# **Eigene Vorlage**

# Dossier zur Nutzenbewertung gemäß § 35a SGB V

*Mepolizumab (Nucala) – HES*GlaxoSmithKline GmbH & Co. KG

Separater Anhang 4-G zu Modul 4C

Tabellen und Abbildungen

Stand: 24.11.2021

# Inhaltsverzeichnis

- 1 Ergebnisse für Veränderung des Gesamt-BFI Scores aus RCT mit dem zu bewertenden Arzneimittel
- 2 Ergebnisse für Veränderung des BFI Item 3 aus RCT mit dem zu bewertenden Arzneimittel
- 3 Ergebnisse für Veränderung der HES-DS (am stärksten belastende Symptome) aus RCT mit dem zu bewertenden Arzneimittel
- 4 Ergebnisse für Veränderung der am stärksten belastenden HES-DS nach Symptomen aus RCT mit dem zu bewertenden Arzneimittel
- 5 Ergebnise für Gesamtansprechen auf die Therapie aus RCT mit dem zu bewertenden Arzneimittel
- 6 Ergebnisse für Veränderung in der Schwere der Symptome (durch den Patienten beurteilt) aus RCT mit dem zu bewertenden Arzneimittel
- 7 Ergebnisse für Veränderung der modifizierten MSAS-SF (Gesamtscore und Subskalen Scores) aus RCT mit dem zu bewertenden Arzneimittel
- 8 Ergebnisse für Veränderung des PROMIS Körperliche Funktion Score aus RCT mit dem zu bewertenden Arzneimittel
- 9 Ergebnisse für Veränderung des PROMIS Schlaf Score aus RCT mit dem zu bewertenden Arzneimittel
- 10 Ergebnisse für Veränderung des SF-36 PCS aus RCT mit dem zu bewertenden Arzneimittel
- 11 Ergebnisse für Veränderung des SF-36 MCS aus RCT mit dem zu bewertenden Arzneimittel
- 12 Ergebnisse für Veränderung der Gesundheitsdomänen des SF-36 aus RCT mit dem zu bewertenden Arzneimittel
- 13 Ergebnisse für Veränderung WPAI aus RCT mit dem zu bewertenden Arzneimittel
- 14 Subgruppenanalyse zu Anteil der Patienten mit einem HES-Schub aus RCT mit dem zu bewertenden Arzneimittel (Woche 32)

- 15 Subgruppenanalysen zu Anteil Patienten mit einem HES-Schub aus RCT mit dem zu bewertenden Arzneimittel (Woche 20-32)
- 16 Subgruppenanalysen zu Zeit bis zum ersten HES-Schub aus RCT mit dem zu bewertenden Arzneimittel
- 17 Subgruppenanalysen zu Rate an HES-Schüben aus RCT mit dem zu bewertenden Arzneimittel
- 18 Subgruppenanalysen zu Veränderung des Gesamt-BFI Scores aus RCT mit dem zu bewertenden Arzneimittel
- 19 Subgruppenanalysen zu Veränderung des BFI Item 3 aus RCT mit dem zu bewertenden Arzneimittel
- 20 Subgruppenanalysen zu Veränderung der HES-DS aus RCT mit dem zu bewertenden Arzneimittel
- 21 Subgruppenanalysen zu Gesamtansprechen auf die Therapie aus RCT mit dem zu bewertenden Arzneimittel
- 22 Subgruppenanalysen zu Veränderung in der Schwere der Symptome (durch den Patienten beurteilt) aus RCT mit dem zu bewertenden Arzneimittel
- 23 Subgruppenanalysen zu Veränderung der modifizierten MSAS-SF aus RCT mit dem zu bewertenden Arzneimittel
- 24 Subgruppenanalysen zu Veränderung des PROMIS Körperliche Funktion Score aus RCT mit dem zu bewertenden Arzneimittel
- 25 Subgruppenanalysen zu Veränderung des PROMIS Schlaf Score aus RCT mit dem zu bewertenden Arzneimittel
- 26 Subgruppenanalysen zu SF-36 Responder (Physical Component Summary Scores ≥5 Punkte) aus RCT mit dem zu bewertenden Arzneimittel
- 27 Subgruppenanalysen zu SF-36 Responder (Mental Component Summary Scores ≥ 5 Punkte) aus RCT mit dem zu bewertenden Arzneimittel
- 28 Subgruppenanalysen zu WPAI (Versäumte Arbeitszeit aufgrund aufgrund von Krankheit) aus RCT mit dem zu bewertenden Arzneimittel

