2.66%)	50 (14.04%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.980 (2.647 , 18.403)
	Relative Risk (95% CI)		4.458 (1.921 , 10.346)
	Common Risk Difference (95% CI)		24.928 (15.931 , 33.925)
	CMH p-value		0.000014

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Sleep-Loss-Score, reduction >= 2 points by Region from baseline at Week 16, NRi (mITT, patients with baseline >= 2)

Region: Rest of the World

		PBO N=188	LEB250Q2W N=356
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (Observed up to ICE), n(%)	Total	54 (28.72%)	102 (28.65%)
	Non-responder	17 (9.04%)	39 (10.96%)
	Responder	3 (1.60%)	33 (9.27%)
	Missing	34 (18.09%)	30 (8.43%)
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (NRI) [1] [2], n(%)	Total	54 (28.72%)	102 (28.65%)
	Non-responder	51 (27.13%)	69 (19.38%)
	Responder	3 (1.60%)	33 (9.27%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.951 (2.030 , 23.806)
	Relative Risk (95% CI)		4.611 (1.604 , 13.254)
	Common Risk Difference (95% CI)		25.631 (14.319 , 36.942)
	CMH p-value		0.000377

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.40 **ADvocate 1 + ADvocate 2. Responder analysis of Sleep-Loss-Score, reduction >= 2 points by Race from baseline at Week 16, NRi (mITT, patients with baseline >= 2)**

Race: Overall

		PBO N=188	LEB250Q2W N=356
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (Observed up to ICE), n(%)	Total	188 (100.00%)	356 (100.00%)
	Non-responder	81 (43.09%)	160 (44.94%)
	Responder	10 (5.32%)	117 (32.87%)
	Missing	97 (51.60%)	79 (22.19%)
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (NRI) [1] [2], n(%)	Total	188 (100.00%)	356 (100.00%)
	Non-responder	178 (94.68%)	239 (67.13%)
	Responder	10 (5.32%)	117 (32.87%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		8.156 (4.150 , 16.031)
	Relative Risk (95% CI)		5.204 (2.864 , 9.455)
	Common Risk Difference (95% CI)		26.854 (20.900 , 32.809)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.259587

	PBO N=188	LEB250Q2W N=356

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Sleep-Loss-Score, reduction >= 2 points by Race from baseline at Week 16, NRi (mITT, patients with baseline >= 2)

Race: ASIAN

		PBO N=188	LEB250Q2W N=356
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (Observed up to ICE), n(%)	Total	56 (29.79%)	74 (20.79%)
	Non-responder	18 (9.57%)	29 (8.15%)
	Responder	4 (2.13%)	28 (7.87%)
	Missing	34 (18.09%)	17 (4.78%)
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (NRI) [1] [2], n(%)	Total	56 (29.79%)	74 (20.79%)
	Non-responder	52 (27.66%)	46 (12.92%)
	Responder	4 (2.13%)	28 (7.87%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		7.138 (2.216 , 22.989)
	Relative Risk (95% CI)		3.994 (1.618 , 9.859)
	Common Risk Difference (95% CI)		30.091 (16.571 , 43.611)
	CMH p-value		0.000148

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Sleep-Loss-Score, reduction >= 2 points by Race from baseline at Week 16, NRi (mITT, patients with baseline >= 2)

Race: BLACK OR AFRICAN AMERICAN

		PBO N=188	LEB250Q2W N=356
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (Observed up to ICE), n(%)	Total	21 (11.17%)	42 (11.80%)
	Non-responder	7 (3.72%)	25 (7.02%)
	Responder	1 (0.53%)	9 (2.53%)
	Missing	13 (6.91%)	8 (2.25%)
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (NRI) [1] [2], n(%)	Total	21 (11.17%)	42 (11.80%)
	Non-responder	20 (10.64%)	33 (9.27%)
	Responder	1 (0.53%)	9 (2.53%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.410 (0.429 , 27.107)
	Relative Risk (95% CI)		2.607 (0.436 , 15.573)
	Common Risk Difference (95% CI)		11.356 (-4.877 , 27.588)
	CMH p-value		0.207356

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Sleep-Loss-Score, reduction >= 2 points by Race from baseline at Week 16, NRi (mITT, patients with baseline >= 2)

Race: WHITE

		PBO N=188	LEB250Q2W N=356
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (Observed up to ICE), n(%)	Total	105 (55.85%)	222 (62.36%)
	Non-responder	55 (29.26%)	99 (27.81%)
	Responder	4 (2.13%)	76 (21.35%)
	Missing	46 (24.47%)	47 (13.20%)
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (NRI) [1] [2], n(%)	Total	105 (55.85%)	222 (62.36%)
	Non-responder	101 (53.72%)	146 (41.01%)
	Responder	4 (2.13%)	76 (21.35%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		13.618 (4.728 , 39.224)
	Relative Risk (95% CI)		8.090 (3.081 , 21.243)
	Common Risk Difference (95% CI)		30.637 (23.092 , 38.183)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis of Sleep-Loss-Score, reduction >= 2 points by Race from baseline at Week 16, NRi (mITT, patients with baseline >= 2)

Race: OTHER

		PBO N=188	LEB250Q2W N=356
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (Observed up to ICE), n(%)	Total	6 (3.19%)	18 (5.06%)
	Non-responder	1 (0.53%)	7 (1.97%)
	Responder	1 (0.53%)	4 (1.12%)
	Missing	4 (2.13%)	7 (1.97%)
Sleep-Loss-Score, Baseline >=2 points and reduction >= 2 points (NRI) [1] [2], n(%)	Total	6 (3.19%)	18 (5.06%)
	Non-responder	5 (2.66%)	14 (3.93%)
	Responder	1 (0.53%)	4 (1.12%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		0.000 (. , .)
	Relative Risk (95% CI)		0.333 (0.067 , 1.652)
	Common Risk Difference (95% CI)		-16.67 (-48.41 , 15.079)
	CMH p-value		0.317311

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.41 **ADvocate 1 + ADvocate 2. Responder analysis EQ-5D VAS by Gender, reduction >= 15 points, baseline to Week 16 NRI (mITT)**

Gender: Overall

		PBO N=287	LEB250Q2W N=564
EQ-5D VAS, reduction >= 15 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	139 (48.43%)	123 (21.81%)
	Non responder	117 (40.77%)	282 (50.00%)
	Responder	31 (10.80%)	159 (28.19%)
EQ-5D VAS, reduction >= 15 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	256 (89.20%)	405 (71.81%)
	Responder	31 (10.80%)	159 (28.19%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.218 (2.113 , 4.899)
	Relative Risk (95% CI)		2.395 (1.702 , 3.371)
	Common Risk Difference (95% CI)		16.788 (11.669 , 21.906)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.915742

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis EQ-5D VAS by Gender, reduction >= 15 points, baseline to Week 16 NRI (mITT)

Gender: F

		PBO N=287	LEB250Q2W N=564
EQ-5D VAS, reduction >= 15 points (Observed up to ICE), n(%)	Missing	70 (24.39%)	57 (10.11%)
	Total	148 (51.57%)	277 (49.11%)
	Non responder	60 (20.91%)	133 (23.58%)
	Responder	18 (6.27%)	87 (15.43%)
EQ-5D VAS, reduction >= 15 points (NRI) [1] [2], n(%)	Total	148 (51.57%)	277 (49.11%)
	Non responder	130 (45.30%)	190 (33.69%)
	Responder	18 (6.27%)	87 (15.43%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.442 (1.935 , 6.124)
	Relative Risk (95% CI)		2.478 (1.561 , 3.934)
	Common Risk Difference (95% CI)		18.956 (11.394 , 26.517)
	CMH p-value		0.000015

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis EQ-5D VAS by Gender, reduction >= 15 points, baseline to Week 16 NRI (mITT)

Gender: M

		PBO N=287	LEB250Q2W N=564
EQ-5D VAS, reduction >= 15 points (Observed up to ICE), n(%)	Missing	69 (24.04%)	66 (11.70%)
	Total	139 (48.43%)	287 (50.89%)
	Non responder	57 (19.86%)	149 (26.42%)
	Responder	13 (4.53%)	72 (12.77%)
EQ-5D VAS, reduction >= 15 points (NRI) [1] [2], n(%)	Total	139 (48.43%)	287 (50.89%)
	Non responder	126 (43.90%)	215 (38.12%)
	Responder	13 (4.53%)	72 (12.77%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.144 (1.663 , 5.941)
	Relative Risk (95% CI)		2.406 (1.416 , 4.090)
	Common Risk Difference (95% CI)		15.390 (8.178 , 22.602)
	CMH p-value		0.000223

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.42 **ADvocate 1 + ADvocate 2. Responder analysis EQ-5D VAS by Age Group I, reduction >= 15 points, baseline to Week 16 NRI (mITT)**

Age Group I: Overall

		PBO N=287	LEB250Q2W N=564
EQ-5D VAS, reduction >= 15 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	139 (48.43%)	123 (21.81%)
	Non responder	117 (40.77%)	282 (50.00%)
	Responder	31 (10.80%)	159 (28.19%)
EQ-5D VAS, reduction >= 15 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	256 (89.20%)	405 (71.81%)
	Responder	31 (10.80%)	159 (28.19%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.218 (2.113 , 4.899)
	Relative Risk (95% CI)		2.395 (1.702 , 3.371)
	Common Risk Difference (95% CI)		16.788 (11.669 , 21.906)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.613303

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis EQ-5D VAS by Age Group I, reduction >= 15 points, baseline to Week 16 NRI (mITT)

Age Group I: Adolescents (12<18) years

		PBO N=287	LEB250Q2W N=564
EQ-5D VAS, reduction >= 15 points (Observed up to ICE), n(%)	Missing	14 (4.88%)	11 (1.95%)
	Total	35 (12.20%)	67 (11.88%)
	Non responder	17 (5.92%)	31 (5.50%)
	Responder	4 (1.39%)	25 (4.43%)
EQ-5D VAS, reduction >= 15 points (NRI) [1] [2], n(%)	Total	35 (12.20%)	67 (11.88%)
	Non responder	31 (10.80%)	42 (7.45%)
	Responder	4 (1.39%)	25 (4.43%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.854 (1.159 , 12.818)
	Relative Risk (95% CI)		3.151 (1.040 , 9.547)
	Common Risk Difference (95% CI)		21.070 (5.331 , 36.808)
	CMH p-value		0.020103

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis EQ-5D VAS by Age Group I, reduction >= 15 points, baseline to Week 16 NRI (mITT)

Age Group I: Adults >= 18 years

		PBO N=287	LEB250Q2W N=564
EQ-5D VAS, reduction >= 15 points (Observed up to ICE), n(%)	Missing	125 (43.55%)	112 (19.86%)
	Total	252 (87.80%)	497 (88.12%)
	Non responder	100 (34.84%)	251 (44.50%)
	Responder	27 (9.41%)	134 (23.76%)
EQ-5D VAS, reduction >= 15 points (NRI) [1] [2], n(%)	Total	252 (87.80%)	497 (88.12%)
	Non responder	225 (78.40%)	363 (64.36%)
	Responder	27 (9.41%)	134 (23.76%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.136 (2.001 , 4.914)
	Relative Risk (95% CI)		2.316 (1.617 , 3.316)
	Common Risk Difference (95% CI)		16.219 (10.810 , 21.629)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.43 **ADvocate 1 + ADvocate 2. Responder analysis EQ-5D VAS by Disease Severity II, reduction >= 15 points, baseline to Week 16 NRI (mITT)**

Disease Severity II: Overall

		PBO N=287	LEB250Q2W N=564
EQ-5D VAS, reduction >= 15 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	139 (48.43%)	123 (21.81%)
	Non responder	117 (40.77%)	282 (50.00%)
	Responder	31 (10.80%)	159 (28.19%)
EQ-5D VAS, reduction >= 15 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	256 (89.20%)	405 (71.81%)
	Responder	31 (10.80%)	159 (28.19%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.218 (2.113 , 4.899)
	Relative Risk (95% CI)		2.395 (1.702 , 3.371)
	Common Risk Difference (95% CI)		16.788 (11.669 , 21.906)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.480163

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis EQ-5D VAS by Disease Severity II, reduction >= 15 points, baseline to Week 16 NRI (mITT)

Disease Severity II: IGA = 3

		PBO N=287	LEB250Q2W N=564
EQ-5D VAS, reduction >= 15 points (Observed up to ICE), n(%)	Missing	78 (27.18%)	68 (12.06%)
	Total	178 (62.02%)	345 (61.17%)
	Non responder	81 (28.22%)	190 (33.69%)
	Responder	19 (6.62%)	87 (15.43%)
EQ-5D VAS, reduction >= 15 points (NRI) [1] [2], n(%)	Total	178 (62.02%)	345 (61.17%)
	Non responder	159 (55.40%)	258 (45.74%)
	Responder	19 (6.62%)	87 (15.43%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		2.920 (1.683 , 5.067)
	Relative Risk (95% CI)		2.214 (1.418 , 3.455)
	Common Risk Difference (95% CI)		14.133 (7.854 , 20.412)
	CMH p-value		0.000089

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis EQ-5D VAS by Disease Severity II, reduction >= 15 points, baseline to Week 16 NRI (mITT)

Disease Severity II: IGA = 4

		PBO N=287	LEB250Q2W N=564
EQ-5D VAS, reduction >= 15 points (Observed up to ICE), n(%)	Missing	61 (21.25%)	55 (9.75%)
	Total	109 (37.98%)	219 (38.83%)
	Non responder	36 (12.54%)	92 (16.31%)
	Responder	12 (4.18%)	72 (12.77%)
EQ-5D VAS, reduction >= 15 points (NRI) [1] [2], n(%)	Total	109 (37.98%)	219 (38.83%)
	Non responder	97 (33.80%)	147 (26.06%)
	Responder	12 (4.18%)	72 (12.77%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.667 (1.911 , 7.035)
	Relative Risk (95% CI)		2.666 (1.563 , 4.546)
	Common Risk Difference (95% CI)		21.082 (12.382 , 29.782)
	CMH p-value		0.000042

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.44 **ADvocate 1 + ADvocate 2. Responder analysis EQ-5D VAS by Region, reduction >= 15 points, baseline to Week 16 NRI (mITT)**

Region: Overall

		PBO N=287	LEB250Q2W N=564
EQ-5D VAS, reduction >= 15 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	139 (48.43%)	123 (21.81%)
	Non responder	117 (40.77%)	282 (50.00%)
	Responder	31 (10.80%)	159 (28.19%)
EQ-5D VAS, reduction >= 15 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	256 (89.20%)	405 (71.81%)
	Responder	31 (10.80%)	159 (28.19%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.218 (2.113 , 4.899)
	Relative Risk (95% CI)		2.395 (1.702 , 3.371)
	Common Risk Difference (95% CI)		16.788 (11.669 , 21.906)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.226047

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis EQ-5D VAS by Region, reduction >= 15 points, baseline to Week 16 NRI (mITT)

Region: Europe

		PBO N=287	LEB250Q2W N=564
EQ-5D VAS, reduction >= 15 points (Observed up to ICE), n(%)	Missing	34 (11.85%)	23 (4.08%)
	Total	84 (29.27%)	168 (29.79%)
	Non responder	40 (13.94%)	79 (14.01%)
	Responder	10 (3.48%)	66 (11.70%)
EQ-5D VAS, reduction >= 15 points (NRI) [1] [2], n(%)	Total	84 (29.27%)	168 (29.79%)
	Non responder	74 (25.78%)	102 (18.09%)
	Responder	10 (3.48%)	66 (11.70%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.725 (2.274 , 9.815)
	Relative Risk (95% CI)		3.171 (1.739 , 5.780)
	Common Risk Difference (95% CI)		26.962 (16.841 , 37.083)
	CMH p-value		0.000011

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis EQ-5D VAS by Region, reduction >= 15 points, baseline to Week 16 NRI (mITT)

Region: US

		PBO N=287	LEB250Q2W N=564
EQ-5D VAS, reduction >= 15 points (Observed up to ICE), n(%)	Missing	55 (19.16%)	53 (9.40%)
	Total	122 (42.51%)	235 (41.67%)
	Non responder	53 (18.47%)	132 (23.40%)
	Responder	14 (4.88%)	50 (8.87%)
EQ-5D VAS, reduction >= 15 points (NRI) [1] [2], n(%)	Total	122 (42.51%)	235 (41.67%)
	Non responder	108 (37.63%)	185 (32.80%)
	Responder	14 (4.88%)	50 (8.87%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		2.030 (1.068 , 3.858)
	Relative Risk (95% CI)		1.662 (1.019 , 2.709)
	Common Risk Difference (95% CI)		9.274 (1.602 , 16.946)
	CMH p-value		0.029397

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis EQ-5D VAS by Region, reduction >= 15 points, baseline to Week 16 NRI (mITT)

Region: Rest of the World

		PBO N=287	LEB250Q2W N=564
EQ-5D VAS, reduction >= 15 points (Observed up to ICE), n(%)	Missing	50 (17.42%)	47 (8.33%)
	Total	81 (28.22%)	161 (28.55%)
	Non responder	24 (8.36%)	71 (12.59%)
	Responder	7 (2.44%)	43 (7.62%)
EQ-5D VAS, reduction >= 15 points (NRI) [1] [2], n(%)	Total	81 (28.22%)	161 (28.55%)
	Non responder	74 (25.78%)	118 (20.92%)
	Responder	7 (2.44%)	43 (7.62%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.012 (1.648 , 9.765)
	Relative Risk (95% CI)		3.008 (1.367 , 6.619)
	Common Risk Difference (95% CI)		17.393 (8.463 , 26.322)
	CMH p-value		0.001226

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.45 **ADvocate 1 + ADvocate 2. Responder analysis EQ-5D VAS by Race, reduction >= 15 points, baseline to Week 16 NRI (mITT)**

Race: Overall

		PBO N=287	LEB250Q2W N=564
EQ-5D VAS, reduction >= 15 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	139 (48.43%)	123 (21.81%)
	Non responder	117 (40.77%)	282 (50.00%)
	Responder	31 (10.80%)	159 (28.19%)
EQ-5D VAS, reduction >= 15 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	256 (89.20%)	405 (71.81%)
	Responder	31 (10.80%)	159 (28.19%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.218 (2.113 , 4.899)
	Relative Risk (95% CI)		2.395 (1.702 , 3.371)
	Common Risk Difference (95% CI)		16.788 (11.669 , 21.906)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.836886

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis EQ-5D VAS by Race, reduction >= 15 points, baseline to Week 16 NRI (mITT)

Race: ASIAN

		PBO N=287	LEB250Q2W N=564
EQ-5D VAS, reduction >= 15 points (Observed up to ICE), n(%)	Missing	43 (14.98%)	32 (5.67%)
	Total	75 (26.13%)	117 (20.74%)
	Non responder	25 (8.71%)	51 (9.04%)
	Responder	7 (2.44%)	34 (6.03%)
EQ-5D VAS, reduction >= 15 points (NRI) [1] [2], n(%)	Total	75 (26.13%)	117 (20.74%)
	Non responder	68 (23.69%)	83 (14.72%)
	Responder	7 (2.44%)	34 (6.03%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.861 (1.892 , 12.493)
	Relative Risk (95% CI)		3.192 (1.433 , 7.113)
	Common Risk Difference (95% CI)		20.793 (10.473 , 31.114)
	CMH p-value		0.000548

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis EQ-5D VAS by Race, reduction >= 15 points, baseline to Week 16 NRI (mITT)

Race: BLACK OR AFRICAN AMERICAN

		PBO N=287	LEB250Q2W N=564
EQ-5D VAS, reduction >= 15 points (Observed up to ICE), n(%)	Missing	14 (4.88%)	10 (1.77%)
	Total	26 (9.06%)	58 (10.28%)
	Non responder	9 (3.14%)	36 (6.38%)
	Responder	3 (1.05%)	12 (2.13%)
EQ-5D VAS, reduction >= 15 points (NRI) [1] [2], n(%)	Total	26 (9.06%)	58 (10.28%)
	Non responder	23 (8.01%)	46 (8.16%)
	Responder	3 (1.05%)	12 (2.13%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		2.879 (0.644 , 12.865)
	Relative Risk (95% CI)		2.052 (0.675 , 6.240)
	Common Risk Difference (95% CI)		13.425 (-3.050 , 29.900)
	CMH p-value		0.169554

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis EQ-5D VAS by Race, reduction >= 15 points, baseline to Week 16 NRI (mITT)

Race: WHITE

		PBO N=287	LEB250Q2W N=564
EQ-5D VAS, reduction >= 15 points (Observed up to ICE), n(%)	Missing	78 (27.18%)	72 (12.77%)
	Total	178 (62.02%)	364 (64.54%)
	Non responder	79 (27.53%)	185 (32.80%)
	Responder	21 (7.32%)	107 (18.97%)
EQ-5D VAS, reduction >= 15 points (NRI) [1] [2], n(%)	Total	178 (62.02%)	364 (64.54%)
	Non responder	157 (54.70%)	257 (45.57%)
	Responder	21 (7.32%)	107 (18.97%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.128 (1.875 , 5.219)
	Relative Risk (95% CI)		2.315 (1.545 , 3.468)
	Common Risk Difference (95% CI)		17.690 (10.923 , 24.457)
	CMH p-value		0.000006