- 29 Subgruppenanalysen zu WPAI (Beeinträchtigung im Berufsleben aufgrund aufgrund von Krankheit) aus RCT mit dem zu bewertenden Arzneimittel
- 30 Subgruppenanalysen zu WPAI (Beeinträchtigung der Arbeitsleistung insgesamt aufgrund von Krankheit) aus RCT mit dem zu bewertenden Arzneimittel
- 31 Subgruppenanalysen zu WPAI (Beeinträchtigung der Aktivität aufgrund aufgrund von Krankheit) aus RCT mit dem zu bewertenden Arzneimittel
- 32 Subgruppenanalysen zu Unerwünschte Ereignisse aus RCT mit dem zu bewertenden Arzneimittel
- 33 Subgruppenanalysen zu Schwerwiegende unerwünschte Ereignisse aus RCT mit dem zu bewertenden Arzneimittel
- 34 Subgruppenanalysen zu Unerwünschte Ereignisse von besonderem Interesse aus RCT mit dem zu bewertenden Arzneimittel

### 2019N406842 00 CONFIDENTIAL $200\overline{6}22$

Protocol: 200622 Page 1 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	BFI Total	n Mean SD Median Min. Max.	49 3.92 2.610 3.67 0.0 8.4	50 4.23 2.565 4.11 0.1 9.1
Week 1	BFI Total	n Mean SD Median Min. Max.	46 3.73 2.563 3.56 0.0 10.0	50 3.88 2.529 3.83 0.0 9.4
	Change from Baseline	n Mean SD Median Min. Max.	43 -0.33 1.681 -0.22 -8.0 2.9	46 -0.19 1.293 -0.06 -3.0 2.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

# 2019N406842 00 $200\overline{6}22$

# CONFIDENTIAL

Protocol: 200622 Page 2 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 2	BFI Total	n Mean SD Median Min. Max.	48 3.55 2.444 3.67 0.0 9.8	48 3.56 2.454 3.06 0.0 8.6
	Change from Baseline	n Mean SD Median Min. Max.	45 -0.34 1.350 -0.22 -3.8 2.1	46 -0.60 1.318 -0.39 -2.9 2.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatique to 10 = As bad as you can imagine.

### 2019N406842 00 CONFIDENTIAL $200\overline{6}22$

Protocol: 200622 Page 3 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 3	BFI Total	n Mean SD Median Min. Max.	48 3.29 2.440 3.17 0.0 10.0	49 3.24 2.529 2.56 0.0 9.3
	Change from Baseline	n Mean SD Median Min. Max.	45 -0.41 1.207 -0.22 -4.2 1.6	45 -0.90 2.155 -0.33 -7.2 2.2

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 4 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 4	BFI Total	n Mean SD Median Min. Max.	47 3.15 2.508 3.00 0.0 10.0	49 3.31 2.355 2.78 0.0 9.0
	Change from Baseline	n Mean SD Median Min. Max.	43 -0.58 1.923 -0.11 -8.2 2.9	47 -0.82 1.916 -0.44 -6.2 2.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 5 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 5	BFI Total	n Mean SD Median Min. Max.	35 3.08 2.771 2.22 0.0 10.0	43 2.97 2.480 1.89 0.0 9.0
	Change from Baseline	n Mean SD Median Min. Max.	35 -0.92 1.868 -0.56 -5.8 2.1	41 -1.12 2.104 -0.67 -6.2 2.4

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatique to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Page 6 of 32

Protocol: 200622

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 6	BFI Total	n Mean SD Median Min. Max.	44 3.60 2.646 3.39 0.0 10.0	50 3.47 2.463 3.67 0.0 9.3
	Change from Baseline	n Mean SD Median Min. Max.	44 -0.53 1.612 -0.39 -5.8 1.8	48 -0.84 2.217 -0.33 -6.9 2.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 7 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 7	BFI Total	n Mean SD Median Min. Max.	46 3.21 2.560 3.06 0.0 10.0	51 3.44 2.690 3.00 0.0 8.9
	Change from Baseline	n Mean SD Median Min. Max.	43 -0.56 1.965 0.00 -5.9 3.8	48 -0.90 1.964 -0.67 -6.7 3.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

### 2019N406842 00 CONFIDENTIAL $200\overline{6}22$

Protocol: 200622 Page 8 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	BFI Total	n Mean SD Median Min. Max.	45 3.03 2.582 2.67 0.0 8.3	47 3.40 2.455 3.00 0.0 8.2
	Change from Baseline	n Mean SD Median Min. Max.	42 -0.64 1.640 -0.11 -6.7 1.9	46 -0.69 2.261 -0.22 -6.3 6.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

### 2019N406842 00 CONFIDENTIAL $200\overline{6}22$

Protocol: 200622 Page 9 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 9	BFI Total	n Mean SD Median Min. Max.	38 2.68 2.353 2.28 0.0 6.8	42 3.21 2.390 2.67 0.0 8.0
	Change from Baseline	n Mean SD Median Min. Max.	37 -0.79 1.980 -0.11 -6.3 2.2	39 -0.74 1.903 -0.33 -5.8 2.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 10 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 10	BFI Total	n Mean SD Median Min. Max.	44 3.23 2.495 3.00 0.0 9.7	49 3.32 2.464 3.11 0.0 8.4
	Change from Baseline	n Mean SD Median Min. Max.	42 -0.73 1.906 -0.17 -6.7 2.0	47 -0.96 1.901 -0.67 -6.7 2.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 11 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 11	BFI Total	n Mean SD Median Min. Max.	39 3.21 2.552 3.11 0.0 9.8	43 3.11 2.475 2.33 0.0 8.7
	Change from Baseline	n Mean SD Median Min. Max.	39 -0.74 1.922 -0.33 -6.0 2.9	40 -0.96 2.064 -0.67 -6.3 3.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 12 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 12	BFI Total	n Mean SD Median Min. Max.	42 3.08 2.431 2.78 0.0 9.9	46 3.35 2.453 2.94 0.0 8.2
	Change from Baseline	n Mean SD Median Min. Max.	41 -0.83 1.947 -0.33 -6.6 2.4	42 -0.79 2.044 -0.61 -6.4 6.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

### 2019N406842 00 CONFIDENTIAL $200\overline{6}22$

Protocol: 200622 Page 13 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 13	BFI Total	n Mean SD Median Min. Max.	31 2.78 2.634 2.33 0.0 10.0	40 3.57 2.325 3.06 0.3 8.0
	Change from Baseline	n Mean SD Median Min. Max.	31 -1.25 1.929 -0.78 -5.7 2.6	37 -0.76 2.069 -0.11 -6.3 2.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 14 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 14	BFI Total	n Mean SD Median Min. Max.	45 2.95 2.526 2.78 0.0 9.1	47 3.13 2.392 2.67 0.0 8.4
	Change from Baseline	n Mean SD Median Min. Max.	43 -0.91 2.075 -0.22 -6.1 2.6	45 -0.89 1.699 -0.78 -5.7 2.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 15 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 15	BFI Total	n Mean SD Median Min. Max.	38 3.61 2.464 3.56 0.0 9.6	45 3.35 2.552 2.78 0.0 9.6
	Change from Baseline	n Mean SD Median Min. Max.	38 -0.25 2.070 -0.06 -5.9 4.7	42 -0.67 2.140 -0.83 -6.0 7.4

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 16 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	BFI Total	n Mean SD Median Min. Max.	45 3.04 2.399 2.44 0.0 8.0	47 3.06 2.338 2.33 0.0 8.3
	Change from Baseline	n Mean SD Median Min. Max.	44 -0.96 1.822 -0.33 -5.9 2.3	44 -1.02 1.663 -0.94 -6.1 3.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatique to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 17 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 17	BFI Total	n Mean SD Median Min. Max.	33 2.54 2.030 2.00 0.0 6.9	33 2.82 1.887 2.33 0.0 8.1
	Change from Baseline	n Mean SD Median Min. Max.	31 -0.83 1.721 -0.44 -5.8 1.7	30 -1.40 1.520 -1.67 -4.4 1.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 18 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 18	BFI Total	n Mean SD Median Min. Max.	40 2.86 2.443 2.28 0.0 8.6	44 3.09 2.247 2.78 0.0 8.0
	Change from Baseline	n Mean SD Median Min. Max.	39 -0.83 1.970 0.00 -5.2 2.1	41 -1.04 1.965 -0.89 -4.9 5.2

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 19 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 19	BFI Total	n Mean SD Median Min. Max.	45 3.20 2.644 2.89 0.0 9.0	47 3.03 2.085 2.78 0.0 7.9
	Change from Baseline	n Mean SD Median Min. Max.	44 -0.59 2.003 -0.22 -6.0 2.6	46 -1.13 2.032 -1.28 -6.2 3.2