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis EQ-5D VAS by Race, reduction >= 15 points, baseline to Week 16 NRI (mITT)

Race: OTHER

		PBO N=287	LEB250Q2W N=564
EQ-5D VAS, reduction >= 15 points (Observed up to ICE), n(%)	Missing	4 (1.39%)	9 (1.60%)
	Total	8 (2.79%)	25 (4.43%)
	Non responder	4 (1.39%)	10 (1.77%)
	Responder	0 (0.00%)	6 (1.06%)
EQ-5D VAS, reduction >= 15 points (NRI) [1] [2], n(%)	Total	8 (2.79%)	25 (4.43%)
	Non responder	8 (2.79%)	19 (3.37%)
	Responder	0 (0.00%)	6 (1.06%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		17.035 (-8.208 , 42.277)
	CMH p-value		0.292171

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.46 **ADvocate 1 + ADvocate 2. Responder analysis POEM 0-2 points by Gender, baseline to Week 16 NRI (mITT)**

Gender: Overall

		PBO N=287	LEB250Q2W N=564
POEM of 0-2 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	151 (52.61%)	170 (30.14%)
	Non responder	129 (44.95%)	334 (59.22%)
	Responder	7 (2.44%)	60 (10.64%)
POEM of 0-2 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	280 (97.56%)	504 (89.36%)
	Responder	7 (2.44%)	60 (10.64%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.957 (2.188 , 11.233)
	Relative Risk (95% CI)		3.575 (1.718 , 7.443)
	Common Risk Difference (95% CI)		8.071 (5.009 , 11.133)
	CMH p-value		0.000033
	Treatment by subgroup interaction test p-value [7]		0.694001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM 0-2 points by Gender, baseline to Week 16 NRI (mITT)

Gender: F

		PBO N=287	LEB250Q2W N=564
POEM of 0-2 points (Observed up to ICE), n(%)	Missing	82 (28.57%)	83 (14.72%)
	Total	148 (51.57%)	277 (49.11%)
	Non responder	63 (21.95%)	165 (29.26%)
	Responder	3 (1.05%)	29 (5.14%)
POEM of 0-2 points (NRI) [1] [2], n(%)	Total	148 (51.57%)	277 (49.11%)
	Non responder	145 (50.52%)	248 (43.97%)
	Responder	3 (1.05%)	29 (5.14%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		9.204 (2.102 , 40.298)
	Relative Risk (95% CI)		5.900 (1.530 , 22.752)
	Common Risk Difference (95% CI)		9.409 (5.261 , 13.556)
	CMH p-value		0.000568

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM 0-2 points by Gender, baseline to Week 16 NRI (mITT)

Gender: M

		PBO N=287	LEB250Q2W N=564
POEM of 0-2 points (Observed up to ICE), n(%)	Missing	69 (24.04%)	87 (15.43%)
	Total	139 (48.43%)	287 (50.89%)
	Non responder	66 (23.00%)	169 (29.96%)
	Responder	4 (1.39%)	31 (5.50%)
POEM of 0-2 points (NRI) [1] [2], n(%)	Total	139 (48.43%)	287 (50.89%)
	Non responder	135 (47.04%)	256 (45.39%)
	Responder	4 (1.39%)	31 (5.50%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.665 (1.273 , 10.546)
	Relative Risk (95% CI)		2.878 (1.117 , 7.413)
	Common Risk Difference (95% CI)		7.302 (2.598 , 12.006)
	CMH p-value		0.010754

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.47 **ADvocate 1 + ADvocate 2. Responder analysis POEM 0-2 points by Age Group I, baseline to Week 16 NRI (mITT)**

Age Group I: Overall

		PBO N=287	LEB250Q2W N=564
POEM of 0-2 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	151 (52.61%)	170 (30.14%)
	Non responder	129 (44.95%)	334 (59.22%)
	Responder	7 (2.44%)	60 (10.64%)
POEM of 0-2 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	280 (97.56%)	504 (89.36%)
	Responder	7 (2.44%)	60 (10.64%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.957 (2.188 , 11.233)
	Relative Risk (95% CI)		3.575 (1.718 , 7.443)
	Common Risk Difference (95% CI)		8.071 (5.009 , 11.133)
	CMH p-value		0.000033
	Treatment by subgroup interaction test p-value [7]		0.778644

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM 0-2 points by Age Group I, baseline to Week 16 NRI (mITT)

Age Group I: Adolescents (12<18) years

		PBO N=287	LEB250Q2W N=564
POEM of 0-2 points (Observed up to ICE), n(%)	Missing	15 (5.23%)	26 (4.61%)
	Total	35 (12.20%)	67 (11.88%)
	Non responder	19 (6.62%)	33 (5.85%)
	Responder	1 (0.35%)	8 (1.42%)
POEM of 0-2 points (NRI) [1] [2], n(%)	Total	35 (12.20%)	67 (11.88%)
	Non responder	34 (11.85%)	59 (10.46%)
	Responder	1 (0.35%)	8 (1.42%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.365 (0.470 , 86.240)
	Relative Risk (95% CI)		4.576 (0.384 , 54.533)
	Common Risk Difference (95% CI)		8.063 (-0.515 , 16.641)
	CMH p-value		0.159506

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM 0-2 points by Age Group I, baseline to Week 16 NRI (mITT)

Age Group I: Adults >= 18 years

		PBO N=287	LEB250Q2W N=564
POEM of 0-2 points (Observed up to ICE), n(%)	Missing	136 (47.39%)	144 (25.53%)
	Total	252 (87.80%)	497 (88.12%)
	Non responder	110 (38.33%)	301 (53.37%)
	Responder	6 (2.09%)	52 (9.22%)
POEM of 0-2 points (NRI) [1] [2], n(%)	Total	252 (87.80%)	497 (88.12%)
	Non responder	246 (85.71%)	445 (78.90%)
	Responder	6 (2.09%)	52 (9.22%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.824 (2.039 , 11.415)
	Relative Risk (95% CI)		3.483 (1.616 , 7.508)
	Common Risk Difference (95% CI)		8.072 (4.795 , 11.349)
	CMH p-value		0.000094

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.48 **ADvocate 1 + ADvocate 2. Responder analysis POEM 0-2 points by Disease Severity II, baseline to Week 16 NRI (mITT)**

Disease Severity II: Overall

		PBO N=287	LEB250Q2W N=564
POEM of 0-2 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	151 (52.61%)	170 (30.14%)
	Non responder	129 (44.95%)	334 (59.22%)
	Responder	7 (2.44%)	60 (10.64%)
POEM of 0-2 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	280 (97.56%)	504 (89.36%)
	Responder	7 (2.44%)	60 (10.64%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.957 (2.188 , 11.233)
	Relative Risk (95% CI)		3.575 (1.718 , 7.443)
	Common Risk Difference (95% CI)		8.071 (5.009 , 11.133)
	CMH p-value		0.000033
	Treatment by subgroup interaction test p-value [7]		0.950583

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM 0-2 points by Disease Severity II, baseline to Week 16 NRI (mITT)

Disease Severity II: IGA = 3

		PBO N=287	LEB250Q2W N=564
POEM of 0-2 points (Observed up to ICE), n(%)	Missing	89 (31.01%)	99 (17.55%)
	Total	178 (62.02%)	345 (61.17%)
	Non responder	84 (29.27%)	206 (36.52%)
	Responder	5 (1.74%)	40 (7.09%)
POEM of 0-2 points (NRI) [1] [2], n(%)	Total	178 (62.02%)	345 (61.17%)
	Non responder	173 (60.28%)	305 (54.08%)
	Responder	5 (1.74%)	40 (7.09%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.734 (1.774 , 12.633)
	Relative Risk (95% CI)		3.429 (1.427 , 8.243)
	Common Risk Difference (95% CI)		8.581 (4.506 , 12.657)
	CMH p-value		0.000807

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM 0-2 points by Disease Severity II, baseline to Week 16 NRI (mITT)

Disease Severity II: IGA = 4

		PBO N=287	LEB250Q2W N=564
POEM of 0-2 points (Observed up to ICE), n(%)	Missing	62 (21.60%)	71 (12.59%)
	Total	109 (37.98%)	219 (38.83%)
	Non responder	45 (15.68%)	128 (22.70%)
	Responder	2 (0.70%)	20 (3.55%)
POEM of 0-2 points (NRI) [1] [2], n(%)	Total	109 (37.98%)	219 (38.83%)
	Non responder	107 (37.28%)	199 (35.28%)
	Responder	2 (0.70%)	20 (3.55%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.470 (1.244 , 24.053)
	Relative Risk (95% CI)		3.911 (1.029 , 14.870)
	Common Risk Difference (95% CI)		7.245 (2.683 , 11.807)
	CMH p-value		0.014157

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.49 **ADvocate 1 + ADvocate 2. Responder analysis POEM 0-2 points by Region, baseline to Week 16 NRI (mITT)**

Region: Overall

		PBO N=287	LEB250Q2W N=564
POEM of 0-2 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	151 (52.61%)	170 (30.14%)
	Non responder	129 (44.95%)	334 (59.22%)
	Responder	7 (2.44%)	60 (10.64%)
POEM of 0-2 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	280 (97.56%)	504 (89.36%)
	Responder	7 (2.44%)	60 (10.64%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.957 (2.188 , 11.233)
	Relative Risk (95% CI)		3.575 (1.718 , 7.443)
	Common Risk Difference (95% CI)		8.071 (5.009 , 11.133)
	CMH p-value		0.000033
	Treatment by subgroup interaction test p-value [7]		0.757287

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM 0-2 points by Region, baseline to Week 16 NRI (mITT)

Region: Europe

		PBO N=287	LEB250Q2W N=564
POEM of 0-2 points (Observed up to ICE), n(%)	Missing	36 (12.54%)	27 (4.79%)
	Total	84 (29.27%)	168 (29.79%)
	Non responder	47 (16.38%)	123 (21.81%)
	Responder	1 (0.35%)	18 (3.19%)
POEM of 0-2 points (NRI) [1] [2], n(%)	Total	84 (29.27%)	168 (29.79%)
	Non responder	83 (28.92%)	150 (26.60%)
	Responder	1 (0.35%)	18 (3.19%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		10.561 (1.334 , 83.611)
	Relative Risk (95% CI)		7.129 (1.003 , 50.675)
	Common Risk Difference (95% CI)		9.513 (4.321 , 14.706)
	CMH p-value		0.007278

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM 0-2 points by Region, baseline to Week 16 NRI (mITT)

Region: US

		PBO N=287	LEB250Q2W N=564
POEM of 0-2 points (Observed up to ICE), n(%)	Missing	66 (23.00%)	83 (14.72%)
	Total	122 (42.51%)	235 (41.67%)
	Non responder	52 (18.12%)	124 (21.99%)
	Responder	4 (1.39%)	28 (4.96%)
POEM of 0-2 points (NRI) [1] [2], n(%)	Total	122 (42.51%)	235 (41.67%)
	Non responder	118 (41.11%)	207 (36.70%)
	Responder	4 (1.39%)	28 (4.96%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.876 (1.333 , 11.273)
	Relative Risk (95% CI)		2.854 (1.137 , 7.164)
	Common Risk Difference (95% CI)		8.437 (3.213 , 13.661)
	CMH p-value		0.008400

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM 0-2 points by Region, baseline to Week 16 NRI (mITT)

Region: Rest of the World

		PBO N=287	LEB250Q2W N=564
POEM of 0-2 points (Observed up to ICE), n(%)	Missing	49 (17.07%)	60 (10.64%)
	Total	81 (28.22%)	161 (28.55%)
	Non responder	30 (10.45%)	87 (15.43%)
	Responder	2 (0.70%)	14 (2.48%)
POEM of 0-2 points (NRI) [1] [2], n(%)	Total	81 (28.22%)	161 (28.55%)
	Non responder	79 (27.53%)	147 (26.06%)
	Responder	2 (0.70%)	14 (2.48%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.356 (0.829 , 22.882)
	Relative Risk (95% CI)		3.256 (0.722 , 14.684)
	Common Risk Difference (95% CI)		6.022 (0.834 , 11.210)
	CMH p-value		0.066052

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.50 **ADvocate 1 + ADvocate 2. Responder analysis POEM 0-2 points by Race, baseline to Week 16 NRI (mITT)**

Race: Overall

		PBO N=287	LEB250Q2W N=564
POEM of 0-2 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	151 (52.61%)	170 (30.14%)
	Non responder	129 (44.95%)	334 (59.22%)
	Responder	7 (2.44%)	60 (10.64%)
POEM of 0-2 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	280 (97.56%)	504 (89.36%)
	Responder	7 (2.44%)	60 (10.64%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.957 (2.188 , 11.233)
	Relative Risk (95% CI)		3.575 (1.718 , 7.443)
	Common Risk Difference (95% CI)		8.071 (5.009 , 11.133)
	CMH p-value		0.000033
	Treatment by subgroup interaction test p-value [7]		0.958104

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM 0-2 points by Race, baseline to Week 16 NRI (mITT)

Race: ASIAN

		PBO N=287	LEB250Q2W N=564
POEM of 0-2 points (Observed up to ICE), n(%)	Missing	46 (16.03%)	43 (7.62%)
	Total	75 (26.13%)	117 (20.74%)
	Non responder	27 (9.41%)	64 (11.35%)
	Responder	2 (0.70%)	10 (1.77%)
POEM of 0-2 points (NRI) [1] [2], n(%)	Total	75 (26.13%)	117 (20.74%)
	Non responder	73 (25.44%)	107 (18.97%)
	Responder	2 (0.70%)	10 (1.77%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.322 (0.592 , 18.638)
	Relative Risk (95% CI)		2.548 (0.544 , 11.926)
	Common Risk Difference (95% CI)		4.742 (-1.080 , 10.565)
	CMH p-value		0.165031

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM 0-2 points by Race, baseline to Week 16 NRI (mITT)

Race: BLACK OR AFRICAN AMERICAN

		PBO N=287	LEB250Q2W N=564
POEM of 0-2 points (Observed up to ICE), n(%)	Missing	15 (5.23%)	18 (3.19%)
	Total	26 (9.06%)	58 (10.28%)
	Non responder	11 (3.83%)	36 (6.38%)
	Responder	0 (0.00%)	4 (0.71%)
POEM of 0-2 points (NRI) [1] [2], n(%)	Total	26 (9.06%)	58 (10.28%)
	Non responder	26 (9.06%)	54 (9.57%)
	Responder	0 (0.00%)	4 (0.71%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		8.934 (0.644 , 17.224)
	CMH p-value		0.120308

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM 0-2 points by Race, baseline to Week 16 NRI (mITT)

Race: WHITE

		PBO N=287	LEB250Q2W N=564
POEM of 0-2 points (Observed up to ICE), n(%)	Missing	85 (29.62%)	98 (17.38%)
	Total	178 (62.02%)	364 (64.54%)
	Non responder	88 (30.66%)	223 (39.54%)
	Responder	5 (1.74%)	43 (7.62%)
POEM of 0-2 points (NRI) [1] [2], n(%)	Total	178 (62.02%)	364 (64.54%)
	Non responder	173 (60.28%)	321 (56.91%)
	Responder	5 (1.74%)	43 (7.62%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.326 (1.687 , 11.091)
	Relative Risk (95% CI)		3.282 (1.405 , 7.663)
	Common Risk Difference (95% CI)		8.628 (4.436 , 12.819)
	CMH p-value		0.000982

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM 0-2 points by Race, baseline to Week 16 NRI (mITT)

Race: OTHER

		PBO N=287	LEB250Q2W N=564
POEM of 0-2 points (Observed up to ICE), n(%)	Missing	5 (1.74%)	11 (1.95%)
	Total	8 (2.79%)	25 (4.43%)
	Non responder	3 (1.05%)	11 (1.95%)
	Responder	0 (0.00%)	3 (0.53%)
POEM of 0-2 points (NRI) [1] [2], n(%)	Total	8 (2.79%)	25 (4.43%)
	Non responder	8 (2.79%)	22 (3.90%)
	Responder	0 (0.00%)	3 (0.53%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		17.035 (-8.208 , 42.277)
	CMH p-value		0.292171

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.51 **ADvocate 1 + ADvocate 2. Responder analysis POEM reduction >= 5 points by Gender, baseline to Week 16 NRI (mITT)**

Gender: Overall

		PBO N=287	LEB250Q2W N=564
POEM reduction >= 5 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	151 (52.61%)	170 (30.14%)
	Non responder	78 (27.18%)	90 (15.96%)
	Responder	58 (20.21%)	304 (53.90%)
POEM reduction >= 5 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	229 (79.79%)	260 (46.10%)
	Responder	58 (20.21%)	304 (53.90%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.615 (3.301 , 6.451)
	Relative Risk (95% CI)		2.985 (2.308 , 3.862)
	Common Risk Difference (95% CI)		33.597 (27.375 , 39.819)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.061318

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM reduction >= 5 points by Gender, baseline to Week 16 NRI (mITT)

Gender: F

		PBO N=287	LEB250Q2W N=564
POEM reduction >= 5 points (Observed up to ICE), n(%)	Missing	82 (28.57%)	83 (14.72%)
	Total	148 (51.57%)	277 (49.11%)
	Non responder	41 (14.29%)	35 (6.21%)
	Responder	25 (8.71%)	159 (28.19%)
POEM reduction >= 5 points (NRI) [1] [2], n(%)	Total	148 (51.57%)	277 (49.11%)
	Non responder	123 (42.86%)	118 (20.92%)
	Responder	25 (8.71%)	159 (28.19%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.847 (3.599 , 9.498)
	Relative Risk (95% CI)		3.635 (2.480 , 5.328)
	Common Risk Difference (95% CI)		39.799 (31.008 , 48.589)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM reduction >= 5 points by Gender, baseline to Week 16 NRI (mITT)

Gender: M

		PBO N=287	LEB250Q2W N=564
POEM reduction >= 5 points (Observed up to ICE), n(%)	Missing	69 (24.04%)	87 (15.43%)
	Total	139 (48.43%)	287 (50.89%)
	Non responder	37 (12.89%)	55 (9.75%)
	Responder	33 (11.50%)	145 (25.71%)
POEM reduction >= 5 points (NRI) [1] [2], n(%)	Total	139 (48.43%)	287 (50.89%)
	Non responder	106 (36.93%)	142 (25.18%)
	Responder	33 (11.50%)	145 (25.71%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.591 (2.243 , 5.749)
	Relative Risk (95% CI)		2.506 (1.741 , 3.607)
	Common Risk Difference (95% CI)		28.689 (19.387 , 37.990)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.52 **ADvocate 1 + ADvocate 2. Responder analysis POEM reduction >= 5 points by Age Group I, baseline to Week 16 NRI (mITT)**

Age Group I: Overall

		PBO N=287	LEB250Q2W N=564
POEM reduction >= 5 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	151 (52.61%)	170 (30.14%)
	Non responder	78 (27.18%)	90 (15.96%)
	Responder	58 (20.21%)	304 (53.90%)
POEM reduction >= 5 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	229 (79.79%)	260 (46.10%)
	Responder	58 (20.21%)	304 (53.90%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.615 (3.301 , 6.451)
	Relative Risk (95% CI)		2.985 (2.308 , 3.862)
	Common Risk Difference (95% CI)		33.597 (27.375 , 39.819)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.399631

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM reduction >= 5 points by Age Group I, baseline to Week 16 NRI (mITT)

Age Group I: Adolescents (12<18) years

		PBO N=287	LEB250Q2W N=564
POEM reduction >= 5 points (Observed up to ICE), n(%)	Missing	15 (5.23%)	26 (4.61%)
	Total	35 (12.20%)	67 (11.88%)
	Non responder	13 (4.53%)	11 (1.95%)
	Responder	7 (2.44%)	30 (5.32%)
POEM reduction >= 5 points (NRI) [1] [2], n(%)	Total	35 (12.20%)	67 (11.88%)
	Non responder	28 (9.76%)	37 (6.56%)
	Responder	7 (2.44%)	30 (5.32%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.153 (1.211 , 8.213)
	Relative Risk (95% CI)		2.396 (1.111 , 5.165)
	Common Risk Difference (95% CI)		25.102 (6.562 , 43.642)
	CMH p-value		0.014896

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM reduction >= 5 points by Age Group I, baseline to Week 16 NRI (mITT)

Age Group I: Adults >= 18 years

		PBO N=287	LEB250Q2W N=564
POEM reduction >= 5 points (Observed up to ICE), n(%)	Missing	136 (47.39%)	144 (25.53%)
	Total	252 (87.80%)	497 (88.12%)
	Non responder	65 (22.65%)	79 (14.01%)
	Responder	51 (17.77%)	274 (48.58%)
POEM reduction >= 5 points (NRI) [1] [2], n(%)	Total	252 (87.80%)	497 (88.12%)
	Non responder	201 (70.03%)	223 (39.54%)
	Responder	51 (17.77%)	274 (48.58%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.866 (3.405 , 6.955)
	Relative Risk (95% CI)		3.069 (2.335 , 4.035)
	Common Risk Difference (95% CI)		34.724 (28.127 , 41.320)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.53 **ADvocate 1 + ADvocate 2. Responder analysis POEM reduction >= 5 points by Disease Severity II, baseline to Week 16 NRI (mITT)**

Disease Severity II: Overall

		PBO N=287	LEB250Q2W N=564
POEM reduction >= 5 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	151 (52.61%)	170 (30.14%)
	Non responder	78 (27.18%)	90 (15.96%)
	Responder	58 (20.21%)	304 (53.90%)
POEM reduction >= 5 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	229 (79.79%)	260 (46.10%)
	Responder	58 (20.21%)	304 (53.90%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.615 (3.301 , 6.451)
	Relative Risk (95% CI)		2.985 (2.308 , 3.862)
	Common Risk Difference (95% CI)		33.597 (27.375 , 39.819)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.600377

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM reduction >= 5 points by Disease Severity II, baseline to Week 16 NRI (mITT)

Disease Severity II: IGA = 3

		PBO N=287	LEB250Q2W N=564
POEM reduction >= 5 points (Observed up to ICE), n(%)	Missing	89 (31.01%)	99 (17.55%)
	Total	178 (62.02%)	345 (61.17%)
	Non responder	51 (17.77%)	60 (10.64%)
	Responder	38 (13.24%)	186 (32.98%)
POEM reduction >= 5 points (NRI) [1] [2], n(%)	Total	178 (62.02%)	345 (61.17%)
	Non responder	140 (48.78%)	159 (28.19%)
	Responder	38 (13.24%)	186 (32.98%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.252 (2.794 , 6.471)
	Relative Risk (95% CI)		2.800 (2.033 , 3.857)
	Common Risk Difference (95% CI)		32.199 (24.177 , 40.221)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM reduction >= 5 points by Disease Severity II, baseline to Week 16 NRI (mITT)

Disease Severity II: IGA = 4

		PBO N=287	LEB250Q2W N=564
POEM reduction >= 5 points (Observed up to ICE), n(%)	Missing	62 (21.60%)	71 (12.59%)
	Total	109 (37.98%)	219 (38.83%)
	Non responder	27 (9.41%)	30 (5.32%)
	Responder	20 (6.97%)	118 (20.92%)
POEM reduction >= 5 points (NRI) [1] [2], n(%)	Total	109 (37.98%)	219 (38.83%)
	Non responder	89 (31.01%)	101 (17.91%)
	Responder	20 (6.97%)	118 (20.92%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.314 (3.045 , 9.272)
	Relative Risk (95% CI)		3.334 (2.160 , 5.146)
	Common Risk Difference (95% CI)		35.858 (26.032 , 45.683)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.54 **ADvocate 1 + ADvocate 2. Responder analysis POEM reduction >= 5 points by Region, baseline to Week 16 NRI (mITT)**

Region: Overall

		PBO N=287	LEB250Q2W N=564
POEM reduction >= 5 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	151 (52.61%)	170 (30.14%)
	Non responder	78 (27.18%)	90 (15.96%)
	Responder	58 (20.21%)	304 (53.90%)
POEM reduction >= 5 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	229 (79.79%)	260 (46.10%)
	Responder	58 (20.21%)	304 (53.90%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.615 (3.301 , 6.451)
	Relative Risk (95% CI)		2.985 (2.308 , 3.862)
	Common Risk Difference (95% CI)		33.597 (27.375 , 39.819)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.336749

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM reduction >= 5 points by Region, baseline to Week 16 NRI (mITT)

Region: Europe

		PBO N=287	LEB250Q2W N=564
POEM reduction >= 5 points (Observed up to ICE), n(%)	Missing	36 (12.54%)	27 (4.79%)
	Total	84 (29.27%)	168 (29.79%)
	Non responder	27 (9.41%)	32 (5.67%)
	Responder	21 (7.32%)	109 (19.33%)
POEM reduction >= 5 points (NRI) [1] [2], n(%)	Total	84 (29.27%)	168 (29.79%)
	Non responder	63 (21.95%)	59 (10.46%)
	Responder	21 (7.32%)	109 (19.33%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.405 (3.001 , 9.734)
	Relative Risk (95% CI)		3.253 (2.119 , 4.995)
	Common Risk Difference (95% CI)		39.777 (27.922 , 51.633)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM reduction >= 5 points by Region, baseline to Week 16 NRI (mITT)

Region: US

		PBO N=287	LEB250Q2W N=564
POEM reduction >= 5 points (Observed up to ICE), n(%)	Missing	66 (23.00%)	83 (14.72%)
	Total	122 (42.51%)	235 (41.67%)
	Non responder	29 (10.10%)	34 (6.03%)
	Responder	27 (9.41%)	118 (20.92%)
POEM reduction >= 5 points (NRI) [1] [2], n(%)	Total	122 (42.51%)	235 (41.67%)
	Non responder	95 (33.10%)	117 (20.74%)
	Responder	27 (9.41%)	118 (20.92%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.464 (2.110 , 5.686)
	Relative Risk (95% CI)		2.400 (1.653 , 3.485)
	Common Risk Difference (95% CI)		27.911 (18.056 , 37.766)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM reduction >= 5 points by Region, baseline to Week 16 NRI (mITT)

Region: Rest of the World

		PBO N=287	LEB250Q2W N=564
POEM reduction >= 5 points (Observed up to ICE), n(%)	Missing	49 (17.07%)	60 (10.64%)
	Total	81 (28.22%)	161 (28.55%)
	Non responder	22 (7.67%)	24 (4.26%)
	Responder	10 (3.48%)	77 (13.65%)
POEM reduction >= 5 points (NRI) [1] [2], n(%)	Total	81 (28.22%)	161 (28.55%)
	Non responder	71 (24.74%)	84 (14.89%)
	Responder	10 (3.48%)	77 (13.65%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.452 (3.108 , 13.396)
	Relative Risk (95% CI)		4.053 (2.186 , 7.515)
	Common Risk Difference (95% CI)		35.637 (25.038 , 46.236)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.55 **ADvocate 1 + ADvocate 2. Responder analysis POEM reduction >= 5 points by Race, baseline to Week 16 NRI (mITT)**

Race: Overall

		PBO N=287	LEB250Q2W N=564
POEM reduction >= 5 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	151 (52.61%)	170 (30.14%)
	Non responder	78 (27.18%)	90 (15.96%)
	Responder	58 (20.21%)	304 (53.90%)
POEM reduction >= 5 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	229 (79.79%)	260 (46.10%)
	Responder	58 (20.21%)	304 (53.90%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.615 (3.301 , 6.451)
	Relative Risk (95% CI)		2.985 (2.308 , 3.862)
	Common Risk Difference (95% CI)		33.597 (27.375 , 39.819)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.835783

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM reduction >= 5 points by Race, baseline to Week 16 NRI (mITT)

Race: ASIAN

		PBO N=287	LEB250Q2W N=564
POEM reduction >= 5 points (Observed up to ICE), n(%)	Missing	46 (16.03%)	43 (7.62%)
	Total	75 (26.13%)	117 (20.74%)
	Non responder	18 (6.27%)	17 (3.01%)
	Responder	11 (3.83%)	57 (10.11%)
POEM reduction >= 5 points (NRI) [1] [2], n(%)	Total	75 (26.13%)	117 (20.74%)
	Non responder	64 (22.30%)	60 (10.64%)
	Responder	11 (3.83%)	57 (10.11%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.546 (2.648 , 11.618)
	Relative Risk (95% CI)		3.240 (1.834 , 5.722)
	Common Risk Difference (95% CI)		35.605 (23.087 , 48.124)
	CMH p-value		0.000002

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM reduction >= 5 points by Race, baseline to Week 16 NRI (mITT)

Race: BLACK OR AFRICAN AMERICAN

		PBO N=287	LEB250Q2W N=564
POEM reduction >= 5 points (Observed up to ICE), n(%)	Missing	15 (5.23%)	18 (3.19%)
	Total	26 (9.06%)	58 (10.28%)
	Non responder	8 (2.79%)	11 (1.95%)
	Responder	3 (1.05%)	29 (5.14%)
POEM reduction >= 5 points (NRI) [1] [2], n(%)	Total	26 (9.06%)	58 (10.28%)
	Non responder	23 (8.01%)	29 (5.14%)
	Responder	3 (1.05%)	29 (5.14%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		7.582 (1.994 , 28.827)
	Relative Risk (95% CI)		5.129 (1.437 , 18.307)
	Common Risk Difference (95% CI)		38.061 (18.534 , 57.587)
	CMH p-value		0.001256

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM reduction >= 5 points by Race, baseline to Week 16 NRI (mITT)

Race: WHITE

		PBO N=287	LEB250Q2W N=564
POEM reduction >= 5 points (Observed up to ICE), n(%)	Missing	85 (29.62%)	98 (17.38%)
	Total	178 (62.02%)	364 (64.54%)
	Non responder	50 (17.42%)	59 (10.46%)
	Responder	43 (14.98%)	207 (36.70%)
POEM reduction >= 5 points (NRI) [1] [2], n(%)	Total	178 (62.02%)	364 (64.54%)
	Non responder	135 (47.04%)	157 (27.84%)
	Responder	43 (14.98%)	207 (36.70%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.220 (2.810 , 6.338)
	Relative Risk (95% CI)		2.748 (2.039 , 3.705)
	Common Risk Difference (95% CI)		33.548 (25.332 , 41.764)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis POEM reduction >= 5 points by Race, baseline to Week 16 NRI (mITT)

Race: OTHER

		PBO N=287	LEB250Q2W N=564
POEM reduction >= 5 points (Observed up to ICE), n(%)	Missing	5 (1.74%)	11 (1.95%)
	Total	8 (2.79%)	25 (4.43%)
	Non responder	2 (0.70%)	3 (0.53%)
	Responder	1 (0.35%)	11 (1.95%)
POEM reduction >= 5 points (NRI) [1] [2], n(%)	Total	8 (2.79%)	25 (4.43%)
	Non responder	7 (2.44%)	14 (2.48%)
	Responder	1 (0.35%)	11 (1.95%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		7.429 (0.339 , 162.84)
	Relative Risk (95% CI)		3.143 (0.520 , 18.984)
	Common Risk Difference (95% CI)		28.391 (-9.880 , 66.662)
	CMH p-value		0.198689

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.56 **ADvocate 1 + ADvocate 2. Responder analysis DQLI of 0-1 points by Gender, baseline to Week 16, NRi (mITT)**

Gender: Overall

		PBO N=287	LEB250Q2W N=564
DQLI of 0-1 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	149 (51.92%)	165 (29.26%)
	Non responder	122 (42.51%)	288 (51.06%)
	Responder	16 (5.57%)	111 (19.68%)
DQLI of 0-1 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	271 (94.43%)	453 (80.32%)
	Responder	16 (5.57%)	111 (19.68%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.279 (2.461 , 7.438)
	Relative Risk (95% CI)		3.065 (1.907 , 4.927)
	Common Risk Difference (95% CI)		14.051 (9.865 , 18.237)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.717005

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI of 0-1 points by Gender, baseline to Week 16, NRi (mITT)

Gender: F

		PBO N=287	LEB250Q2W N=564
DQLI of 0-1 points (Observed up to ICE), n(%)	Missing	76 (26.48%)	77 (13.65%)
	Total	148 (51.57%)	277 (49.11%)
	Non responder	65 (22.65%)	149 (26.42%)
	Responder	7 (2.44%)	51 (9.04%)
DQLI of 0-1 points (NRI) [1] [2], n(%)	Total	148 (51.57%)	277 (49.11%)
	Non responder	141 (49.13%)	226 (40.07%)
	Responder	7 (2.44%)	51 (9.04%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.410 (1.969 , 9.877)
	Relative Risk (95% CI)		3.172 (1.582 , 6.360)
	Common Risk Difference (95% CI)		13.916 (8.001 , 19.831)
	CMH p-value		0.000089

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI of 0-1 points by Gender, baseline to Week 16, NRi (mITT)

Gender: M

		PBO N=287	LEB250Q2W N=564
DQLI of 0-1 points (Observed up to ICE), n(%)	Missing	73 (25.44%)	88 (15.60%)
	Total	139 (48.43%)	287 (50.89%)
	Non responder	57 (19.86%)	139 (24.65%)
	Responder	9 (3.14%)	60 (10.64%)
DQLI of 0-1 points (NRI) [1] [2], n(%)	Total	139 (48.43%)	287 (50.89%)
	Non responder	130 (45.30%)	227 (40.25%)
	Responder	9 (3.14%)	60 (10.64%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.025 (1.890 , 8.571)
	Relative Risk (95% CI)		2.945 (1.534 , 5.657)
	Common Risk Difference (95% CI)		14.769 (8.364 , 21.174)
	CMH p-value		0.000139

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.57 **ADvocate 1 + ADvocate 2. Responder analysis DQLI of 0-1 points by Age Group I, baseline to Week 16, NRi (mITT)**

Age Group I: Overall

		PBO N=287	LEB250Q2W N=564
DQLI of 0-1 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	149 (51.92%)	165 (29.26%)
	Non responder	122 (42.51%)	288 (51.06%)
	Responder	16 (5.57%)	111 (19.68%)
DQLI of 0-1 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	271 (94.43%)	453 (80.32%)
	Responder	16 (5.57%)	111 (19.68%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.279 (2.461 , 7.438)
	Relative Risk (95% CI)		3.065 (1.907 , 4.927)
	Common Risk Difference (95% CI)		14.051 (9.865 , 18.237)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.813536

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI of 0-1 points by Age Group I, baseline to Week 16, NRi (mITT)

Age Group I: Adolescents (12<18) years

		PBO N=287	LEB250Q2W N=564
DQLI of 0-1 points (Observed up to ICE), n(%)	Missing	29 (10.10%)	58 (10.28%)
	Total	35 (12.20%)	67 (11.88%)
	Non responder	6 (2.09%)	7 (1.24%)
	Responder	0 (0.00%)	2 (0.35%)
DQLI of 0-1 points (NRI) [1] [2], n(%)	Total	35 (12.20%)	67 (11.88%)
	Non responder	35 (12.20%)	65 (11.52%)
	Responder	0 (0.00%)	2 (0.35%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		2.652 (-1.342 , 6.646)
	CMH p-value		0.345779

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI of 0-1 points by Age Group I, baseline to Week 16, NRi (mITT)

Age Group I: Adults >= 18 years

		PBO N=287	LEB250Q2W N=564
DQLI of 0-1 points (Observed up to ICE), n(%)	Missing	120 (41.81%)	107 (18.97%)
	Total	252 (87.80%)	497 (88.12%)
	Non responder	116 (40.42%)	281 (49.82%)
	Responder	16 (5.57%)	109 (19.33%)
DQLI of 0-1 points (NRI) [1] [2], n(%)	Total	252 (87.80%)	497 (88.12%)
	Non responder	236 (82.23%)	388 (68.79%)
	Responder	16 (5.57%)	109 (19.33%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.206 (2.418 , 7.317)
	Relative Risk (95% CI)		3.019 (1.880 , 4.851)
	Common Risk Difference (95% CI)		15.564 (10.868 , 20.260)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.58 **ADvocate 1 + ADvocate 2. Responder analysis DQLI of 0-1 points by Disease Severity II, baseline to Week 16, NRi (mITT)**

Disease Severity II: Overall

		PBO N=287	LEB250Q2W N=564
DQLI of 0-1 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	149 (51.92%)	165 (29.26%)
	Non responder	122 (42.51%)	288 (51.06%)
	Responder	16 (5.57%)	111 (19.68%)
DQLI of 0-1 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	271 (94.43%)	453 (80.32%)
	Responder	16 (5.57%)	111 (19.68%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.279 (2.461 , 7.438)
	Relative Risk (95% CI)		3.065 (1.907 , 4.927)
	Common Risk Difference (95% CI)		14.051 (9.865 , 18.237)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.570544

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI of 0-1 points by Disease Severity II, baseline to Week 16, NRi (mITT)

Disease Severity II: IGA = 3

		PBO N=287	LEB250Q2W N=564
DQLI of 0-1 points (Observed up to ICE), n(%)	Missing	86 (29.97%)	89 (15.78%)
	Total	178 (62.02%)	345 (61.17%)
	Non responder	82 (28.57%)	181 (32.09%)
	Responder	10 (3.48%)	75 (13.30%)
DQLI of 0-1 points (NRI) [1] [2], n(%)	Total	178 (62.02%)	345 (61.17%)
	Non responder	168 (58.54%)	270 (47.87%)
	Responder	10 (3.48%)	75 (13.30%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.609 (2.309 , 9.198)
	Relative Risk (95% CI)		3.273 (1.799 , 5.955)
	Common Risk Difference (95% CI)		15.794 (10.293 , 21.295)
	CMH p-value		0.000003

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI of 0-1 points by Disease Severity II, baseline to Week 16, NRi (mITT)

Disease Severity II: IGA = 4

		PBO N=287	LEB250Q2W N=564
DQLI of 0-1 points (Observed up to ICE), n(%)	Missing	63 (21.95%)	76 (13.48%)
	Total	109 (37.98%)	219 (38.83%)
	Non responder	40 (13.94%)	107 (18.97%)
	Responder	6 (2.09%)	36 (6.38%)
DQLI of 0-1 points (NRI) [1] [2], n(%)	Total	109 (37.98%)	219 (38.83%)
	Non responder	103 (35.89%)	183 (32.45%)
	Responder	6 (2.09%)	36 (6.38%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.714 (1.474 , 9.358)
	Relative Risk (95% CI)		2.710 (1.244 , 5.902)
	Common Risk Difference (95% CI)		11.231 (4.847 , 17.616)
	CMH p-value		0.003470

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.59 **ADvocate 1 + ADvocate 2. Responder analysis DQLI of 0-1 points by Region, baseline to Week 16, NRi (mITT)**

Region: Overall

		PBO N=287	LEB250Q2W N=564
DQLI of 0-1 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	149 (51.92%)	165 (29.26%)
	Non responder	122 (42.51%)	288 (51.06%)
	Responder	16 (5.57%)	111 (19.68%)
DQLI of 0-1 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	271 (94.43%)	453 (80.32%)
	Responder	16 (5.57%)	111 (19.68%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.279 (2.461 , 7.438)
	Relative Risk (95% CI)		3.065 (1.907 , 4.927)
	Common Risk Difference (95% CI)		14.051 (9.865 , 18.237)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.225269

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI of 0-1 points by Region, baseline to Week 16, NRi (mITT)

Region: Europe

		PBO N=287	LEB250Q2W N=564
DQLI of 0-1 points (Observed up to ICE), n(%)	Missing	38 (13.24%)	32 (5.67%)
	Total	84 (29.27%)	168 (29.79%)
	Non responder	42 (14.63%)	100 (17.73%)
	Responder	4 (1.39%)	36 (6.38%)
DQLI of 0-1 points (NRI) [1] [2], n(%)	Total	84 (29.27%)	168 (29.79%)
	Non responder	80 (27.87%)	132 (23.40%)
	Responder	4 (1.39%)	36 (6.38%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.708 (1.933 , 16.855)
	Relative Risk (95% CI)		3.882 (1.499 , 10.056)
	Common Risk Difference (95% CI)		16.633 (9.008 , 24.259)
	CMH p-value		0.000593

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI of 0-1 points by Region, baseline to Week 16, NRi (mITT)

Region: US

		PBO N=287	LEB250Q2W N=564
DQLI of 0-1 points (Observed up to ICE), n(%)	Missing	58 (20.21%)	70 (12.41%)
	Total	122 (42.51%)	235 (41.67%)
	Non responder	52 (18.12%)	111 (19.68%)
	Responder	12 (4.18%)	54 (9.57%)
DQLI of 0-1 points (NRI) [1] [2], n(%)	Total	122 (42.51%)	235 (41.67%)
	Non responder	110 (38.33%)	181 (32.09%)
	Responder	12 (4.18%)	54 (9.57%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		2.673 (1.370 , 5.214)
	Relative Risk (95% CI)		2.064 (1.212 , 3.514)
	Common Risk Difference (95% CI)		12.857 (5.282 , 20.431)
	CMH p-value		0.002898

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI of 0-1 points by Region, baseline to Week 16, NRi (mITT)

Region: Rest of the World

		PBO N=287	LEB250Q2W N=564
DQLI of 0-1 points (Observed up to ICE), n(%)	Missing	53 (18.47%)	63 (11.17%)
	Total	81 (28.22%)	161 (28.55%)
	Non responder	28 (9.76%)	77 (13.65%)
	Responder	0 (0.00%)	21 (3.72%)
DQLI of 0-1 points (NRI) [1] [2], n(%)	Total	81 (28.22%)	161 (28.55%)
	Non responder	81 (28.22%)	140 (24.82%)
	Responder	0 (0.00%)	21 (3.72%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		13.142 (7.891 , 18.394)
	CMH p-value		0.000542

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.60 **ADvocate 1 + ADvocate 2. Responder analysis DQLI of 0-1 points by Race, baseline to Week 16, NRi (mITT)**