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 20 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 20	BFI Total	n Mean SD Median Min. Max.	43 3.10 2.786 2.33 0.0 9.9	43 2.66 2.160 2.33 0.0 8.6
	Change from Baseline	n Mean SD Median Min. Max.	43 -0.58 1.927 0.00 -5.0 3.7	41 -1.17 1.931 -1.00 -6.0 3.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatique to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 21 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 21	BFI Total	n Mean SD Median Min. Max.	39 3.08 2.732 2.11 0.0 10.0	40 2.74 2.460 2.22 0.0 7.8
	Change from Baseline	n Mean SD Median Min. Max.	38 -0.63 2.010 -0.11 -6.3 3.3	38 -1.42 2.234 -0.94 -6.1 3.4

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatique to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 22 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 22	BFI Total	n Mean SD Median Min. Max.	41 3.16 2.663 2.44 0.0 9.9	46 2.94 2.391 2.50 0.0 8.9
	Change from Baseline	n Mean SD Median Min. Max.	41 -0.52 1.897 0.00 -5.2 1.8	43 -1.34 2.060 -1.44 -5.8 3.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 23 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 23	BFI Total	n Mean SD Median Min. Max.	39 3.19 2.976 2.44 0.0	42 2.91 2.526 2.11 0.0 8.6
	Change from Baseline	n Mean SD Median Min. Max.	38 -0.63 2.018 -0.11 -5.6 4.2	40 -1.23 1.874 -1.11 -5.8 3.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 24 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	BFI Total	n Mean SD Median Min. Max.	40 2.91 2.623 2.17 0.0 7.8	41 2.82 2.536 2.22 0.0 8.8
	Change from Baseline	n Mean SD Median Min. Max.	39 -1.04 2.016 -0.33 -5.9 1.9	38 -1.33 2.074 -1.17 -6.3 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatique to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 25 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 25	BFI Total	n Mean SD Median Min. Max.	39 2.79 2.247 2.22 0.0 8.0	38 2.56 1.986 2.00 0.0 7.6
	Change from Baseline	n Mean SD Median Min. Max.	38 -0.76 2.225 -0.33 -5.3 3.2	36 -1.21 2.263 -1.22 -6.2 5.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatique to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 26 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 26	BFI Total	n Mean SD Median Min. Max.	42 2.83 2.374 2.44 0.0 8.0	41 2.54 1.959 2.00 0.0 7.8
	Change from Baseline	n Mean SD Median Min. Max.	40 -1.14 1.993 -0.44 -5.9 1.6	39 -1.47 2.101 -1.44 -7.1 3.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatique to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 27 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 27	BFI Total	n Mean SD Median Min. Max.	41 2.99 2.468 2.56 0.0 8.3	47 2.68 2.252 2.11 0.0 8.0
	Change from Baseline	n Mean SD Median Min. Max.	40 -0.68 2.008 -0.11 -5.7 2.3	44 -1.56 1.996 -1.17 -9.1 1.2

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatique to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 28 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 28	BFI Total	n Mean SD Median Min. Max.	43 2.98 2.648 2.89 0.0 8.9	44 3.04 2.557 2.72 0.0 8.0
	Change from Baseline	n Mean SD Median Min. Max.	41 -0.81 1.711 -0.33 -4.3 2.1	41 -0.99 1.949 -0.89 -5.8 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatique to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 29 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 29	BFI Total	n Mean SD Median Min. Max.	2.72 2.355 2.67 0.0	34 2.59 2.276 1.83 0.0 8.0
	Change from Baseline	n Mean SD Median Min. Max.	31 -1.01 2.134 0.00 -6.2 1.8	34 -1.89 2.003 -1.33 -6.4 0.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatique to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 30 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 30	BFI Total	n Mean SD Median Min. Max.	43 2.87 2.576 2.56 0.0 8.2	45 2.69 2.141 2.22 0.0 7.0
	Change from Baseline	n Mean SD Median Min. Max.	41 -0.98 2.208 -0.33 -6.4 3.0	43 -1.35 2.197 -1.56 -6.3 6.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 31 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 31	BFI Total	n Mean SD Median Min. Max.	42 3.30 2.494 3.06 0.0 8.4	45 2.94 2.241 2.44 0.0 8.1
	Change from Baseline	n Mean SD Median Min. Max.	41 -0.50 2.032 0.00 -5.6 3.4	44 -1.05 2.245 -0.89 -6.1 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatique to 10 = As bad as you can imagine.