Race: Overall

		PBO N=287	LEB250Q2W N=564
DQLI of 0-1 points (Observed up to ICE), n(%)	Total	287 (100.00%)	564 (100.00%)
	Missing	149 (51.92%)	165 (29.26%)
	Non responder	122 (42.51%)	288 (51.06%)
	Responder	16 (5.57%)	111 (19.68%)
DQLI of 0-1 points (NRI) [1] [2], n(%)	Total	287 (100.00%)	564 (100.00%)
	Non responder	271 (94.43%)	453 (80.32%)
	Responder	16 (5.57%)	111 (19.68%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.279 (2.461 , 7.438)
	Relative Risk (95% CI)		3.065 (1.907 , 4.927)
	Common Risk Difference (95% CI)		14.051 (9.865 , 18.237)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.708811

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI of 0-1 points by Race, baseline to Week 16, NRi (mITT)

Race: ASIAN

		PBO N=287	LEB250Q2W N=564
DQLI of 0-1 points (Observed up to ICE), n(%)	Missing	46 (16.03%)	43 (7.62%)
	Total	75 (26.13%)	117 (20.74%)
	Non responder	28 (9.76%)	61 (10.82%)
	Responder	1 (0.35%)	13 (2.30%)
DQLI of 0-1 points (NRI) [1] [2], n(%)	Total	75 (26.13%)	117 (20.74%)
	Non responder	74 (25.78%)	104 (18.44%)
	Responder	1 (0.35%)	13 (2.30%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		10.870 (1.188 , 99.500)
	Relative Risk (95% CI)		7.169 (0.786 , 65.407)
	Common Risk Difference (95% CI)		9.332 (3.175 , 15.490)
	CMH p-value		0.011746

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI of 0-1 points by Race, baseline to Week 16, NRi (mITT)

Race: BLACK OR AFRICAN AMERICAN

		PBO N=287	LEB250Q2W N=564
DQLI of 0-1 points (Observed up to ICE), n(%)	Missing	14 (4.88%)	14 (2.48%)
	Total	26 (9.06%)	58 (10.28%)
	Non responder	10 (3.48%)	36 (6.38%)
	Responder	2 (0.70%)	8 (1.42%)
DQLI of 0-1 points (NRI) [1] [2], n(%)	Total	26 (9.06%)	58 (10.28%)
	Non responder	24 (8.36%)	50 (8.87%)
	Responder	2 (0.70%)	8 (1.42%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		2.169 (0.379 , 12.397)
	Relative Risk (95% CI)		1.671 (0.476 , 5.863)
	Common Risk Difference (95% CI)		6.919 (-7.109 , 20.947)
	CMH p-value		0.397333

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI of 0-1 points by Race, baseline to Week 16, NRi (mITT)

Race: WHITE

		PBO N=287	LEB250Q2W N=564
DQLI of 0-1 points (Observed up to ICE), n(%)	Missing	86 (29.97%)	97 (17.20%)
	Total	178 (62.02%)	364 (64.54%)
	Non responder	79 (27.53%)	183 (32.45%)
	Responder	13 (4.53%)	84 (14.89%)
DQLI of 0-1 points (NRI) [1] [2], n(%)	Total	178 (62.02%)	364 (64.54%)
	Non responder	165 (57.49%)	280 (49.65%)
	Responder	13 (4.53%)	84 (14.89%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.732 (2.002 , 6.957)
	Relative Risk (95% CI)		2.733 (1.621 , 4.606)
	Common Risk Difference (95% CI)		15.330 (9.487 , 21.174)
	CMH p-value		0.000013

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI of 0-1 points by Race, baseline to Week 16, NRi (mITT)

Race: OTHER

		PBO N=287	LEB250Q2W N=564
DQLI of 0-1 points (Observed up to ICE), n(%)	Missing	3 (1.05%)	11 (1.95%)
	Total	8 (2.79%)	25 (4.43%)
	Non responder	5 (1.74%)	8 (1.42%)
	Responder	0 (0.00%)	6 (1.06%)
DQLI of 0-1 points (NRI) [1] [2], n(%)	Total	8 (2.79%)	25 (4.43%)
	Non responder	8 (2.79%)	19 (3.37%)
	Responder	0 (0.00%)	6 (1.06%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		. (. , .)
	Common Risk Difference (95% CI)		20.189 (-8.247 , 48.625)
	CMH p-value		0.264948

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.

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Global Clinical Statistics ALMIRALL

4.5.2.61 **ADvocate 1 + ADvocate 2. Responder analysis DQLI reduction >= 4 points by Gender, baseline to Week 16, NRi (mITT, patients with baseline >= 4)**

Gender: Overall

		PBO N=222	LEB250Q2W N=433
DQLI of >= 4 points (Observed up to ICE), n(%)	Total	222 (100.00%)	433 (100.00%)
	Missing	105 (47.30%)	91 (21.02%)
	Non responder	52 (23.42%)	52 (12.01%)
	Responder	65 (29.28%)	290 (66.97%)
DQLI of >= 4 points (NRI) [1] [2], n(%)	Total	222 (100.00%)	433 (100.00%)
	Non responder	157 (70.72%)	143 (33.03%)
	Responder	65 (29.28%)	290 (66.97%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.082 (3.542 , 7.292)
	Relative Risk (95% CI)		3.053 (2.350 , 3.968)
	Common Risk Difference (95% CI)		37.701 (30.337 , 45.066)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.213899

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing DQLI baseline value.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI reduction >= 4 points by Gender, baseline to Week 16, NRi (mITT, patients with baseline >= 4)

Gender: F

		PBO N=222	LEB250Q2W N=433
DQLI of >= 4 points (Observed up to ICE), n(%)	Missing	54 (24.32%)	38 (8.78%)
	Total	115 (51.80%)	207 (47.81%)
	Non responder	19 (8.56%)	22 (5.08%)
	Responder	42 (18.92%)	147 (33.95%)
DQLI of >= 4 points (NRI) [1] [2], n(%)	Total	115 (51.80%)	207 (47.81%)
	Non responder	73 (32.88%)	60 (13.86%)
	Responder	42 (18.92%)	147 (33.95%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.336 (2.645 , 7.110)
	Relative Risk (95% CI)		2.559 (1.850 , 3.541)
	Common Risk Difference (95% CI)		34.474 (23.692 , 45.256)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing DQLI baseline value.

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI reduction >= 4 points by Gender, baseline to Week 16, NRi (mITT, patients with baseline >= 4)

Gender: M

		PBO N=222	LEB250Q2W N=433
DQLI of >= 4 points (Observed up to ICE), n(%)	Missing	51 (22.97%)	53 (12.24%)
	Total	107 (48.20%)	226 (52.19%)
	Non responder	33 (14.86%)	30 (6.93%)
	Responder	23 (10.36%)	143 (33.03%)
DQLI of >= 4 points (NRI) [1] [2], n(%)	Total	107 (48.20%)	226 (52.19%)
	Non responder	84 (37.84%)	83 (19.17%)
	Responder	23 (10.36%)	143 (33.03%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		8.043 (4.403 , 14.692)
	Relative Risk (95% CI)		4.544 (2.839 , 7.274)
	Common Risk Difference (95% CI)		44.506 (34.984 , 54.027)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing DQLI baseline value.

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Global Clinical Statistics ALMIRALL

4.5.2.62 **ADvocate 1 + ADvocate 2. Responder analysis DQLI reduction >= 4 points by Disease Severity II, baseline to Week 16, NRi (mITT, patients with baseline >= 4)**

Disease Severity II: Overall

		PBO N=222	LEB250Q2W N=433
DQLI of >= 4 points (Observed up to ICE), n(%)	Total	222 (100.00%)	433 (100.00%)
	Missing	105 (47.30%)	91 (21.02%)
	Non responder	52 (23.42%)	52 (12.01%)
	Responder	65 (29.28%)	290 (66.97%)
DQLI of >= 4 points (NRI) [1] [2], n(%)	Total	222 (100.00%)	433 (100.00%)
	Non responder	157 (70.72%)	143 (33.03%)
	Responder	65 (29.28%)	290 (66.97%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.082 (3.542 , 7.292)
	Relative Risk (95% CI)		3.053 (2.350 , 3.968)
	Common Risk Difference (95% CI)		37.701 (30.337 , 45.066)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.935965

	PBO N=222	LEB250Q2W N=433

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing DQLI baseline value.

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Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI reduction >= 4 points by Disease Severity II, baseline to Week 16, NRi (mITT, patients with baseline >= 4)

Disease Severity II: IGA = 3

		PBO N=222	LEB250Q2W N=433
DQLI of >= 4 points (Observed up to ICE), n(%)	Missing	61 (27.48%)	48 (11.09%)
	Total	137 (61.71%)	264 (60.97%)
	Non responder	32 (14.41%)	31 (7.16%)
	Responder	44 (19.82%)	185 (42.73%)
DQLI of >= 4 points (NRI) [1] [2], n(%)	Total	137 (61.71%)	264 (60.97%)
	Non responder	93 (41.89%)	79 (18.24%)
	Responder	44 (19.82%)	185 (42.73%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.102 (3.241 , 8.031)
	Relative Risk (95% CI)		3.035 (2.193 , 4.199)
	Common Risk Difference (95% CI)		38.339 (28.837 , 47.840)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing DQLI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI reduction >= 4 points by Disease Severity II, baseline to Week 16, NRi (mITT, patients with baseline >= 4)

Disease Severity II: IGA = 4

		PBO N=222	LEB250Q2W N=433
DQLI of >= 4 points (Observed up to ICE), n(%)	Missing	44 (19.82%)	43 (9.93%)
	Total	85 (38.29%)	169 (39.03%)
	Non responder	20 (9.01%)	21 (4.85%)
	Responder	21 (9.46%)	105 (24.25%)
DQLI of >= 4 points (NRI) [1] [2], n(%)	Total	85 (38.29%)	169 (39.03%)
	Non responder	64 (28.83%)	64 (14.78%)
	Responder	21 (9.46%)	105 (24.25%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.049 (2.782 , 9.164)
	Relative Risk (95% CI)		3.086 (1.983 , 4.801)
	Common Risk Difference (95% CI)		36.683 (25.035 , 48.330)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing DQLI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.63 **ADvocate 1 + ADvocate 2. Responder analysis DQLI reduction >= 4 points by Region, baseline to Week 16, NRi (mITT, patients with baseline >= 4)**

Region: Overall

		PBO N=222	LEB250Q2W N=433
DQLI of >= 4 points (Observed up to ICE), n(%)	Total	222 (100.00%)	433 (100.00%)
	Missing	105 (47.30%)	91 (21.02%)
	Non responder	52 (23.42%)	52 (12.01%)
	Responder	65 (29.28%)	290 (66.97%)
DQLI of >= 4 points (NRI) [1] [2], n(%)	Total	222 (100.00%)	433 (100.00%)
	Non responder	157 (70.72%)	143 (33.03%)
	Responder	65 (29.28%)	290 (66.97%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.082 (3.542 , 7.292)
	Relative Risk (95% CI)		3.053 (2.350 , 3.968)
	Common Risk Difference (95% CI)		37.701 (30.337 , 45.066)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.093351

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing DQLI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI reduction >= 4 points by Region, baseline to Week 16, NRi (mITT, patients with baseline >= 4)

Region: Europe

		PBO N=222	LEB250Q2W N=433
DQLI of >= 4 points (Observed up to ICE), n(%)	Missing	26 (11.71%)	14 (3.23%)
	Total	64 (28.83%)	133 (30.72%)
	Non responder	15 (6.76%)	18 (4.16%)
	Responder	23 (10.36%)	101 (23.33%)
DQLI of >= 4 points (NRI) [1] [2], n(%)	Total	64 (28.83%)	133 (30.72%)
	Non responder	41 (18.47%)	32 (7.39%)
	Responder	23 (10.36%)	101 (23.33%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		6.242 (3.167 , 12.303)
	Relative Risk (95% CI)		3.438 (2.145 , 5.509)
	Common Risk Difference (95% CI)		41.094 (27.575 , 54.613)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing DQLI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI reduction >= 4 points by Region, baseline to Week 16, NRi (mITT, patients with baseline >= 4)

Region: US

		PBO N=222	LEB250Q2W N=433
DQLI of >= 4 points (Observed up to ICE), n(%)	Missing	44 (19.82%)	41 (9.47%)
	Total	96 (43.24%)	183 (42.26%)
	Non responder	18 (8.11%)	23 (5.31%)
	Responder	34 (15.32%)	119 (27.48%)
DQLI of >= 4 points (NRI) [1] [2], n(%)	Total	96 (43.24%)	183 (42.26%)
	Non responder	62 (27.93%)	64 (14.78%)
	Responder	34 (15.32%)	119 (27.48%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.405 (2.028 , 5.719)
	Relative Risk (95% CI)		2.260 (1.582 , 3.228)
	Common Risk Difference (95% CI)		29.743 (17.948 , 41.539)
	CMH p-value		0.000002

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing DQLI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI reduction >= 4 points by Region, baseline to Week 16, NRi (mITT, patients with baseline >= 4)

Region: Rest of the World

		PBO N=222	LEB250Q2W N=433
DQLI of >= 4 points (Observed up to ICE), n(%)	Missing	35 (15.77%)	36 (8.31%)
	Total	62 (27.93%)	117 (27.02%)
	Non responder	19 (8.56%)	11 (2.54%)
	Responder	8 (3.60%)	70 (16.17%)
DQLI of >= 4 points (NRI) [1] [2], n(%)	Total	62 (27.93%)	117 (27.02%)
	Non responder	54 (24.32%)	47 (10.85%)
	Responder	8 (3.60%)	70 (16.17%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		8.946 (4.010 , 19.957)
	Relative Risk (95% CI)		4.945 (2.576 , 9.492)
	Common Risk Difference (95% CI)		46.480 (34.030 , 58.930)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing DQLI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.64 **ADvocate 1 + ADvocate 2. Responder analysis DQLI reduction >= 4 points by Race, baseline to Week 16, NRi (mITT, patients with baseline >= 4)**

Race: Overall

		PBO N=222	LEB250Q2W N=433
DQLI of >= 4 points (Observed up to ICE), n(%)	Total	222 (100.00%)	433 (100.00%)
	Missing	105 (47.30%)	91 (21.02%)
	Non responder	52 (23.42%)	52 (12.01%)
	Responder	65 (29.28%)	290 (66.97%)
DQLI of >= 4 points (NRI) [1] [2], n(%)	Total	222 (100.00%)	433 (100.00%)
	Non responder	157 (70.72%)	143 (33.03%)
	Responder	65 (29.28%)	290 (66.97%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.082 (3.542 , 7.292)
	Relative Risk (95% CI)		3.053 (2.350 , 3.968)
	Common Risk Difference (95% CI)		37.701 (30.337 , 45.066)
	CMH p-value		<0.000001
	Treatment by subgroup interaction test p-value [7]		0.629441

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing DQLI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI reduction >= 4 points by Race, baseline to Week 16, NRi (mITT, patients with baseline >= 4)

Race: ASIAN

		PBO N=222	LEB250Q2W N=433
DQLI of >= 4 points (Observed up to ICE), n(%)	Missing	31 (13.96%)	22 (5.08%)
	Total	58 (26.13%)	82 (18.94%)
	Non responder	15 (6.76%)	7 (1.62%)
	Responder	12 (5.41%)	53 (12.24%)
DQLI of >= 4 points (NRI) [1] [2], n(%)	Total	58 (26.13%)	82 (18.94%)
	Non responder	46 (20.72%)	29 (6.70%)
	Responder	12 (5.41%)	53 (12.24%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		7.637 (3.309 , 17.626)
	Relative Risk (95% CI)		3.683 (2.006 , 6.761)
	Common Risk Difference (95% CI)		43.179 (28.519 , 57.840)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing DQLI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI reduction >= 4 points by Race, baseline to Week 16, NRi (mITT, patients with baseline >= 4)

Race: BLACK OR AFRICAN AMERICAN

		PBO N=222	LEB250Q2W N=433
DQLI of >= 4 points (Observed up to ICE), n(%)	Missing	11 (4.95%)	7 (1.62%)
	Total	21 (9.46%)	44 (10.16%)
	Non responder	4 (1.80%)	8 (1.85%)
	Responder	6 (2.70%)	29 (6.70%)
DQLI of >= 4 points (NRI) [1] [2], n(%)	Total	21 (9.46%)	44 (10.16%)
	Non responder	15 (6.76%)	15 (3.46%)
	Responder	6 (2.70%)	29 (6.70%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.549 (1.412 , 14.658)
	Relative Risk (95% CI)		2.715 (1.223 , 6.026)
	Common Risk Difference (95% CI)		35.740 (11.223 , 60.257)
	CMH p-value		0.009756

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing DQLI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI reduction >= 4 points by Race, baseline to Week 16, NRi (mITT, patients with baseline >= 4)

Race: WHITE

		PBO N=222	LEB250Q2W N=433
DQLI of >= 4 points (Observed up to ICE), n(%)	Missing	61 (27.48%)	55 (12.70%)
	Total	137 (61.71%)	290 (66.97%)
	Non responder	31 (13.96%)	36 (8.31%)
	Responder	45 (20.27%)	199 (45.96%)
DQLI of >= 4 points (NRI) [1] [2], n(%)	Total	137 (61.71%)	290 (66.97%)
	Non responder	92 (41.44%)	91 (21.02%)
	Responder	45 (20.27%)	199 (45.96%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.938 (3.132 , 7.785)
	Relative Risk (95% CI)		2.998 (2.170 , 4.141)
	Common Risk Difference (95% CI)		37.082 (27.761 , 46.403)
	CMH p-value		<0.000001

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing DQLI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis DQLI reduction >= 4 points by Race, baseline to Week 16, NRi (mITT, patients with baseline >= 4)

Race: OTHER

		PBO N=222	LEB250Q2W N=433
DQLI of >= 4 points (Observed up to ICE), n(%)	Missing	2 (0.90%)	7 (1.62%)
	Total	6 (2.70%)	17 (3.93%)
	Non responder	2 (0.90%)	1 (0.23%)
	Responder	2 (0.90%)	9 (2.08%)
DQLI of >= 4 points (NRI) [1] [2], n(%)	Total	6 (2.70%)	17 (3.93%)
	Non responder	4 (1.80%)	8 (1.85%)
	Responder	2 (0.90%)	9 (2.08%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		8.000 (0.414 , 154.43)
	Relative Risk (95% CI)		2.167 (0.747 , 6.281)
	Common Risk Difference (95% CI)		50.000 (-5.117 , 100.00)
	CMH p-value		0.154750

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing DQLI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.65 **ADvocate 1 + ADvocate 2. Responder analysis CLDQI, reduction >= 4 points by Gender, baseline to Week 16, NRi (mITT, patients with baseline >= 4)**

Gender: Overall

		PBO N=24	LEB250Q2W N=48
CLDQI reduction of >= 4 points (Observed up to ICE), n(%)	Total	24 (100.00%)	48 (100.00%)
	Missing	10 (41.67%)	8 (16.67%)
	Non responder	7 (29.17%)	5 (10.42%)
	Responder	7 (29.17%)	35 (72.92%)
CLDQI reduction of >= 4 points (NRI) [1] [2], n(%)	Total	24 (100.00%)	48 (100.00%)
	Non responder	17 (70.83%)	13 (27.08%)
	Responder	7 (29.17%)	35 (72.92%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		7.021 (1.884 , 26.172)
	Relative Risk (95% CI)		3.571 (1.682 , 7.581)
	Common Risk Difference (95% CI)		42.505 (20.548 , 64.462)
	CMH p-value		0.000617
	Treatment by subgroup interaction test p-value [7]		0.918576

	PBO N=24	LEB250Q2W N=48

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing CLDQI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis CLDQI, reduction >= 4 points by Gender, baseline to Week 16, NRi (mITT, patients with baseline >= 4)

Gender: F

		PBO N=24	LEB250Q2W N=48
CLDQI reduction of >= 4 points (Observed up to ICE), n(%)	Missing	5 (20.83%)	5 (10.42%)
	Total	14 (58.33%)	27 (56.25%)
	Non responder	4 (16.67%)	1 (2.08%)
	Responder	5 (20.83%)	21 (43.75%)
CLDQI reduction of >= 4 points (NRI) [1] [2], n(%)	Total	14 (58.33%)	27 (56.25%)
	Non responder	9 (37.50%)	6 (12.50%)
	Responder	5 (20.83%)	21 (43.75%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.714 (1.040 , 31.382)
	Relative Risk (95% CI)		4.000 (0.918 , 17.432)
	Common Risk Difference (95% CI)		36.407 (4.080 , 68.733)
	CMH p-value		0.037538

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing CLDQI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis CLDQI, reduction >= 4 points by Gender, baseline to Week 16, NRi (mITT, patients with baseline >= 4)

Gender: M

		PBO N=24	LEB250Q2W N=48
CLDQI reduction of >= 4 points (Observed up to ICE), n(%)	Missing	5 (20.83%)	3 (6.25%)
	Total	10 (41.67%)	21 (43.75%)
	Non responder	3 (12.50%)	4 (8.33%)
	Responder	2 (8.33%)	14 (29.17%)
CLDQI reduction of >= 4 points (NRI) [1] [2], n(%)	Total	10 (41.67%)	21 (43.75%)
	Non responder	8 (33.33%)	7 (14.58%)
	Responder	2 (8.33%)	14 (29.17%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		5.171 (1.014 , 26.377)
	Common Risk Difference (95% CI)		55.725 (22.707 , 88.744)
	CMH p-value		0.027099

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing CLDQI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.66 **ADvocate 1 + ADvocate 2. Responder analysis CLDQI, reduction >= 4 points by Disease Severity II, baseline to Week 16, NRi (mITT, patients with baseline >= 4)**

Disease Severity II: Overall

		PBO N=24	LEB250Q2W N=48
CLDQI reduction of >= 4 points (Observed up to ICE), n(%)	Total	24 (100.00%)	48 (100.00%)
	Missing	10 (41.67%)	8 (16.67%)
	Non responder	7 (29.17%)	5 (10.42%)
	Responder	7 (29.17%)	35 (72.92%)
CLDQI reduction of >= 4 points (NRI) [1] [2], n(%)	Total	24 (100.00%)	48 (100.00%)
	Non responder	17 (70.83%)	13 (27.08%)
	Responder	7 (29.17%)	35 (72.92%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		7.021 (1.884 , 26.172)
	Relative Risk (95% CI)		3.571 (1.682 , 7.581)
	Common Risk Difference (95% CI)		42.505 (20.548 , 64.462)
	CMH p-value		0.000617
	Treatment by subgroup interaction test p-value [7]		0.539629

	PBO N=24	LEB250Q2W N=48

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing CLDQI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis CLDQI, reduction >= 4 points by Disease Severity II, baseline to Week 16, NRi (mITT, patients with baseline >= 4)

Disease Severity II: IGA = 3

		PBO N=24	LEB250Q2W N=48
CLDQI reduction of >= 4 points (Observed up to ICE), n(%)	Missing	5 (20.83%)	6 (12.50%)
	Total	15 (62.50%)	27 (56.25%)
	Non responder	5 (20.83%)	2 (4.17%)
	Responder	5 (20.83%)	19 (39.58%)
CLDQI reduction of >= 4 points (NRI) [1] [2], n(%)	Total	15 (62.50%)	27 (56.25%)
	Non responder	10 (41.67%)	8 (16.67%)
	Responder	5 (20.83%)	19 (39.58%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		5.631 (1.125 , 28.195)
	Relative Risk (95% CI)		3.083 (1.207 , 7.874)
	Common Risk Difference (95% CI)		35.653 (7.799 , 63.507)
	CMH p-value		0.016959

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing CLDQI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis CLDQI, reduction >= 4 points by Disease Severity II, baseline to Week 16, NRi (mITT, patients with baseline >= 4)

Disease Severity II: IGA = 4

		PBO N=24	LEB250Q2W N=48
CLDQI reduction of >= 4 points (Observed up to ICE), n(%)	Missing	5 (20.83%)	2 (4.17%)
	Total	9 (37.50%)	21 (43.75%)
	Non responder	2 (8.33%)	3 (6.25%)
	Responder	2 (8.33%)	16 (33.33%)
CLDQI reduction of >= 4 points (NRI) [1] [2], n(%)	Total	9 (37.50%)	21 (43.75%)
	Non responder	7 (29.17%)	5 (10.42%)
	Responder	2 (8.33%)	16 (33.33%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		10.034 (0.956 , 105.34)
	Relative Risk (95% CI)		4.475 (1.262 , 15.862)
	Common Risk Difference (95% CI)		54.040 (19.582 , 88.497)
	CMH p-value		0.013426

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing CLDQI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

4.5.2.67 **ADvocate 1 + ADvocate 2. Responder analysis CLDQI, reduction >= 4 points by Region, baseline to Week 16, NRi (mITT, patients with baseline >= 4)**

Region: Overall

		PBO N=24	LEB250Q2W N=48
CLDQI reduction of >= 4 points (Observed up to ICE), n(%)	Total	24 (100.00%)	48 (100.00%)
	Missing	10 (41.67%)	8 (16.67%)
	Non responder	7 (29.17%)	5 (10.42%)
	Responder	7 (29.17%)	35 (72.92%)
CLDQI reduction of >= 4 points (NRI) [1] [2], n(%)	Total	24 (100.00%)	48 (100.00%)
	Non responder	17 (70.83%)	13 (27.08%)
	Responder	7 (29.17%)	35 (72.92%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		7.021 (1.884 , 26.172)
	Relative Risk (95% CI)		3.571 (1.682 , 7.581)
	Common Risk Difference (95% CI)		42.505 (20.548 , 64.462)
	CMH p-value		0.000617
	Treatment by subgroup interaction test p-value [7]		0.918375

	PBO N=24	LEB250Q2W N=48

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4). When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing CLDQI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis CLDQI, reduction >= 4 points by Region, baseline to Week 16, NRi (mITT, patients with baseline >= 4)

Region: Europe

		PBO N=24	LEB250Q2W N=48
CLDQI reduction of >= 4 points (Observed up to ICE), n(%)	Missing	1 (4.17%)	3 (6.25%)
	Total	6 (25.00%)	13 (27.08%)
	Non responder	3 (12.50%)	1 (2.08%)
	Responder	2 (8.33%)	9 (18.75%)
CLDQI reduction of >= 4 points (NRI) [1] [2], n(%)	Total	6 (25.00%)	13 (27.08%)
	Non responder	4 (16.67%)	4 (8.33%)
	Responder	2 (8.33%)	9 (18.75%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		3.300 (0.400 , 27.204)
	Relative Risk (95% CI)		2.211 (0.760 , 6.432)
	Common Risk Difference (95% CI)		29.677 (-18.03 , 77.386)
	CMH p-value		0.199035

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing CLDQI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

Lebrikizumab

ADvocate 1 + ADvocate 2. Responder analysis CLDQI, reduction >= 4 points by Region, baseline to Week 16, NRi (mITT, patients with baseline >= 4)

Region: US

		PBO N=24	LEB250Q2W N=48
CLDQI reduction of >= 4 points (Observed up to ICE), n(%)	Missing	5 (20.83%)	4 (8.33%)
	Total	10 (41.67%)	20 (41.67%)
	Non responder	2 (8.33%)	1 (2.08%)
	Responder	3 (12.50%)	15 (31.25%)
CLDQI reduction of >= 4 points (NRI) [1] [2], n(%)	Total	10 (41.67%)	20 (41.67%)
	Non responder	7 (29.17%)	5 (10.42%)
	Responder	3 (12.50%)	15 (31.25%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		. (. , .)
	Relative Risk (95% CI)		11.990 (1.217 , 118.16)
	Common Risk Difference (95% CI)		50.092 (24.062 , 76.122)
	CMH p-value		0.005541

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World), age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction. P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing CLDQI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

Global Clinical Statistics ALMIRALL

Lebrikizumab
ADvocate 1 + ADvocate 2. Responder analysis CLDQI, reduction >= 4 points by Region, baseline to Week 16, NRi (mITT, patients with baseline >= 4)
Region: Rest of the World

		PBO N=24	LEB250Q2W N=48
CLDQI reduction of >= 4 points (Observed up to ICE), n(%)	Missing	4 (16.67%)	1 (2.08%)
	Total	8 (33.33%)	15 (31.25%)
	Non responder	2 (8.33%)	3 (6.25%)
	Responder	2 (8.33%)	11 (22.92%)
CLDQI reduction of >= 4 points (NRI) [1] [2], n(%)	Total	8 (33.33%)	15 (31.25%)
	Non responder	6 (25.00%)	4 (8.33%)
	Responder	2 (8.33%)	11 (22.92%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI)		4.436 (0.690 , 28.498)
	Relative Risk (95% CI)		2.562 (0.872 , 7.526)
	Common Risk Difference (95% CI)		42.454 (-3.243 , 88.150)
	CMH p-value		0.085381

	PBO N=24	LEB250Q2W N=48

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, ICE = Intercurrent Event, NRi = Non-responder imputation, mITT = Modified Intention-to-treat
Note 1: Subjects with missing have been considered as Non-Responder.
Note 2: Subjects with rescue medication have been considered as Non-Responder.
Note 3: The stratification factors are: studyid (KGAB vs KGAC), geographic region (US vs EU vs Rest of the World),
age (adolescent patients <12 to 18 and adults >= 18), disease severity at baseline (IGA 3 vs IGA 4).
When subgroup factor is also included in the latter stratification factors, such will be excluded from strata.
Note 4: Odds Ratio and Relative Risk are computed by Mantel-Haenzel method and adjusted by stratification factors.
Note 5: Common Risk Difference adjusted by stratification factors.
Note 6: CHM p-value obtained from stratified Cochran-Mantel-Haenszel test (CMH).
Note 7: Logistic regression with Firth correction. Covariates: treatment, stratification factors, subgroup, treatment-by-subgroup interaction.
P-value for global effect of treatment-by-subgroup interaction is provided.
Note 8: Observed results exclude data from subjects with missing CLDQI baseline value.

Source: I:\Bioestad\SEGURTEM\Proyecto\Lebrikizumab\Results\R01_01_01_Responder_Analysis_KGABC.sas (Date: 01MAR23)

4.5.3 Jegliche UE, UE nach SOC und PT, UESI - Subgruppen

4.5.3.1 ADvocate 1

4.5.3.2 **ADvocate 1. Safety analysis, patients with at least one AE by Gender, up to Week 16 (mSAFETY)**

Gender: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		74 (52.48%)	130 (46.10%)
Number of patients with no event, n(%)		67 (47.52%)	152 (53.90%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.774 (0.506 , 1.185)
	Relative Risk (95% CI) [3]		0.918 (0.802 , 1.052)
	Relative Risk (95% CI) [4]		0.918 (0.795 , 1.052)
	Common Risk Difference (95% CI) [3]		-6.355 (-16.45 , 3.736)
	Treatment by subgroup interaction test p-value [5]		0.646557

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE by Gender, up to Week 16 (mSAFETY)
Gender: F

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		40 (28.37%)	65 (23.05%)
Number of patients with no event, n(%)		33 (23.40%)	76 (26.95%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.706 (0.384 , 1.294)
	Relative Risk (95% CI) [3]		0.888 (0.731 , 1.078)
	Relative Risk (95% CI) [4]		0.888 (0.715 , 1.079)
	Common Risk Difference (95% CI) [3]		-8.695 (-22.77 , 5.378)
	Fisher's Exact test p-value		0.250498

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE by Gender, up to Week 16 (mSAFETY)
Gender: M

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		34 (24.11%)	65 (23.05%)
Number of patients with no event, n(%)		34 (24.11%)	76 (26.95%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.855 (0.460 , 1.591)
	Relative Risk (95% CI) [3]		0.950 (0.786 , 1.149)
	Relative Risk (95% CI) [4]		0.950 (0.770 , 1.150)
	Common Risk Difference (95% CI) [3]		-3.901 (-18.36 , 10.554)
	Fisher's Exact test p-value		0.658111

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.3 ADvocate 1. Safety analysis, patients with at least one AE by Age Group I, up to Week 16 (mSAFETY)

Age Group I: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		74 (52.48%)	130 (46.10%)
Number of patients with no event, n(%)		67 (47.52%)	152 (53.90%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.774 (0.506 , 1.185)
	Relative Risk (95% CI) [3]		0.918 (0.802 , 1.052)
	Relative Risk (95% CI) [4]		0.918 (0.795 , 1.052)
	Common Risk Difference (95% CI) [3]		-6.342 (-16.42 , 3.737)
	Treatment by subgroup interaction test p-value [5]		0.401110

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adolescents (12<18) years

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		9 (6.38%)	12 (4.26%)
Number of patients with no event, n(%)		9 (6.38%)	25 (8.87%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.480 (0.131 , 1.779)
	Relative Risk (95% CI) [3]		0.777 (0.510 , 1.185)
	Relative Risk (95% CI) [4]		0.777 (0.458 , 1.158)
	Common Risk Difference (95% CI) [3]		-17.57 (-45.15 , 10.020)
	Fisher's Exact test p-value		0.246319

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adults >= 18 years

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		65 (46.10%)	118 (41.84%)
Number of patients with no event, n(%)		58 (41.13%)	127 (45.04%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.829 (0.525 , 1.309)
	Relative Risk (95% CI) [3]		0.939 (0.812 , 1.086)
	Relative Risk (95% CI) [4]		0.939 (0.808 , 1.090)
	Common Risk Difference (95% CI) [3]		-4.682 (-15.50 , 6.133)
	Fisher's Exact test p-value		0.439562

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.4 **ADvocate 1. Safety analysis, patients with at least one AE by Disease Severity II, up to Week 16 (mSAFETY)**

Disease Severity II: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		74 (52.48%)	130 (46.10%)
Number of patients with no event, n(%)		67 (47.52%)	152 (53.90%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.774 (0.506 , 1.185)
	Relative Risk (95% CI) [3]		0.918 (0.802 , 1.052)
	Relative Risk (95% CI) [4]		0.918 (0.795 , 1.052)
	Common Risk Difference (95% CI) [3]		-6.242 (-16.38 , 3.894)
	Treatment by subgroup interaction test p-value [5]		0.012594

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE by Disease Severity II, up to Week 16 (mSAFETY)
Disease Severity II: IGA = 3

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		45 (31.91%)	63 (22.34%)
Number of patients with no event, n(%)		38 (26.95%)	106 (37.59%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.502 (0.284 , 0.885)
	Relative Risk (95% CI) [3]		0.792 (0.657 , 0.955)
	Relative Risk (95% CI) [4]		0.792 (0.642 , 0.974)
	Common Risk Difference (95% CI) [3]		-16.94 (-29.90 , -3.976)
	Fisher's Exact test p-value		0.014551

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE by Disease Severity II, up to Week 16 (mSAFETY)
Disease Severity II: IGA = 4

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		29 (20.57%)	67 (23.76%)
Number of patients with no event, n(%)		29 (20.57%)	46 (16.31%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.457 (0.732 , 2.892)
	Relative Risk (95% CI) [3]		1.138 (0.911 , 1.422)
	Relative Risk (95% CI) [4]		1.138 (0.912 , 1.461)
	Common Risk Difference (95% CI) [3]		9.292 (-6.444 , 25.028)
	Fisher's Exact test p-value		0.259054

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.5 **ADvocate 1. Safety analysis, patients with at least one AE by Region, up to Week 16 (mSAFETY)**

Region: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		74 (52.48%)	130 (46.10%)
Number of patients with no event, n(%)		67 (47.52%)	152 (53.90%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.774 (0.506 , 1.185)
	Relative Risk (95% CI) [3]		0.918 (0.802 , 1.052)
	Relative Risk (95% CI) [4]		0.918 (0.795 , 1.052)
	Common Risk Difference (95% CI) [3]		-6.288 (-16.30 , 3.720)
	Treatment by subgroup interaction test p-value [5]		0.492722

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE by Region, up to Week 16 (mSAFETY)
Region: Europe

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		30 (21.28%)	49 (17.38%)
Number of patients with no event, n(%)		16 (11.35%)	43 (15.25%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.608 (0.271 , 1.337)
	Relative Risk (95% CI) [3]		0.851 (0.675 , 1.074)
	Relative Risk (95% CI) [4]		0.851 (0.668 , 1.101)
	Common Risk Difference (95% CI) [3]		-11.96 (-29.08 , 5.172)
	Fisher's Exact test p-value		0.204712

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE by Region, up to Week 16 (mSAFETY)
Region: US

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		29 (20.57%)	50 (17.73%)
Number of patients with no event, n(%)		33 (23.40%)	78 (27.66%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.729 (0.378 , 1.412)
	Relative Risk (95% CI) [3]		0.901 (0.732 , 1.108)
	Relative Risk (95% CI) [4]		0.901 (0.705 , 1.110)
	Common Risk Difference (95% CI) [3]		-7.712 (-22.73 , 7.311)
	Fisher's Exact test p-value		0.347893

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE by Region, up to Week 16 (mSAFETY)
Region: Rest of the World

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		15 (10.64%)	31 (10.99%)
Number of patients with no event, n(%)		18 (12.77%)	31 (10.99%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.200 (0.474 , 3.060)
	Relative Risk (95% CI) [3]		1.065 (0.795 , 1.428)
	Relative Risk (95% CI) [4]		1.065 (0.771 , 1.477)
	Common Risk Difference (95% CI) [3]		4.545 (-16.51 , 25.605)
	Fisher's Exact test p-value		0.829534

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.6 **ADvocate 1. Safety analysis, patients with at least one AE by Race, up to Week 16 (mSAFETY)**

Race: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		74 (52.48%)	130 (46.10%)
Number of patients with no event, n(%)		67 (47.52%)	152 (53.90%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.774 (0.506 , 1.185)
	Relative Risk (95% CI) [3]		0.918 (0.802 , 1.052)
	Relative Risk (95% CI) [4]		0.918 (0.795 , 1.052)
	Common Risk Difference (95% CI) [3]		-6.566 (-16.76 , 3.623)
	Treatment by subgroup interaction test p-value [5]		0.553841

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE by Race, up to Week 16 (mSAFETY)
Race: ASIAN

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		16 (11.35%)	16 (5.67%)
Number of patients with no event, n(%)		15 (10.64%)	23 (8.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.652 (0.227 , 1.871)
	Relative Risk (95% CI) [3]		0.826 (0.537 , 1.271)
	Relative Risk (95% CI) [4]		0.826 (0.488 , 1.272)
	Common Risk Difference (95% CI) [3]		-10.59 (-33.99 , 12.818)
	Fisher's Exact test p-value		0.470511

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE by Race, up to Week 16 (mSAFETY)
Race: BLACK OR AFRICAN AMERICAN

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		5 (3.55%)	15 (5.32%)
Number of patients with no event, n(%)		11 (7.80%)	18 (6.38%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.833 (0.450 , 8.218)
	Relative Risk (95% CI) [3]		1.208 (0.826 , 1.768)
	Relative Risk (95% CI) [4]		1.208 (0.759 , 1.835)
	Common Risk Difference (95% CI) [3]		14.205 (-14.16 , 42.567)
	Fisher's Exact test p-value		0.374749

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE by Race, up to Week 16 (mSAFETY)
Race: WHITE

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		52 (36.88%)	93 (32.98%)
Number of patients with no event, n(%)		41 (29.08%)	102 (36.17%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.719 (0.424 , 1.216)
	Relative Risk (95% CI) [3]		0.899 (0.766 , 1.055)
	Relative Risk (95% CI) [4]		0.899 (0.761 , 1.060)
	Common Risk Difference (95% CI) [3]		-8.222 (-20.51 , 4.065)
	Fisher's Exact test p-value		0.208982

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE by Race, up to Week 16 (mSAFETY)
Race: OTHER

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		1 (0.71%)	6 (2.13%)
Number of patients with no event, n(%)		0 (0.00%)	9 (3.19%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.000 (0.000 , 14.778)
	Relative Risk (95% CI) [3]		0.857 (0.633 , 1.160)
	Relative Risk (95% CI) [4]		0.857 (0.421 , 1.329)
	Common Risk Difference (95% CI) [3]		-60.00 (-84.79 , -35.21)
	Fisher's Exact test p-value		0.437500

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.7 **ADvocate 1. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Gender, up to Week 16 (mSAFETY)**

Gender: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		58 (41.13%)	118 (41.84%)
Number of patients with no event, n(%)		83 (58.87%)	164 (58.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.030 (0.670 , 1.588)
	Relative Risk (95% CI) [3]		1.010 (0.881 , 1.157)
	Relative Risk (95% CI) [4]		1.010 (0.872 , 1.158)
	Common Risk Difference (95% CI) [3]		0.759 (-9.197 , 10.715)
	Treatment by subgroup interaction test p-value [5]		0.412726

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Gender, up to Week 16 (mSAFETY)
Gender: F

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		33 (23.40%)	59 (20.92%)
Number of patients with no event, n(%)		40 (28.37%)	82 (29.08%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.872 (0.475 , 1.607)
	Relative Risk (95% CI) [3]		0.954 (0.784 , 1.162)
	Relative Risk (95% CI) [4]		0.954 (0.771 , 1.161)
	Common Risk Difference (95% CI) [3]		-3.362 (-17.38 , 10.662)
	Fisher's Exact test p-value		0.664101

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Gender, up to Week 16 (mSAFETY)
Gender: M

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		25 (17.73%)	59 (20.92%)
Number of patients with no event, n(%)		43 (30.50%)	82 (29.08%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.238 (0.656 , 2.359)
	Relative Risk (95% CI) [3]		1.071 (0.887 , 1.293)
	Relative Risk (95% CI) [4]		1.071 (0.874 , 1.295)
	Common Risk Difference (95% CI) [3]		5.079 (-8.979 , 19.137)
	Fisher's Exact test p-value		0.547890

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.8 **ADvocate 1. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Age Group I, up to Week 16 (mSAFETY)**

Age Group I: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		58 (41.13%)	118 (41.84%)
Number of patients with no event, n(%)		83 (58.87%)	164 (58.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.030 (0.670 , 1.588)
	Relative Risk (95% CI) [3]		1.010 (0.881 , 1.157)
	Relative Risk (95% CI) [4]		1.010 (0.872 , 1.158)
	Common Risk Difference (95% CI) [3]		0.760 (-9.161 , 10.681)
	Treatment by subgroup interaction test p-value [5]		0.562216