### 2019N406842 00 CONFIDENTIAL $200\overline{6}22$

Protocol: 200622 Page 32 of 32

Table 2.41 Summary of Total BFI Score

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	BFI Total	n Mean SD Median Min. Max.	37 3.16 2.700 2.56 0.0 8.8	37 2.53 2.260 1.78 0.0 7.8
	Change from Baseline	n Mean SD Median Min. Max.	36 -0.76 2.157 -0.17 -6.2 2.0	36 -1.55 1.911 -1.11 -6.1 1.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

Protocol: 200622
Population: Intent-to-Treat
Page 1 of 8

Table 90.49
Analysis of Change from Baseline in Total BFI Score
(Mixed Model Repeated Measures)

Visit: Week 4

<b>.</b> 1	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	49 43 3.38 (0.268) -0.56 (0.268)	50 47 3.12 (0.258) -0.82 (0.258)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.26 (-1.00, 0.48) 0.487	
Corrected Hedges g [3] 95% CI		-0.15 (-0.56, 0.27)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

Mepolizumab (Nucala) - HES Seite 37 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 8 Population: Intent-to-Treat

Table 90.49 Analysis of Change from Baseline in Total BFI Score

(Mixed Model Repeated Measures)

Mara a 1 d - . . . . . . la

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	49 42 3.19 (0.270) -0.75 (0.270)	50 46 3.24 (0.261) -0.71 (0.261)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.04 (-0.70, 0.79) 0.906	
Corrected Hedges g [3] 95% CI		0.03 (-0.39, 0.44)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

Mepolizumab (Nucala) - HES Seite 38 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622
Population: Intent-to-Treat
Page 3 of 8

Table 90.49
Analysis of Change from Baseline in Total BFI Score

(Mixed Model Repeated Measures)

Mara a 1 d - . . . . . . la

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	49 41 3.17 (0.272) -0.78 (0.272)	50 42 3.23 (0.266) -0.72 (0.266)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.06 (-0.70, 0.81) 0.881	
Corrected Hedges g [3] 95% CI		0.03 (-0.40, 0.46)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

. . –

Mepolizumab (Nucala) - HES Seite 39 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622
Population: Intent-to-Treat
Page 4 of 8

Table 90.49
Analysis of Change from Baseline in Total BFI Score

(Mixed Model Repeated Measures)

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	49 44 2.99 (0.229) -0.95 (0.229)	50 44 3.03 (0.228) -0.91 (0.228)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.04 (-0.61, 0.68) 0.910
Corrected Hedges g [3] 95% CI		0.02 (-0.39, 0.44)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

Mepolizumab (Nucala) - HES Seite 40 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622
Population: Intent-to-Treat
Page 5 of 8

Menolizumah

Table 90.49
Analysis of Change from Baseline in Total BFI Score

(Mixed Model Repeated Measures)

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	49 43 3.28 (0.273) -0.66 (0.273)	50 41 2.77 (0.274) -1.17 (0.274)	_
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.51 (-1.28, 0.26) 0.190	
Corrected Hedges g [3] 95% CI		-0.29 (-0.72, 0.14)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

Mepolizumab (Nucala) - HES Seite 41 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622
Population: Intent-to-Treat
Page 6 of 8

Table 90.49
Analysis of Change from Baseline in Total BFI Score

(Mixed Model Repeated Measures)

Mara a 1 d - . . . . . . la

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	49 39 3.06 (0.274) -0.88 (0.274)	50 38 2.74 (0.275) -1.20 (0.275)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.32 (-1.09, 0.45) 0.416	
Corrected Hedges g [3] 95% CI		-0.18 (-0.63, 0.26)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

Mepolizumab (Nucala) - HES Seite 42 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622
Population: Intent-to-Treat
Page 7 of 8

Table 90.49
Analysis of Change from Baseline in Total BFI Score

(Mixed Model Repeated Measures)

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	49 41 3.21 (0.265) -0.74 (0.265)	50 41 3.08 (0.265) -0.86 (0.265)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.13 (-0.87, 0.62) 0.732	
Corrected Hedges g [3] 95% CI		-0.08 (-0.51, 0.36)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

Mepolizumab (Nucala) - HES Seite 43 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622
Population: Intent-to-Treat

Table 90.49
Analysis of Change from Baseline in Total BFI Score

(Mixed Model Repeated Measures)

Menolizumah

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	49 36 3.39 (0.286) -0.56 (0.286)	50 36 2.75 (0.286) -1.19 (0.286)	_
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.64 (-1.44, 0.17) 0.118	
Corrected Hedges g [3] 95% CI		-0.37 (-0.83, 0.10)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