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adolescents (12<18) years

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		6 (4.26%)	10 (3.55%)
Number of patients with no event, n(%)		12 (8.51%)	27 (9.57%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.741 (0.189 , 3.099)
	Relative Risk (95% CI) [3]		0.903 (0.585 , 1.393)
	Relative Risk (95% CI) [4]		0.903 (0.466 , 1.347)
	Common Risk Difference (95% CI) [3]		-6.306 (-32.36 , 19.752)
	Fisher's Exact test p-value		0.753756

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adults >= 18 years

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		52 (36.88%)	108 (38.30%)
Number of patients with no event, n(%)		71 (50.35%)	137 (48.58%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.076 (0.679 , 1.710)
	Relative Risk (95% CI) [3]		1.025 (0.886 , 1.185)
	Relative Risk (95% CI) [4]		1.025 (0.872 , 1.187)
	Common Risk Difference (95% CI) [3]		1.805 (-8.912 , 12.523)
	Fisher's Exact test p-value		0.823666

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.9 **ADvocate 1. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Disease Severity II, up to Week 16 (mSAFETY)**

Disease Severity II: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		58 (41.13%)	118 (41.84%)
Number of patients with no event, n(%)		83 (58.87%)	164 (58.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.030 (0.670 , 1.588)
	Relative Risk (95% CI) [3]		1.010 (0.881 , 1.157)
	Relative Risk (95% CI) [4]		1.010 (0.872 , 1.158)
	Common Risk Difference (95% CI) [3]		0.812 (-9.193 , 10.817)
	Treatment by subgroup interaction test p-value [5]		0.030487

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Disease Severity II, up to Week 16 (mSAFETY)
Disease Severity II: IGA = 3

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		36 (25.53%)	59 (20.92%)
Number of patients with no event, n(%)		47 (33.33%)	110 (39.01%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.700 (0.396 , 1.245)
	Relative Risk (95% CI) [3]		0.886 (0.735 , 1.069)
	Relative Risk (95% CI) [4]		0.886 (0.710 , 1.063)
	Common Risk Difference (95% CI) [3]		-8.462 (-21.32 , 4.396)
	Fisher's Exact test p-value		0.214390

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Disease Severity II, up to Week 16 (mSAFETY)
Disease Severity II: IGA = 4

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		22 (15.60%)	59 (20.92%)
Number of patients with no event, n(%)		36 (25.53%)	54 (19.15%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.788 (0.894 , 3.607)
	Relative Risk (95% CI) [3]		1.214 (0.979 , 1.505)
	Relative Risk (95% CI) [4]		1.214 (0.977 , 1.533)
	Common Risk Difference (95% CI) [3]		14.281 (-1.235 , 29.798)
	Fisher's Exact test p-value		0.105383

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.10 **ADvocate 1. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Region, up to Week 16 (mSAFETY)**

Region: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		58 (41.13%)	118 (41.84%)
Number of patients with no event, n(%)		83 (58.87%)	164 (58.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.030 (0.670 , 1.588)
	Relative Risk (95% CI) [3]		1.010 (0.881 , 1.157)
	Relative Risk (95% CI) [4]		1.010 (0.872 , 1.158)
	Common Risk Difference (95% CI) [3]		0.792 (-9.159 , 10.742)
	Treatment by subgroup interaction test p-value [5]		0.540538

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Region, up to Week 16 (mSAFETY)
Region: Europe

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		21 (14.89%)	43 (15.25%)
Number of patients with no event, n(%)		25 (17.73%)	49 (17.38%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.045 (0.484 , 2.265)
	Relative Risk (95% CI) [3]		1.015 (0.801 , 1.285)
	Relative Risk (95% CI) [4]		1.015 (0.784 , 1.296)
	Common Risk Difference (95% CI) [3]		1.087 (-16.55 , 18.726)
	Fisher's Exact test p-value		1.000000

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Region, up to Week 16 (mSAFETY)
Region: US

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		25 (17.73%)	46 (16.31%)
Number of patients with no event, n(%)		37 (26.24%)	82 (29.08%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.830 (0.427 , 1.631)
	Relative Risk (95% CI) [3]		0.940 (0.762 , 1.160)
	Relative Risk (95% CI) [4]		0.940 (0.733 , 1.152)
	Common Risk Difference (95% CI) [3]		-4.385 (-19.16 , 10.386)
	Fisher's Exact test p-value		0.631884

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Region, up to Week 16 (mSAFETY)
Region: Rest of the World

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		12 (8.51%)	29 (10.28%)
Number of patients with no event, n(%)		21 (14.89%)	33 (11.70%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.538 (0.597 , 4.054)
	Relative Risk (95% CI) [3]		1.157 (0.866 , 1.547)
	Relative Risk (95% CI) [4]		1.157 (0.832 , 1.568)
	Common Risk Difference (95% CI) [3]		10.411 (-10.17 , 30.993)
	Fisher's Exact test p-value		0.387776

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.11 **ADvocate 1. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Race, up to Week 16 (mSAFETY)**

Race: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		58 (41.13%)	118 (41.84%)
Number of patients with no event, n(%)		83 (58.87%)	164 (58.16%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.030 (0.670 , 1.588)
	Relative Risk (95% CI) [3]		1.010 (0.881 , 1.157)
	Relative Risk (95% CI) [4]		1.010 (0.872 , 1.158)
	Common Risk Difference (95% CI) [3]		0.464 (-9.594 , 10.522)
	Treatment by subgroup interaction test p-value [5]		0.442314

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Race, up to Week 16 (mSAFETY)
Race: ASIAN

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		14 (9.93%)	14 (4.96%)
Number of patients with no event, n(%)		17 (12.06%)	25 (8.87%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.680 (0.233 , 1.987)
	Relative Risk (95% CI) [3]		0.840 (0.537 , 1.313)
	Relative Risk (95% CI) [4]		0.840 (0.471 , 1.300)
	Common Risk Difference (95% CI) [3]		-9.264 (-32.36 , 13.835)
	Fisher's Exact test p-value		0.469756

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Race, up to Week 16 (mSAFETY)
Race: BLACK OR AFRICAN AMERICAN

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		3 (2.13%)	13 (4.61%)
Number of patients with no event, n(%)		13 (9.22%)	20 (7.09%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		2.817 (0.588 , 18.038)
	Relative Risk (95% CI) [3]		1.341 (0.933 , 1.925)
	Relative Risk (95% CI) [4]		1.341 (0.806 , 1.986)
	Common Risk Difference (95% CI) [3]		20.644 (-4.727 , 46.015)
	Fisher's Exact test p-value		0.201468

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Race, up to Week 16 (mSAFETY)
Race: WHITE

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		40 (28.37%)	85 (30.14%)
Number of patients with no event, n(%)		53 (37.59%)	110 (39.01%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.024 (0.604 , 1.742)
	Relative Risk (95% CI) [3]		1.008 (0.858 , 1.183)
	Relative Risk (95% CI) [4]		1.008 (0.843 , 1.186)
	Common Risk Difference (95% CI) [3]		0.579 (-11.66 , 12.814)
	Fisher's Exact test p-value		1.000000

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Race, up to Week 16 (mSAFETY)
Race: OTHER

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		1 (0.71%)	6 (2.13%)
Number of patients with no event, n(%)		0 (0.00%)	9 (3.19%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.000 (0.000 , 14.778)
	Relative Risk (95% CI) [3]		0.857 (0.633 , 1.160)
	Relative Risk (95% CI) [4]		0.857 (0.421 , 1.329)
	Common Risk Difference (95% CI) [3]		-60.00 (-84.79 , -35.21)
	Fisher's Exact test p-value		0.437500

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.12 **ADvocate 1. Safety analysis, patients with at least one Severe AE by Age Group I, up to Week 16 (mSAFETY)**

Age Group I: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		7 (4.96%)	6 (2.13%)
Number of patients with no event, n(%)		134 (95.04%)	276 (97.87%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.416 (0.113 , 1.481)
	Relative Risk (95% CI) [3]		0.686 (0.380 , 1.238)
	Relative Risk (95% CI) [4]		0.686 (0.144 , 1.131)
	Common Risk Difference (95% CI) [3]		-2.832 (-6.795 , 1.132)
	Treatment by subgroup interaction test p-value [5]		0.518653

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one Severe AE by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adolescents (12<18) years

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		1 (0.71%)	0 (0.00%)
Number of patients with no event, n(%)		17 (12.06%)	37 (13.12%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.000 (0.000 , 9.243)
	Relative Risk (95% CI) [3]		0.000 (. , .)
	Relative Risk (95% CI) [4]		0.000 (0.000 , 1.430)
	Common Risk Difference (95% CI) [3]		-5.556 (-16.14 , 5.026)
	Fisher's Exact test p-value		0.327273

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, patients with at least one Severe AE by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adults >= 18 years

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		6 (4.26%)	6 (2.13%)
Number of patients with no event, n(%)		117 (82.98%)	239 (84.75%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.490 (0.128 , 1.878)
	Relative Risk (95% CI) [3]		0.745 (0.421 , 1.318)
	Relative Risk (95% CI) [4]		0.745 (0.164 , 1.183)
	Common Risk Difference (95% CI) [3]		-2.429 (-6.700 , 1.841)
	Fisher's Exact test p-value		0.226363

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.13 **ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Age Group I, up to Week 16 (mSAFETY)**

Age Group I: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		6 (4.26%)	9 (3.19%)
Number of patients with no event, n(%)		135 (95.74%)	273 (96.81%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.742 (0.230 , 2.589)
	Relative Risk (95% CI) [3]		0.897 (0.590 , 1.363)
	Relative Risk (95% CI) [4]		0.897 (0.281 , 1.251)
	Common Risk Difference (95% CI) [3]		-1.049 (-4.951 , 2.852)
	Treatment by subgroup interaction test p-value [5]		0.855842

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adolescents (12<18) years

	PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)	0 (0.00%)	0 (0.00%)
Number of patients with no event, n(%)	18 (12.77%)	37 (13.12%)

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adults >= 18 years

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		6 (4.26%)	9 (3.19%)
Number of patients with no event, n(%)		117 (82.98%)	236 (83.69%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.744 (0.230 , 2.605)
	Relative Risk (95% CI) [3]		0.897 (0.590 , 1.365)
	Relative Risk (95% CI) [4]		0.897 (0.312 , 1.252)
	Common Risk Difference (95% CI) [3]		-1.205 (-5.681 , 3.272)
	Fisher's Exact test p-value		0.584811

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.14 **ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Region, up to Week 16 (mSAFETY)**

Region: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		6 (4.26%)	9 (3.19%)
Number of patients with no event, n(%)		135 (95.74%)	273 (96.81%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.742 (0.230 , 2.589)
	Relative Risk (95% CI) [3]		0.897 (0.590 , 1.363)
	Relative Risk (95% CI) [4]		0.897 (0.281 , 1.251)
	Common Risk Difference (95% CI) [3]		-1.049 (-4.932 , 2.833)
	Treatment by subgroup interaction test p-value [5]		0.292120

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Region, up to Week 16 (mSAFETY)
Region: Europe

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		4 (2.84%)	7 (2.48%)
Number of patients with no event, n(%)		42 (29.79%)	85 (30.14%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.865 (0.206 , 4.262)
	Relative Risk (95% CI) [3]		0.951 (0.598 , 1.511)
	Relative Risk (95% CI) [4]		0.951 (0.341 , 1.350)
	Common Risk Difference (95% CI) [3]		-1.087 (-10.87 , 8.693)
	Fisher's Exact test p-value		1.000000

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Region, up to Week 16 (mSAFETY)
Region: US

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		2 (1.42%)	0 (0.00%)
Number of patients with no event, n(%)		60 (42.55%)	128 (45.39%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.000 (0.000 , 1.670)
	Relative Risk (95% CI) [3]		0.000 (. , .)
	Relative Risk (95% CI) [4]		0.000 (0.000 , 1.241)
	Common Risk Difference (95% CI) [3]		-3.226 (-7.624 , 1.172)
	Fisher's Exact test p-value		0.105319

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Region, up to Week 16 (mSAFETY)
Region: Rest of the World

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		0 (0.00%)	2 (0.71%)
Number of patients with no event, n(%)		33 (23.40%)	60 (21.28%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		. (0.153 , .)
	Relative Risk (95% CI) [3]		1.550 (1.333 , 1.802)
	Relative Risk (95% CI) [4]		1.550 (0.122 , 1.941)
	Common Risk Difference (95% CI) [3]		3.226 (-1.172 , 7.624)
	Fisher's Exact test p-value		0.541769

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.15 **ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Race, up to Week 16 (mSAFETY)**

Race: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		6 (4.26%)	9 (3.19%)
Number of patients with no event, n(%)		135 (95.74%)	273 (96.81%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.742 (0.230 , 2.589)
	Relative Risk (95% CI) [3]		0.897 (0.590 , 1.363)
	Relative Risk (95% CI) [4]		0.897 (0.281 , 1.251)
	Common Risk Difference (95% CI) [3]		-1.254 (-5.232 , 2.725)
	Treatment by subgroup interaction test p-value [5]		0.712378

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Race, up to Week 16 (mSAFETY)
Race: ASIAN

	PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)	0 (0.00%)	0 (0.00%)
Number of patients with no event, n(%)	31 (21.99%)	39 (13.83%)

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Race, up to Week 16 (mSAFETY)
Race: BLACK OR AFRICAN AMERICAN

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		1 (0.71%)	0 (0.00%)
Number of patients with no event, n(%)		15 (10.64%)	33 (11.70%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.000 (0.000 , 9.212)
	Relative Risk (95% CI) [3]		0.000 (. , .)
	Relative Risk (95% CI) [4]		0.000 (0.000 , 1.432)
	Common Risk Difference (95% CI) [3]		-6.250 (-18.11 , 5.611)
	Fisher's Exact test p-value		0.326531

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Race, up to Week 16 (mSAFETY)
Race: WHITE

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		5 (3.55%)	9 (3.19%)
Number of patients with no event, n(%)		88 (62.41%)	186 (65.96%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.852 (0.248 , 3.335)
	Relative Risk (95% CI) [3]		0.947 (0.636 , 1.411)
	Relative Risk (95% CI) [4]		0.947 (0.346 , 1.287)
	Common Risk Difference (95% CI) [3]		-0.761 (-6.209 , 4.688)
	Fisher's Exact test p-value		0.774902

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Race, up to Week 16 (mSAFETY)
Race: OTHER

	PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)	0 (0.00%)	0 (0.00%)
Number of patients with no event, n(%)	1 (0.71%)	15 (5.32%)

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.16 **ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Gender, up to Week 16 (mSAFETY)**

Gender: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		5 (3.55%)	28 (9.93%)
Number of patients with no event, n(%)		136 (96.45%)	254 (90.07%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		2.998 (1.106 , 10.151)
	Relative Risk (95% CI) [3]		1.303 (1.109 , 1.531)
	Relative Risk (95% CI) [4]		1.303 (0.805 , 1.492)
	Common Risk Difference (95% CI) [3]		6.323 (1.695 , 10.950)
	Treatment by subgroup interaction test p-value [5]		0.963690

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Gender, up to Week 16 (mSAFETY)
Gender: F

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		2 (1.42%)	11 (3.90%)
Number of patients with no event, n(%)		71 (50.35%)	130 (46.10%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		3.004 (0.627 , 28.518)
	Relative Risk (95% CI) [3]		1.308 (1.016 , 1.685)
	Relative Risk (95% CI) [4]		1.308 (0.554 , 1.584)
	Common Risk Difference (95% CI) [3]		5.062 (-0.736 , 10.860)
	Fisher's Exact test p-value		0.226727

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Gender, up to Week 16 (mSAFETY)
Gender: M

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		3 (2.13%)	17 (6.03%)
Number of patients with no event, n(%)		65 (46.10%)	124 (43.97%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		2.970 (0.812 , 16.324)
	Relative Risk (95% CI) [3]		1.296 (1.049 , 1.600)
	Relative Risk (95% CI) [4]		1.296 (0.648 , 1.546)
	Common Risk Difference (95% CI) [3]		7.645 (0.385 , 14.905)
	Fisher's Exact test p-value		0.085354

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.17 **ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Age Group I, up to Week 16 (mSAFETY)**

Age Group I: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		5 (3.55%)	28 (9.93%)
Number of patients with no event, n(%)		136 (96.45%)	254 (90.07%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		2.998 (1.106 , 10.151)
	Relative Risk (95% CI) [3]		1.303 (1.109 , 1.531)
	Relative Risk (95% CI) [4]		1.303 (0.805 , 1.492)
	Common Risk Difference (95% CI) [3]		6.393 (1.761 , 11.025)
	Treatment by subgroup interaction test p-value [5]		0.804061

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adolescents (12<18) years

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		0 (0.00%)	3 (1.06%)
Number of patients with no event, n(%)		18 (12.77%)	34 (12.06%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		. (0.284 , .)
	Relative Risk (95% CI) [3]		1.529 (1.255 , 1.864)
	Relative Risk (95% CI) [4]		1.529 (0.225 , 1.993)
	Common Risk Difference (95% CI) [3]		8.108 (-0.687 , 16.903)
	Fisher's Exact test p-value		0.543053

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adults >= 18 years

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		5 (3.55%)	25 (8.87%)
Number of patients with no event, n(%)		118 (83.69%)	220 (78.01%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		2.682 (0.972 , 9.185)
	Relative Risk (95% CI) [3]		1.280 (1.071 , 1.530)
	Relative Risk (95% CI) [4]		1.280 (0.765 , 1.486)
	Common Risk Difference (95% CI) [3]		6.139 (0.987 , 11.291)
	Fisher's Exact test p-value		0.044599

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.18 **ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Disease Severity II, up to Week 16 (mSAFETY)**

Disease Severity II: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		5 (3.55%)	28 (9.93%)
Number of patients with no event, n(%)		136 (96.45%)	254 (90.07%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		2.998 (1.106 , 10.151)
	Relative Risk (95% CI) [3]		1.303 (1.109 , 1.531)
	Relative Risk (95% CI) [4]		1.303 (0.805 , 1.492)
	Common Risk Difference (95% CI) [3]		6.464 (1.851 , 11.076)
	Treatment by subgroup interaction test p-value [5]		0.703861

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Disease Severity II, up to Week 16 (mSAFETY)
Disease Severity II: IGA = 3

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		2 (1.42%)	10 (3.55%)
Number of patients with no event, n(%)		81 (57.45%)	159 (56.38%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		2.547 (0.523 , 24.377)
	Relative Risk (95% CI) [3]		1.258 (0.962 , 1.646)
	Relative Risk (95% CI) [4]		1.258 (0.563 , 1.524)
	Common Risk Difference (95% CI) [3]		3.508 (-1.344 , 8.359)
	Fisher's Exact test p-value		0.346712

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Disease Severity II, up to Week 16 (mSAFETY)
Disease Severity II: IGA = 4

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		3 (2.13%)	18 (6.38%)
Number of patients with no event, n(%)		55 (39.01%)	95 (33.69%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		3.474 (0.945 , 19.116)
	Relative Risk (95% CI) [3]		1.353 (1.094 , 1.674)
	Relative Risk (95% CI) [4]		1.353 (0.827 , 1.635)
	Common Risk Difference (95% CI) [3]		10.757 (1.924 , 19.589)
	Fisher's Exact test p-value		0.049656

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.19 **ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Region, up to Week 16 (mSAFETY)**

Region: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		5 (3.55%)	28 (9.93%)
Number of patients with no event, n(%)		136 (96.45%)	254 (90.07%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		2.998 (1.106 , 10.151)
	Relative Risk (95% CI) [3]		1.303 (1.109 , 1.531)
	Relative Risk (95% CI) [4]		1.303 (0.805 , 1.492)
	Common Risk Difference (95% CI) [3]		6.527 (1.916 , 11.138)
	Treatment by subgroup interaction test p-value [5]		0.641945

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Region, up to Week 16 (mSAFETY)
Region: Europe

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		3 (2.13%)	13 (4.61%)
Number of patients with no event, n(%)		43 (30.50%)	79 (28.01%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		2.359 (0.598 , 13.531)
	Relative Risk (95% CI) [3]		1.255 (0.958 , 1.643)
	Relative Risk (95% CI) [4]		1.255 (0.541 , 1.573)
	Common Risk Difference (95% CI) [3]		7.609 (-2.470 , 17.687)
	Fisher's Exact test p-value		0.262495

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Region, up to Week 16 (mSAFETY)
Region: US

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		1 (0.71%)	4 (1.42%)
Number of patients with no event, n(%)		61 (43.26%)	124 (43.97%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.968 (0.189 , 98.471)
	Relative Risk (95% CI) [3]		1.194 (0.761 , 1.871)
	Relative Risk (95% CI) [4]		1.194 (0.189 , 1.550)
	Common Risk Difference (95% CI) [3]		1.512 (-2.837 , 5.862)
	Fisher's Exact test p-value		1.000000

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Region, up to Week 16 (mSAFETY)
Region: Rest of the World

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		1 (0.71%)	11 (3.90%)
Number of patients with no event, n(%)		32 (22.70%)	51 (18.09%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		6.902 (0.908 , 306.19)
	Relative Risk (95% CI) [3]		1.492 (1.172 , 1.899)
	Relative Risk (95% CI) [4]		1.492 (0.748 , 1.881)
	Common Risk Difference (95% CI) [3]		14.712 (3.548 , 25.875)
	Fisher's Exact test p-value		0.051820