Mepolizumab (Nucala) - HES Seite 44 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 1 of 32

Table 2.23 Summary of Mean Daily Fatigue Severity - Worst Level of Fatigue in Past 24 Hours (BFI Item 3) (Treatment Policy Estimand)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	BFI Item 3	n Mean SD Median Min. Max.	54 4.39 2.666 4.69 0.0 9.6	54 4.74 2.575 4.46 0.0 9.3
Week 1	BFI Item 3	n Mean SD Median Min. Max.	54 4.03 2.635 3.99 0.0 9.7	54 4.45 2.651 4.33 0.0 9.9
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.36 1.360 -0.43 -3.8 3.6	54 -0.30 1.140 -0.29 -3.0 2.5

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

Protocol: 200622 Page 2 of 32

Table 2.23 Summary of Mean Daily Fatigue Severity - Worst Level of Fatigue in Past 24 Hours (BFI Item 3) (Treatment Policy Estimand)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 2	BFI Item 3	n Mean SD Median Min. Max.	54 3.88 2.569 4.00 0.0 9.8	54 4.08 2.517 4.08 0.0 9.4
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.51 1.374 -0.43 -4.7 3.4	54 -0.66 1.266 -0.57 -3.8 2.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 3 of 32

Population: Intent-to-Treat

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 3	BFI Item 3	n Mean SD Median Min. Max.	54 3.69 2.593 3.38 0.0	54 3.93 2.530 3.45 0.0 8.2
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.70 1.655 -0.43 -5.5 3.3	54 -0.82 1.726 -0.43 -6.7 1.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

Protocol: 200622 Page 4 of 32

Population: Intent-to-Treat

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 4	BFI Item 3	n Mean SD Median Min. Max.	54 3.63 2.666 3.13 0.0	54 3.82 2.476 3.32 0.0 9.0
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.76 1.783 -0.45 -6.3 2.0	54 -0.92 1.772 -0.68 -6.9 1.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 5 of 32

Population: Intent-to-Treat

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 5	BFI Item 3	n Mean SD Median Min. Max.	47 3.82 2.901 3.57 0.0 10.0	50 3.87 2.682 3.07 0.0 8.4
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.67 1.861 -0.18 -4.3 2.9	50 -1.05 1.963 -0.71 -7.5 2.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

Protocol: 200622 Page 6 of 32

Population: Intent-to-Treat

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 6	BFI Item 3	n Mean SD Median Min. Max.	51 3.92 2.654 4.00 0.0 10.0	54 3.97 2.662 3.57 0.0 8.8
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.41 1.718 0.00 -4.4 5.0	54 -0.77 2.006 -0.50 -7.5

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

Protocol: 200622 Page 7 of 32

Population: Intent-to-Treat

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 7	BFI Item 3	n Mean SD Median Min. Max.	52 3.74 2.713 3.43 0.0 9.4	54 3.86 2.635 3.00 0.0 8.5
	Change from Baseline	n Mean SD Median Min. Max.	52 -0.63 1.682 -0.43 -4.3 3.1	54 -0.88 2.013 -0.83 -7.7 2.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

Protocol: 200622 Page 8 of 32

Population: Intent-to-Treat

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	BFI Item 3	n Mean SD Median Min. Max.	52 3.67 2.707 3.07 0.0 9.0	54 4.00 2.555 3.90 0.0 8.3
	Change from Baseline	n Mean SD Median Min. Max.	52 -0.71 1.687 -0.52 -5.0 2.0	54 -0.75 2.165 -0.69 -7.3 4.2

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 9 of 32

Table 2.23 Summary of Mean Daily Fatigue Severity - Worst Level of Fatigue in Past 24 Hours (BFI Item 3) (Treatment Policy Estimand)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 9	BFI Item 3	n Mean SD Median Min. Max.	47 3.61 2.737 3.20 0.0 8.6	50 3.99 2.555 3.10 0.0 9.0
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.62 1.592 -0.29 -4.5 2.9	50 -0.63 1.846 -0.59 -7.0 3.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 10 of 32

Population: Intent-to-Treat

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 10	BFI Item 3	n Mean SD Median Min. Max.	3.72 2.602 3.14 0.0	52 3.83 2.565 3.41 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.63 1.681 -0.36 -5.3 3.2	52 -0.82 2.139 -0.57 -6.8 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

Protocol: 200622 Page 11 of 32

Table 2.23 Summary of Mean Daily Fatigue Severity - Worst Level of Fatigue in Past 24 Hours (BFI Item 3) (Treatment Policy Estimand)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 11	BFI Item 3	n Mean SD Median Min. Max.	49 3.72 2.624 3.14 0.0 8.9	52 4.12 2.753 3.79 0.3 10.0
	Change from Baseline	n Mean SD Median Min. Max.	49 -0.73 1.839 -0.43 -4.4 3.7	52 -0.57 2.368 -0.69 -6.8 4.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 12 of 32

Table 2.23 Summary of Mean Daily Fatigue Severity - Worst Level of Fatigue in Past 24 Hours (BFI Item 3) (Treatment Policy Estimand)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 12	BFI Item 3	n Mean SD Median Min. Max.	3.73 2.658 3.50 0.0	53 3.98 2.611 4.00 0.0
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.59 1.693 0.00 -4.8 3.0	53 -0.73 2.227 -0.54 -7.5 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 13 of 32

Population: Intent-to-Treat

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 13	BFI Item 3	n Mean SD Median Min. Max.	43 3.81 2.801 4.00 0.0 9.2	48 3.97 2.547 3.83 0.5
	Change from Baseline	n Mean SD Median Min. Max.	43 -0.87 1.774 -0.71 -4.9 2.7	48 -0.84 2.248 -0.32 -7.0 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 14 of 32

Population: Intent-to-Treat

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 14	BFI Item 3	n Mean SD Median Min. Max.	50 3.50 2.745 3.14 0.0 9.0	53 4.03 2.535 4.00 0.4 10.0
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.78 1.933 -0.52 -5.4 4.0	53 -0.68 2.161 -0.43 -7.3 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 15 of 32

Population: Intent-to-Treat

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 15	BFI Item 3	n Mean SD Median Min. Max.	50 3.70 2.634 3.43 0.0 9.3	53 4.01 2.540 3.86 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.57 1.899 -0.21 -5.5 4.0	53 -0.71 2.188 -0.50 -6.3 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 16 of 32

Table 2.23 Summary of Mean Daily Fatigue Severity - Worst Level of Fatigue in Past 24 Hours (BFI Item 3) (Treatment Policy Estimand)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	BFI Item 3	n Mean SD Median Min. Max.	3.78 2.742 3.29 0.0	52 3.86 2.484 3.13 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.54 1.871 -0.29 -4.4 3.4	52 -0.82 2.132 -0.54 -6.6 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

Protocol: 200622 Page 17 of 32

Population: Intent-to-Treat

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 17	BFI Item 3	n Mean SD Median Min. Max.	41 3.43 2.899 2.40 0.0 9.8	42 3.93 2.519 3.86 0.1 10.0
	Change from Baseline	n Mean SD Median Min. Max.	41 -0.69 1.857 -0.29 -4.9 2.8	42 -0.84 2.284 -0.73 -6.5 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

Protocol: 200622 Page 18 of 32

Table 2.23 Summary of Mean Daily Fatigue Severity - Worst Level of Fatigue in Past 24 Hours (BFI Item 3) (Treatment Policy Estimand)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 18	BFI Item 3	n Mean SD Median Min. Max.	48 3.67 2.805 3.25 0.0 9.5	51 3.63 2.411 3.43 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.64 1.859 -0.21 -5.1 4.1	51 -1.03 2.148 -1.14 -6.0 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 19 of 32

Table 2.23 Summary of Mean Daily Fatigue Severity - Worst Level of Fatigue in Past 24 Hours (BFI Item 3) (Treatment Policy Estimand)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 19	BFI Item 3	n Mean SD Median Min. Max.	48 3.85 2.859 3.46 0.0 9.7	51 3.62 2.539 3.29 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.46 1.786 -0.17 -4.7 3.6	51 -1.04 2.418 -0.83 -6.7 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

# CONFIDENTIAL

Protocol: 200622 Page 20 of 32

Population: Intent-to-Treat

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 20	BFI Item 3	n Mean SD Median Min. Max.	48 3.82 2.968 3.85 0.0 9.8	52 3.53 2.465 2.62 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.48 1.803 -0.21 -4.7 4.3	52 -1.11 2.313 -0.85 -6.0 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 21 of 32