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.20 **ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Race, up to Week 16 (mSAFETY)**

Race: Overall

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		5 (3.55%)	28 (9.93%)
Number of patients with no event, n(%)		136 (96.45%)	254 (90.07%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		2.998 (1.106 , 10.151)
	Relative Risk (95% CI) [3]		1.303 (1.109 , 1.531)
	Relative Risk (95% CI) [4]		1.303 (0.805 , 1.492)
	Common Risk Difference (95% CI) [3]		6.088 (1.320 , 10.857)
	Treatment by subgroup interaction test p-value [5]		0.458320

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Race, up to Week 16 (mSAFETY)
Race: ASIAN

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		1 (0.71%)	5 (1.77%)
Number of patients with no event, n(%)		30 (21.28%)	34 (12.06%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		4.412 (0.448 , 215.49)
	Relative Risk (95% CI) [3]		1.569 (1.025 , 2.400)
	Relative Risk (95% CI) [4]		1.569 (0.432 , 2.249)
	Common Risk Difference (95% CI) [3]		9.595 (-2.603 , 21.792)
	Fisher's Exact test p-value		0.217166

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Race, up to Week 16 (mSAFETY)
Race: BLACK OR AFRICAN AMERICAN

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		0 (0.00%)	1 (0.35%)
Number of patients with no event, n(%)		16 (11.35%)	32 (11.35%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		. (0.026 , .)
	Relative Risk (95% CI) [3]		1.500 (1.228 , 1.832)
	Relative Risk (95% CI) [4]		1.500 (0.047 , 2.086)
	Common Risk Difference (95% CI) [3]		3.030 (-2.818 , 8.879)
	Fisher's Exact test p-value		1.000000

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Race, up to Week 16 (mSAFETY)
Race: WHITE

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		3 (2.13%)	20 (7.09%)
Number of patients with no event, n(%)		90 (63.83%)	175 (62.06%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		3.429 (0.975 , 18.429)
	Relative Risk (95% CI) [3]		1.317 (1.100 , 1.577)
	Relative Risk (95% CI) [4]		1.317 (0.771 , 1.530)
	Common Risk Difference (95% CI) [3]		7.031 (1.460 , 12.601)
	Fisher's Exact test p-value		0.060163

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 1. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Race, up to Week 16 (mSAFETY)
Race: OTHER

		PBO N=141	LEB250Q2W N=282
Number of patients with >=1 event [1], n(%)		1 (0.71%)	2 (0.71%)
Number of patients with no event, n(%)		0 (0.00%)	13 (4.61%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.000 (0.000 , 4.385)
	Relative Risk (95% CI) [3]		0.667 (0.300 , 1.484)
	Relative Risk (95% CI) [4]		0.667 (0.080 , 1.106)
	Common Risk Difference (95% CI) [3]		-86.67 (-100.0 , -69.46)
	Fisher's Exact test p-value		0.187500

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.21 ADvocate 2

4.5.3.22 **ADvocate 2. Safety analysis, patients with at least one AE by Gender, up to Week 16 (mSAFETY)**

Gender: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		96 (66.21%)	151 (53.74%)
Number of patients with no event, n(%)		49 (33.79%)	130 (46.26%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.593 (0.382 , 0.917)
	Relative Risk (95% CI) [3]		0.842 (0.736 , 0.963)
	Relative Risk (95% CI) [4]		0.842 (0.734 , 0.973)
	Common Risk Difference (95% CI) [3]		-12.67 (-22.31 , -3.027)
	Treatment by subgroup interaction test p-value [5]		0.504539

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE by Gender, up to Week 16 (mSAFETY)
Gender: F

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		48 (33.10%)	66 (23.49%)
Number of patients with no event, n(%)		26 (17.93%)	70 (24.91%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.511 (0.272 , 0.951)
	Relative Risk (95% CI) [3]		0.794 (0.651 , 0.968)
	Relative Risk (95% CI) [4]		0.794 (0.643 , 0.975)
	Common Risk Difference (95% CI) [3]		-16.34 (-30.08 , -2.593)
	Fisher's Exact test p-value		0.029489

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE by Gender, up to Week 16 (mSAFETY)
Gender: M

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		48 (33.10%)	85 (30.25%)
Number of patients with no event, n(%)		23 (15.86%)	60 (21.35%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.679 (0.355 , 1.280)
	Relative Risk (95% CI) [3]		0.884 (0.735 , 1.063)
	Relative Risk (95% CI) [4]		0.884 (0.734 , 1.081)
	Common Risk Difference (95% CI) [3]		-8.985 (-22.50 , 4.534)
	Fisher's Exact test p-value		0.234632

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.23 **ADvocate 2. Safety analysis, patients with at least one AE by Age Group I, up to Week 16 (mSAFETY)**

Age Group I: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		96 (66.21%)	151 (53.74%)
Number of patients with no event, n(%)		49 (33.79%)	130 (46.26%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.593 (0.382 , 0.917)
	Relative Risk (95% CI) [3]		0.842 (0.736 , 0.963)
	Relative Risk (95% CI) [4]		0.842 (0.734 , 0.973)
	Common Risk Difference (95% CI) [3]		-12.46 (-22.13 , -2.786)
	Treatment by subgroup interaction test p-value [5]		0.215446

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adolescents (12<18) years

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		13 (8.97%)	15 (5.34%)
Number of patients with no event, n(%)		3 (2.07%)	15 (5.34%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.231 (0.036 , 1.121)
	Relative Risk (95% CI) [3]		0.643 (0.430 , 0.961)
	Relative Risk (95% CI) [4]		0.643 (0.406 , 0.983)
	Common Risk Difference (95% CI) [3]		-31.25 (-57.44 , -5.061)
	Fisher's Exact test p-value		0.057910

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adults >= 18 years

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		83 (57.24%)	136 (48.40%)
Number of patients with no event, n(%)		46 (31.72%)	115 (40.93%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.655 (0.412 , 1.037)
	Relative Risk (95% CI) [3]		0.869 (0.754 , 1.002)
	Relative Risk (95% CI) [4]		0.869 (0.753 , 1.011)
	Common Risk Difference (95% CI) [3]		-10.16 (-20.47 , 0.153)
	Fisher's Exact test p-value		0.062903

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.24 **ADvocate 2. Safety analysis, patients with at least one AE by Disease Severity II, up to Week 16 (mSAFETY)**

Disease Severity II: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		96 (66.21%)	151 (53.74%)
Number of patients with no event, n(%)		49 (33.79%)	130 (46.26%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.593 (0.382 , 0.917)
	Relative Risk (95% CI) [3]		0.842 (0.736 , 0.963)
	Relative Risk (95% CI) [4]		0.842 (0.734 , 0.973)
	Common Risk Difference (95% CI) [3]		-12.66 (-22.31 , -3.015)
	Treatment by subgroup interaction test p-value [5]		0.668165

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE by Disease Severity II, up to Week 16 (mSAFETY)
Disease Severity II: IGA = 3

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		62 (42.76%)	89 (31.67%)
Number of patients with no event, n(%)		33 (22.76%)	86 (30.60%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.551 (0.317 , 0.950)
	Relative Risk (95% CI) [3]		0.816 (0.686 , 0.970)
	Relative Risk (95% CI) [4]		0.816 (0.681 , 0.977)
	Common Risk Difference (95% CI) [3]		-14.41 (-26.51 , -2.301)
	Fisher's Exact test p-value		0.028926

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE by Disease Severity II, up to Week 16 (mSAFETY)
Disease Severity II: IGA = 4

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		34 (23.45%)	62 (22.06%)
Number of patients with no event, n(%)		16 (11.03%)	44 (15.66%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.663 (0.303 , 1.417)
	Relative Risk (95% CI) [3]		0.881 (0.712 , 1.089)
	Relative Risk (95% CI) [4]		0.881 (0.706 , 1.122)
	Common Risk Difference (95% CI) [3]		-9.509 (-25.48 , 6.465)
	Fisher's Exact test p-value		0.292627

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.25 **ADvocate 2. Safety analysis, patients with at least one AE by Region, up to Week 16 (mSAFETY)**

Region: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		96 (66.21%)	151 (53.74%)
Number of patients with no event, n(%)		49 (33.79%)	130 (46.26%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.593 (0.382 , 0.917)
	Relative Risk (95% CI) [3]		0.842 (0.736 , 0.963)
	Relative Risk (95% CI) [4]		0.842 (0.734 , 0.973)
	Common Risk Difference (95% CI) [3]		-13.13 (-22.65 , -3.609)
	Treatment by subgroup interaction test p-value [5]		0.532143

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE by Region, up to Week 16 (mSAFETY)
Region: Europe

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		26 (17.93%)	45 (16.01%)
Number of patients with no event, n(%)		12 (8.28%)	31 (11.03%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.670 (0.266 , 1.632)
	Relative Risk (95% CI) [3]		0.879 (0.680 , 1.136)
	Relative Risk (95% CI) [4]		0.879 (0.675 , 1.200)
	Common Risk Difference (95% CI) [3]		-9.211 (-27.66 , 9.242)
	Fisher's Exact test p-value		0.414048

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE by Region, up to Week 16 (mSAFETY)
Region: US

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		36 (24.83%)	42 (14.95%)
Number of patients with no event, n(%)		24 (16.55%)	65 (23.13%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.431 (0.214 , 0.863)
	Relative Risk (95% CI) [3]		0.737 (0.579 , 0.938)
	Relative Risk (95% CI) [4]		0.737 (0.556 , 0.956)
	Common Risk Difference (95% CI) [3]		-20.75 (-36.22 , -5.279)
	Fisher's Exact test p-value		0.014993

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE by Region, up to Week 16 (mSAFETY)
Region: Rest of the World

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		34 (23.45%)	64 (22.78%)
Number of patients with no event, n(%)		13 (8.97%)	34 (12.10%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.720 (0.307 , 1.630)
	Relative Risk (95% CI) [3]		0.903 (0.719 , 1.134)
	Relative Risk (95% CI) [4]		0.903 (0.723 , 1.212)
	Common Risk Difference (95% CI) [3]		-7.034 (-22.92 , 8.851)
	Fisher's Exact test p-value		0.451770

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.26 **ADvocate 2. Safety analysis, patients with at least one AE by Race, up to Week 16 (mSAFETY)**

Race: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		96 (66.21%)	151 (53.74%)
Number of patients with no event, n(%)		49 (33.79%)	130 (46.26%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.593 (0.382 , 0.917)
	Relative Risk (95% CI) [3]		0.842 (0.736 , 0.963)
	Relative Risk (95% CI) [4]		0.842 (0.734 , 0.973)
	Common Risk Difference (95% CI) [3]		-11.96 (-21.65 , -2.269)
	Treatment by subgroup interaction test p-value [5]		0.088545

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE by Race, up to Week 16 (mSAFETY)
Race: ASIAN

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		29 (20.00%)	56 (19.93%)
Number of patients with no event, n(%)		14 (9.66%)	22 (7.83%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.229 (0.501 , 2.948)
	Relative Risk (95% CI) [3]		1.078 (0.797 , 1.458)
	Relative Risk (95% CI) [4]		1.078 (0.811 , 1.571)
	Common Risk Difference (95% CI) [3]		4.353 (-12.85 , 21.555)
	Fisher's Exact test p-value		0.679607

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE by Race, up to Week 16 (mSAFETY)
Race: BLACK OR AFRICAN AMERICAN

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		8 (5.52%)	8 (2.85%)
Number of patients with no event, n(%)		2 (1.38%)	17 (6.05%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.118 (0.011 , 0.827)
	Relative Risk (95% CI) [3]		0.559 (0.334 , 0.934)
	Relative Risk (95% CI) [4]		0.559 (0.289 , 0.911)
	Common Risk Difference (95% CI) [3]		-48.00 (-78.81 , -17.19)
	Fisher's Exact test p-value		0.021770

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE by Race, up to Week 16 (mSAFETY)
Race: WHITE

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		55 (37.93%)	81 (28.83%)
Number of patients with no event, n(%)		30 (20.69%)	87 (30.96%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.508 (0.285 , 0.898)
	Relative Risk (95% CI) [3]		0.801 (0.673 , 0.954)
	Relative Risk (95% CI) [4]		0.801 (0.668 , 0.967)
	Common Risk Difference (95% CI) [3]		-16.49 (-29.15 , -3.831)
	Fisher's Exact test p-value		0.016145

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE by Race, up to Week 16 (mSAFETY)
Race: OTHER

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		4 (2.76%)	6 (2.14%)
Number of patients with no event, n(%)		3 (2.07%)	4 (1.42%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.125 (0.102 , 11.626)
	Relative Risk (95% CI) [3]		1.050 (0.464 , 2.377)
	Relative Risk (95% CI) [4]		1.050 (0.431 , 3.513)
	Common Risk Difference (95% CI) [3]		2.857 (-44.74 , 50.459)
	Fisher's Exact test p-value		1.000000

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.27 **ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Gender, up to Week 16 (mSAFETY)**

Gender: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		82 (56.55%)	139 (49.47%)
Number of patients with no event, n(%)		63 (43.45%)	142 (50.53%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.752 (0.492 , 1.148)
	Relative Risk (95% CI) [3]		0.908 (0.792 , 1.041)
	Relative Risk (95% CI) [4]		0.908 (0.790 , 1.042)
	Common Risk Difference (95% CI) [3]		-7.237 (-17.20 , 2.730)
	Treatment by subgroup interaction test p-value [5]		0.365261

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Gender, up to Week 16 (mSAFETY)
Gender: F

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		42 (28.97%)	61 (21.71%)
Number of patients with no event, n(%)		32 (22.07%)	75 (26.69%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.620 (0.336 , 1.140)
	Relative Risk (95% CI) [3]		0.845 (0.690 , 1.035)
	Relative Risk (95% CI) [4]		0.845 (0.675 , 1.034)
	Common Risk Difference (95% CI) [3]		-11.90 (-25.95 , 2.142)
	Fisher's Exact test p-value		0.113009

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Gender, up to Week 16 (mSAFETY)
Gender: M

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		40 (27.59%)	78 (27.76%)
Number of patients with no event, n(%)		31 (21.38%)	67 (23.84%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.902 (0.488 , 1.660)
	Relative Risk (95% CI) [3]		0.967 (0.802 , 1.165)
	Relative Risk (95% CI) [4]		0.967 (0.799 , 1.187)
	Common Risk Difference (95% CI) [3]		-2.545 (-16.65 , 11.560)
	Fisher's Exact test p-value		0.772074

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.28 **ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Age Group I, up to Week 16 (mSAFETY)**

Age Group I: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		82 (56.55%)	139 (49.47%)
Number of patients with no event, n(%)		63 (43.45%)	142 (50.53%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.752 (0.492 , 1.148)
	Relative Risk (95% CI) [3]		0.908 (0.792 , 1.041)
	Relative Risk (95% CI) [4]		0.908 (0.790 , 1.042)
	Common Risk Difference (95% CI) [3]		-7.085 (-17.09 , 2.922)
	Treatment by subgroup interaction test p-value [5]		0.074933

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adolescents (12<18) years

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		12 (8.28%)	12 (4.27%)
Number of patients with no event, n(%)		4 (2.76%)	18 (6.41%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.222 (0.043 , 0.993)
	Relative Risk (95% CI) [3]		0.611 (0.391 , 0.955)
	Relative Risk (95% CI) [4]		0.611 (0.344 , 0.942)
	Common Risk Difference (95% CI) [3]		-35.00 (-62.52 , -7.478)
	Fisher's Exact test p-value		0.032353

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adults >= 18 years

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		70 (48.28%)	127 (45.20%)
Number of patients with no event, n(%)		59 (40.69%)	124 (44.13%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.863 (0.551 , 1.351)
	Relative Risk (95% CI) [3]		0.951 (0.824 , 1.099)
	Relative Risk (95% CI) [4]		0.951 (0.819 , 1.104)
	Common Risk Difference (95% CI) [3]		-3.666 (-14.26 , 6.925)
	Fisher's Exact test p-value		0.516921

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.29 **ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Disease Severity II, up to Week 16 (mSAFETY)**

Disease Severity II: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		82 (56.55%)	139 (49.47%)
Number of patients with no event, n(%)		63 (43.45%)	142 (50.53%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.752 (0.492 , 1.148)
	Relative Risk (95% CI) [3]		0.908 (0.792 , 1.041)
	Relative Risk (95% CI) [4]		0.908 (0.790 , 1.042)
	Common Risk Difference (95% CI) [3]		-7.193 (-17.16 , 2.770)
	Treatment by subgroup interaction test p-value [5]		0.874018

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Disease Severity II, up to Week 16 (mSAFETY)
Disease Severity II: IGA = 3

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		53 (36.55%)	84 (29.89%)
Number of patients with no event, n(%)		42 (28.97%)	91 (32.38%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.731 (0.429 , 1.245)
	Relative Risk (95% CI) [3]		0.896 (0.751 , 1.069)
	Relative Risk (95% CI) [4]		0.896 (0.746 , 1.073)
	Common Risk Difference (95% CI) [3]		-7.789 (-20.22 , 4.641)
	Fisher's Exact test p-value		0.251939

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Disease Severity II, up to Week 16 (mSAFETY)
Disease Severity II: IGA = 4

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		29 (20.00%)	55 (19.57%)
Number of patients with no event, n(%)		21 (14.48%)	51 (18.15%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.781 (0.373 , 1.622)
	Relative Risk (95% CI) [3]		0.924 (0.746 , 1.146)
	Relative Risk (95% CI) [4]		0.924 (0.737 , 1.163)
	Common Risk Difference (95% CI) [3]		-6.113 (-22.78 , 10.549)
	Fisher's Exact test p-value		0.496286

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.30 **ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Region, up to Week 16 (mSAFETY)**

Region: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		82 (56.55%)	139 (49.47%)
Number of patients with no event, n(%)		63 (43.45%)	142 (50.53%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.752 (0.492 , 1.148)
	Relative Risk (95% CI) [3]		0.908 (0.792 , 1.041)
	Relative Risk (95% CI) [4]		0.908 (0.790 , 1.042)
	Common Risk Difference (95% CI) [3]		-7.742 (-17.62 , 2.137)
	Treatment by subgroup interaction test p-value [5]		0.139528

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Region, up to Week 16 (mSAFETY)
Region: Europe

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		20 (13.79%)	43 (15.30%)
Number of patients with no event, n(%)		18 (12.41%)	33 (11.74%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.173 (0.497 , 2.753)
	Relative Risk (95% CI) [3]		1.055 (0.810 , 1.373)
	Relative Risk (95% CI) [4]		1.055 (0.809 , 1.421)
	Common Risk Difference (95% CI) [3]		3.947 (-15.45 , 23.343)
	Fisher's Exact test p-value		0.695159

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Region, up to Week 16 (mSAFETY)
Region: US

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		32 (22.07%)	36 (12.81%)
Number of patients with no event, n(%)		28 (19.31%)	71 (25.27%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.444 (0.221 , 0.891)
	Relative Risk (95% CI) [3]		0.738 (0.571 , 0.954)
	Relative Risk (95% CI) [4]		0.738 (0.539 , 0.969)
	Common Risk Difference (95% CI) [3]		-19.69 (-35.16 , -4.213)
	Fisher's Exact test p-value		0.014531

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Region, up to Week 16 (mSAFETY)
Region: Rest of the World

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		30 (20.69%)	60 (21.35%)
Number of patients with no event, n(%)		17 (11.72%)	38 (13.52%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.895 (0.405 , 1.943)
	Relative Risk (95% CI) [3]		0.965 (0.767 , 1.214)
	Relative Risk (95% CI) [4]		0.965 (0.769 , 1.249)
	Common Risk Difference (95% CI) [3]		-2.605 (-19.39 , 14.180)
	Fisher's Exact test p-value		0.855507

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.31 **ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Race, up to Week 16 (mSAFETY)**

Race: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		82 (56.55%)	139 (49.47%)
Number of patients with no event, n(%)		63 (43.45%)	142 (50.53%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.752 (0.492 , 1.148)
	Relative Risk (95% CI) [3]		0.908 (0.792 , 1.041)
	Relative Risk (95% CI) [4]		0.908 (0.790 , 1.042)
	Common Risk Difference (95% CI) [3]		-6.612 (-16.56 , 3.337)
	Treatment by subgroup interaction test p-value [5]		0.234337

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Race, up to Week 16 (mSAFETY)
Race: ASIAN

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		26 (17.93%)	52 (18.51%)
Number of patients with no event, n(%)		17 (11.72%)	26 (9.25%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.308 (0.559 , 3.021)
	Relative Risk (95% CI) [3]		1.103 (0.827 , 1.471)
	Relative Risk (95% CI) [4]		1.103 (0.836 , 1.607)
	Common Risk Difference (95% CI) [3]		6.202 (-11.77 , 24.174)
	Fisher's Exact test p-value		0.553813

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Race, up to Week 16 (mSAFETY)
Race: BLACK OR AFRICAN AMERICAN

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		7 (4.83%)	8 (2.85%)
Number of patients with no event, n(%)		3 (2.07%)	17 (6.05%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.202 (0.028 , 1.231)
	Relative Risk (95% CI) [3]		0.627 (0.378 , 1.043)
	Relative Risk (95% CI) [4]		0.627 (0.323 , 1.011)
	Common Risk Difference (95% CI) [3]		-38.00 (-71.78 , -4.220)
	Fisher's Exact test p-value		0.061912

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Race, up to Week 16 (mSAFETY)
Race: WHITE

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		45 (31.03%)	74 (26.33%)
Number of patients with no event, n(%)		40 (27.59%)	94 (33.45%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.700 (0.401 , 1.222)
	Relative Risk (95% CI) [3]		0.886 (0.742 , 1.060)
	Relative Risk (95% CI) [4]		0.886 (0.729 , 1.061)
	Common Risk Difference (95% CI) [3]		-8.894 (-21.89 , 4.104)
	Fisher's Exact test p-value		0.185761

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one AE without PT of Pruritus and Dermatitis Atopics by Race, up to Week 16 (mSAFETY)
Race: OTHER

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		4 (2.76%)	5 (1.78%)
Number of patients with no event, n(%)		3 (2.07%)	5 (1.78%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.750 (0.070 , 7.551)
	Relative Risk (95% CI) [3]		0.889 (0.402 , 1.965)
	Relative Risk (95% CI) [4]		0.889 (0.319 , 2.483)
	Common Risk Difference (95% CI) [3]		-7.143 (-55.15 , 40.860)
	Fisher's Exact test p-value		1.000000

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.32 **ADvocate 2. Safety analysis, patients with at least one Severe AE by Gender, up to Week 16 (mSAFETY)**

Gender: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		7 (4.83%)	7 (2.49%)
Number of patients with no event, n(%)		138 (95.17%)	274 (97.51%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.504 (0.148 , 1.722)
	Relative Risk (95% CI) [3]		0.752 (0.443 , 1.275)
	Relative Risk (95% CI) [4]		0.752 (0.185 , 1.167)
	Common Risk Difference (95% CI) [3]		-2.410 (-6.334 , 1.515)
	Treatment by subgroup interaction test p-value [5]		0.337703

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one Severe AE by Gender, up to Week 16 (mSAFETY)
Gender: F

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		3 (2.07%)	1 (0.36%)
Number of patients with no event, n(%)		71 (48.97%)	135 (48.04%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.175 (0.003 , 2.248)
	Relative Risk (95% CI) [3]		0.381 (0.070 , 2.089)
	Relative Risk (95% CI) [4]		0.381 (0.011 , 1.232)
	Common Risk Difference (95% CI) [3]		-3.319 (-8.036 , 1.399)
	Fisher's Exact test p-value		0.126579

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one Severe AE by Gender, up to Week 16 (mSAFETY)
Gender: M

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		4 (2.76%)	6 (2.14%)
Number of patients with no event, n(%)		67 (46.21%)	139 (49.47%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.723 (0.165 , 3.609)
	Relative Risk (95% CI) [3]		0.889 (0.531 , 1.488)
	Relative Risk (95% CI) [4]		0.889 (0.206 , 1.303)
	Common Risk Difference (95% CI) [3]		-1.496 (-7.763 , 4.771)
	Fisher's Exact test p-value		0.732453

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.33 **ADvocate 2. Safety analysis, patients with at least one Severe AE by Age Group I, up to Week 16 (mSAFETY)**

Age Group I: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		7 (4.83%)	7 (2.49%)
Number of patients with no event, n(%)		138 (95.17%)	274 (97.51%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.504 (0.148 , 1.722)
	Relative Risk (95% CI) [3]		0.752 (0.443 , 1.275)
	Relative Risk (95% CI) [4]		0.752 (0.185 , 1.167)
	Common Risk Difference (95% CI) [3]		-2.350 (-6.279 , 1.580)
	Treatment by subgroup interaction test p-value [5]		0.971571

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one Severe AE by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adolescents (12<18) years

	PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)	0 (0.00%)	0 (0.00%)
Number of patients with no event, n(%)	16 (11.03%)	30 (10.68%)

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one Severe AE by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adults >= 18 years

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		7 (4.83%)	7 (2.49%)
Number of patients with no event, n(%)		122 (84.14%)	244 (86.83%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.500 (0.146 , 1.715)
	Relative Risk (95% CI) [3]		0.750 (0.442 , 1.273)
	Relative Risk (95% CI) [4]		0.750 (0.182 , 1.165)
	Common Risk Difference (95% CI) [3]		-2.638 (-7.046 , 1.771)
	Fisher's Exact test p-value		0.250059

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.34 **ADvocate 2. Safety analysis, patients with at least one Severe AE without PT of Pruritus and Dermatitis Atopic by Age Group I, up to Week 16 (mSAFETY)**

Age Group I: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		5 (3.45%)	6 (2.14%)
Number of patients with no event, n(%)		140 (96.55%)	275 (97.86%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.611 (0.153 , 2.580)
	Relative Risk (95% CI) [3]		0.823 (0.478 , 1.418)
	Relative Risk (95% CI) [4]		0.823 (0.168 , 1.255)
	Common Risk Difference (95% CI) [3]		-1.323 (-4.736 , 2.089)
	Treatment by subgroup interaction test p-value [5]		0.962013

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one Severe AE without PT of Pruritus and Dermatitis Atopic by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adolescents (12<18) years

	PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)	0 (0.00%)	0 (0.00%)
Number of patients with no event, n(%)	16 (11.03%)	30 (10.68%)

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, patients with at least one Severe AE without PT of Pruritus and Dermatitis Atopic by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adults >= 18 years

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		5 (3.45%)	6 (2.14%)
Number of patients with no event, n(%)		124 (85.52%)	245 (87.19%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.607 (0.151 , 2.572)
	Relative Risk (95% CI) [3]		0.822 (0.477 , 1.416)
	Relative Risk (95% CI) [4]		0.822 (0.172 , 1.253)
	Common Risk Difference (95% CI) [3]		-1.486 (-5.315 , 2.344)
	Fisher's Exact test p-value		0.519761

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.35 **ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Gender, up to Week 16 (mSAFETY)**

Gender: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		7 (4.83%)	9 (3.20%)
Number of patients with no event, n(%)		138 (95.17%)	272 (96.80%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.652 (0.211 , 2.110)
	Relative Risk (95% CI) [3]		0.848 (0.547 , 1.313)
	Relative Risk (95% CI) [4]		0.848 (0.260 , 1.216)
	Common Risk Difference (95% CI) [3]		-1.673 (-5.732 , 2.387)
	Treatment by subgroup interaction test p-value [5]		0.472635

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Gender, up to Week 16 (mSAFETY)
Gender: F

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		2 (1.38%)	4 (1.42%)
Number of patients with no event, n(%)		72 (49.66%)	132 (46.98%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		1.091 (0.152 , 12.329)
	Relative Risk (95% CI) [3]		1.030 (0.580 , 1.831)
	Relative Risk (95% CI) [4]		1.030 (0.168 , 1.487)
	Common Risk Difference (95% CI) [3]		0.238 (-4.421 , 4.898)
	Fisher's Exact test p-value		1.000000

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Gender, up to Week 16 (mSAFETY)
Gender: M

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		5 (3.45%)	5 (1.78%)
Number of patients with no event, n(%)		66 (45.52%)	140 (49.82%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.471 (0.105 , 2.132)
	Relative Risk (95% CI) [3]		0.736 (0.393 , 1.377)
	Relative Risk (95% CI) [4]		0.736 (0.140 , 1.202)
	Common Risk Difference (95% CI) [3]		-3.594 (-10.25 , 3.057)
	Fisher's Exact test p-value		0.302741

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.36 **ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Age Group I, up to Week 16 (mSAFETY)**

Age Group I: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		7 (4.83%)	9 (3.20%)
Number of patients with no event, n(%)		138 (95.17%)	272 (96.80%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.652 (0.211 , 2.110)
	Relative Risk (95% CI) [3]		0.848 (0.547 , 1.313)
	Relative Risk (95% CI) [4]		0.848 (0.260 , 1.216)
	Common Risk Difference (95% CI) [3]		-1.622 (-5.684 , 2.439)
	Treatment by subgroup interaction test p-value [5]		0.189779

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adolescents (12<18) years

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		2 (1.38%)	0 (0.00%)
Number of patients with no event, n(%)		14 (9.66%)	30 (10.68%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.000 (0.000 , 1.803)
	Relative Risk (95% CI) [3]		0.000 (. , .)
	Relative Risk (95% CI) [4]		0.000 (0.000 , 1.215)
	Common Risk Difference (95% CI) [3]		-12.50 (-28.70 , 3.705)
	Fisher's Exact test p-value		0.115942

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adults >= 18 years

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		5 (3.45%)	9 (3.20%)
Number of patients with no event, n(%)		124 (85.52%)	242 (86.12%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.922 (0.271 , 3.582)
	Relative Risk (95% CI) [3]		0.972 (0.654 , 1.446)
	Relative Risk (95% CI) [4]		0.972 (0.338 , 1.321)
	Common Risk Difference (95% CI) [3]		-0.290 (-4.338 , 3.758)
	Fisher's Exact test p-value		1.000000

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.37 **ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Disease Severity II, up to Week 16 (mSAFETY)**

Disease Severity II: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		7 (4.83%)	9 (3.20%)
Number of patients with no event, n(%)		138 (95.17%)	272 (96.80%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.652 (0.211 , 2.110)
	Relative Risk (95% CI) [3]		0.848 (0.547 , 1.313)
	Relative Risk (95% CI) [4]		0.848 (0.260 , 1.216)
	Common Risk Difference (95% CI) [3]		-1.598 (-5.648 , 2.452)
	Treatment by subgroup interaction test p-value [5]		0.970179

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Disease Severity II, up to Week 16 (mSAFETY)
Disease Severity II: IGA = 3

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		5 (3.45%)	6 (2.14%)
Number of patients with no event, n(%)		90 (62.07%)	169 (60.14%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.639 (0.158 , 2.729)
	Relative Risk (95% CI) [3]		0.836 (0.484 , 1.444)
	Relative Risk (95% CI) [4]		0.836 (0.188 , 1.274)
	Common Risk Difference (95% CI) [3]		-1.835 (-7.072 , 3.403)
	Fisher's Exact test p-value		0.525222

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - herpes infection or zoster by Disease Severity II, up to Week 16 (mSAFETY)
Disease Severity II: IGA = 4

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		2 (1.38%)	3 (1.07%)
Number of patients with no event, n(%)		48 (33.10%)	103 (36.65%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.699 (0.078 , 8.645)
	Relative Risk (95% CI) [3]		0.880 (0.426 , 1.814)
	Relative Risk (95% CI) [4]		0.880 (0.105 , 1.389)
	Common Risk Difference (95% CI) [3]		-1.170 (-7.452 , 5.113)
	Fisher's Exact test p-value		0.655814

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.38 **ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Gender, up to Week 16 (mSAFETY)**

Gender: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		5 (3.45%)	31 (11.03%)
Number of patients with no event, n(%)		140 (96.55%)	250 (88.97%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		3.472 (1.295 , 11.670)
	Relative Risk (95% CI) [3]		1.343 (1.155 , 1.562)
	Relative Risk (95% CI) [4]		1.343 (0.878 , 1.528)
	Common Risk Difference (95% CI) [3]		7.520 (2.809 , 12.232)
	Treatment by subgroup interaction test p-value [5]		0.906367

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Gender, up to Week 16 (mSAFETY)
Gender: F

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		2 (1.38%)	13 (4.63%)
Number of patients with no event, n(%)		72 (49.66%)	123 (43.77%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		3.805 (0.821 , 35.507)
	Relative Risk (95% CI) [3]		1.374 (1.096 , 1.722)
	Relative Risk (95% CI) [4]		1.374 (0.820 , 1.650)
	Common Risk Difference (95% CI) [3]		6.856 (0.686 , 13.026)
	Fisher's Exact test p-value		0.091278

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Gender, up to Week 16 (mSAFETY)
Gender: M

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		3 (2.07%)	18 (6.41%)
Number of patients with no event, n(%)		68 (46.90%)	127 (45.20%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		3.213 (0.888 , 17.546)
	Relative Risk (95% CI) [3]		1.316 (1.075 , 1.612)
	Relative Risk (95% CI) [4]		1.316 (0.686 , 1.565)
	Common Risk Difference (95% CI) [3]		8.188 (1.068 , 15.309)
	Fisher's Exact test p-value		0.084565

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.39 **ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Age Group I, up to Week 16 (mSAFETY)**

Age Group I: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		5 (3.45%)	31 (11.03%)
Number of patients with no event, n(%)		140 (96.55%)	250 (88.97%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		3.472 (1.295 , 11.670)
	Relative Risk (95% CI) [3]		1.343 (1.155 , 1.562)
	Relative Risk (95% CI) [4]		1.343 (0.878 , 1.528)
	Common Risk Difference (95% CI) [3]		7.585 (2.853 , 12.317)
	Treatment by subgroup interaction test p-value [5]		0.047645

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adolescents (12<18) years

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		2 (1.38%)	2 (0.71%)
Number of patients with no event, n(%)		14 (9.66%)	28 (9.96%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.500 (0.034 , 7.694)
	Relative Risk (95% CI) [3]		0.750 (0.275 , 2.045)
	Relative Risk (95% CI) [4]		0.750 (0.069 , 1.479)
	Common Risk Difference (95% CI) [3]		-5.833 (-24.33 , 12.667)
	Fisher's Exact test p-value		0.601924

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Age Group I, up to Week 16 (mSAFETY)
Age Group I: Adults >= 18 years

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		3 (2.07%)	29 (10.32%)
Number of patients with no event, n(%)		126 (86.90%)	222 (79.00%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		5.486 (1.644 , 28.612)
	Relative Risk (95% CI) [3]		1.421 (1.239 , 1.629)
	Relative Risk (95% CI) [4]		1.421 (0.949 , 1.600)
	Common Risk Difference (95% CI) [3]		9.228 (4.495 , 13.961)
	Fisher's Exact test p-value		0.001496

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.40 **ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Disease Severity II, up to Week 16 (mSAFETY)**

Disease Severity II: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		5 (3.45%)	31 (11.03%)
Number of patients with no event, n(%)		140 (96.55%)	250 (88.97%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		3.472 (1.295 , 11.670)
	Relative Risk (95% CI) [3]		1.343 (1.155 , 1.562)
	Relative Risk (95% CI) [4]		1.343 (0.878 , 1.528)
	Common Risk Difference (95% CI) [3]		7.532 (2.820 , 12.244)
	Treatment by subgroup interaction test p-value [5]		0.422273

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Disease Severity II, up to Week 16 (mSAFETY)
Disease Severity II: IGA = 3

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		4 (2.76%)	17 (6.05%)
Number of patients with no event, n(%)		91 (62.76%)	158 (56.23%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		2.448 (0.764 , 10.275)
	Relative Risk (95% CI) [3]		1.276 (1.016 , 1.602)
	Relative Risk (95% CI) [4]		1.276 (0.788 , 1.534)
	Common Risk Difference (95% CI) [3]		5.504 (-0.460 , 11.467)
	Fisher's Exact test p-value		0.152450

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Disease Severity II, up to Week 16 (mSAFETY)
Disease Severity II: IGA = 4

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		1 (0.69%)	14 (4.98%)
Number of patients with no event, n(%)		49 (33.79%)	92 (32.74%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		7.457 (1.064 , 321.61)
	Relative Risk (95% CI) [3]		1.430 (1.193 , 1.714)
	Relative Risk (95% CI) [4]		1.430 (0.678 , 1.689)
	Common Risk Difference (95% CI) [3]		11.208 (3.684 , 18.731)
	Fisher's Exact test p-value		0.038074

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.41 **ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Region, up to Week 16 (mSAFETY)**

Region: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		5 (3.45%)	31 (11.03%)
Number of patients with no event, n(%)		140 (96.55%)	250 (88.97%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		3.472 (1.295 , 11.670)
	Relative Risk (95% CI) [3]		1.343 (1.155 , 1.562)
	Relative Risk (95% CI) [4]		1.343 (0.878 , 1.528)
	Common Risk Difference (95% CI) [3]		7.187 (2.587 , 11.786)
	Treatment by subgroup interaction test p-value [5]		0.901799

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Region, up to Week 16 (mSAFETY)
Region: Europe

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		1 (0.69%)	9 (3.20%)
Number of patients with no event, n(%)		37 (25.52%)	67 (23.84%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		4.970 (0.638 , 223.63)
	Relative Risk (95% CI) [3]		1.397 (1.087 , 1.796)
	Relative Risk (95% CI) [4]		1.397 (0.695 , 1.727)
	Common Risk Difference (95% CI) [3]		9.211 (0.341 , 18.080)
	Fisher's Exact test p-value		0.160885

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Region, up to Week 16 (mSAFETY)
Region: US

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		0 (0.00%)	3 (1.07%)
Number of patients with no event, n(%)		60 (41.38%)	104 (37.01%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		. (0.328 , .)
	Relative Risk (95% CI) [3]		1.577 (1.404 , 1.771)
	Relative Risk (95% CI) [4]		1.577 (0.189 , 1.850)
	Common Risk Difference (95% CI) [3]		2.804 (-0.324 , 5.932)
	Fisher's Exact test p-value		0.553673

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Region, up to Week 16 (mSAFETY)
Region: Rest of the World

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		4 (2.76%)	19 (6.76%)
Number of patients with no event, n(%)		43 (29.66%)	79 (28.11%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		2.585 (0.784 , 11.056)
	Relative Risk (95% CI) [3]		1.276 (1.015 , 1.604)
	Relative Risk (95% CI) [4]		1.276 (0.855 , 1.570)
	Common Risk Difference (95% CI) [3]		10.877 (-0.299 , 22.053)
	Fisher's Exact test p-value		0.143537

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

4.5.3.42 **ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Race, up to Week 16 (mSAFETY)**

Race: Overall

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		5 (3.45%)	31 (11.03%)
Number of patients with no event, n(%)		140 (96.55%)	250 (88.97%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		3.472 (1.295 , 11.670)
	Relative Risk (95% CI) [3]		1.343 (1.155 , 1.562)
	Relative Risk (95% CI) [4]		1.343 (0.878 , 1.528)
	Common Risk Difference (95% CI) [3]		7.901 (3.193 , 12.609)
	Treatment by subgroup interaction test p-value [5]		0.321890

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction. p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Race, up to Week 16 (mSAFETY)
Race: ASIAN

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		2 (1.38%)	17 (6.05%)
Number of patients with no event, n(%)		41 (28.28%)	61 (21.71%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		5.713 (1.234 , 53.035)
	Relative Risk (95% CI) [3]		1.496 (1.199 , 1.867)
	Relative Risk (95% CI) [4]		1.496 (1.008 , 1.858)
	Common Risk Difference (95% CI) [3]		17.144 (6.028 , 28.260)
	Fisher's Exact test p-value		0.017088

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Race, up to Week 16 (mSAFETY)
Race: BLACK OR AFRICAN AMERICAN

	PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)	0 (0.00%)	0 (0.00%)
Number of patients with no event, n(%)	10 (6.90%)	25 (8.90%)

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Race, up to Week 16 (mSAFETY)
Race: WHITE

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		2 (1.38%)	14 (4.98%)
Number of patients with no event, n(%)		83 (57.24%)	154 (54.80%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		3.773 (0.832 , 34.859)
	Relative Risk (95% CI) [3]		1.347 (1.094 , 1.657)
	Relative Risk (95% CI) [4]		1.347 (0.769 , 1.583)
	Common Risk Difference (95% CI) [3]		5.980 (0.703 , 11.258)
	Fisher's Exact test p-value		0.098122

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.

ADvocate 2. Safety analysis, Adverse Events of Special Interest (AESIs) - conjunctivitis by Race, up to Week 16 (mSAFETY)
Race: OTHER

		PBO N=145	LEB250Q2W N=281
Number of patients with >=1 event [1], n(%)		1 (0.69%)	0 (0.00%)
Number of patients with no event, n(%)		6 (4.14%)	10 (3.56%)
Lebrikizumab vs. PBO	Odds Ratio (95% CI) [2]		0.000 (0.000 , 13.300)
	Relative Risk (95% CI) [3]		0.000 (. , .)
	Relative Risk (95% CI) [4]		0.000 (0.000 , 1.809)
	Common Risk Difference (95% CI) [3]		-14.29 (-40.21 , 11.637)
	Fisher's Exact test p-value		0.411765

Abbreviations: PBO = Placebo, LEB = Lebrikizumab, mSAFETY = Modified Safety Population, CI = Confidence Interval.
Note 1: Patients with multiple occurrences of these categories are counted once for each category.
Note 2: Odds Ratio is computed by Mantel-Haenzel method. Odds Ratio CI are computed by Thomas and Gart exact method.
Note 3: Relative risk, Common risk difference and its CI are computed by Mantel-Haenszel. CI are asymptotic.
Note 4: Relative risk score, CI are computed by exact method.
Note 5: Logistic regression with Firth correction. Covariates: treatment, subgroup, treatment-by-subgroup interaction.
p-value for global effect of treatment-by-subgroup interaction is provided.