Table 2.23 Summary of Mean Daily Fatigue Severity - Worst Level of Fatigue in Past 24 Hours (BFI Item 3) (Treatment Policy Estimand)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 21	BFI Item 3	n Mean SD Median Min. Max.	46 3.69 2.902 3.21 0.0 9.3	46 3.68 2.446 3.17 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	46 -0.54 1.701 -0.29 -3.8 2.7	46 -1.15 2.349 -0.96 -6.5 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 22 of 32

Table 2.23 Summary of Mean Daily Fatigue Severity - Worst Level of Fatigue in Past 24 Hours (BFI Item 3) (Treatment Policy Estimand)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 22	BFI Item 3	n Mean SD Median Min. Max.	47 3.77 2.851 3.43 0.0 9.0	51 3.43 2.400 2.86 0.0 9.5
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.48 1.979 -0.14 -4.7 4.1	51 -1.24 2.280 -1.17 -6.0 3.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 23 of 32

Population: Intent-to-Treat

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 23	BFI Item 3	n Mean SD Median Min. Max.	47 3.84 3.036 4.00 0.0 10.0	49 3.32 2.649 2.43 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.46 2.033 -0.19 -5.0 4.1	49 -1.39 2.409 -1.20 -6.3 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

2019N406842<u>00</u> 200<del>6</del>22

## CONFIDENTIAL

Protocol: 200622 Page 24 of 32

Population: Intent-to-Treat

Table 2.23

Summary of Mean Daily Fatigue Severity - Worst Level of Fatigue in Past 24 Hours (BFI Item 3)

(Treatment Policy Estimand)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	BFI Item 3	n Mean SD Median Min. Max.	47 3.75 3.001 3.33 0.0 10.0	48 3.44 2.600 2.60 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.45 2.013 0.00 -4.6 4.0	48 -1.24 2.450 -0.93 -6.3 4.1

### Note:

378

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

# CONFIDENTIAL

Protocol: 200622 Page 25 of 32

Table 2.23 Summary of Mean Daily Fatigue Severity - Worst Level of Fatigue in Past 24 Hours (BFI Item 3) (Treatment Policy Estimand)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 25	BFI Item 3	n Mean SD Median Min. Max.	45 3.84 2.682 3.17 0.0 9.3	44 3.29 2.506 2.34 0.0 9.0
	Change from Baseline	n Mean SD Median Min. Max.	45 -0.58 2.124 0.00 -4.5 3.2	44 -1.10 2.572 -0.51 -6.8 5.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

Protocol: 200622 Page 26 of 32

Population: Intent-to-Treat

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 26	BFI Item 3	n Mean SD Median Min. Max.	49 3.72 2.958 3.14 0.0 10.0	50 3.62 2.617 2.93 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	49 -0.64 1.986 -0.29 -4.5 4.3	50 -1.06 2.694 -0.86 -8.5 5.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 27 of 32

Population: Intent-to-Treat

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 27	BFI Item 3	n Mean SD Median Min. Max.	50 3.96 3.021 3.83 0.0 10.0	50 3.59 2.584 2.69 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.45 2.068 -0.12 -5.0 4.4	50 -1.09 2.509 -0.58 -8.8 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 28 of 32

Population: Intent-to-Treat

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 28	BFI Item 3	n Mean SD Median Min. Max.	48 4.13 2.900 3.86 0.0 10.0	50 3.67 2.771 3.25 0.0
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.12 1.860 -0.08 -5.5 4.3	50 -1.02 2.535 -0.81 -8.2 4.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

Protocol: 200622 Page 29 of 32

Population: Intent-to-Treat

Table 2.23 Summary of Mean Daily Fatigue Severity - Worst Level of Fatigue in Past 24 Hours (BFI Item 3) (Treatment Policy Estimand)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 29	BFI Item 3	n Mean SD Median Min. Max.	44 3.68 2.544 3.30 0.0 9.0	40 3.44 2.592 2.45 0.0 8.5
	Change from Baseline	n Mean SD Median Min. Max.	44 -0.47 1.807 -0.21 -5.3 3.4	40 -1.45 2.306 -0.93 -7.2 2.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

Protocol: 200622 Page 30 of 32

Population: Intent-to-Treat

Table 2.23

Summary of Mean Daily Fatigue Severity - Worst Level of Fatigue in Past 24 Hours (BFI Item 3)

(Treatment Policy Estimand)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 30	BFI Item 3	n Mean SD Median Min. Max.	47 3.83 2.773 3.50 0.0 9.0	51 3.68 2.674 2.75 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.41 2.038 -0.21 -5.5 5.0	51 -0.99 2.709 -0.86 -6.8 6.3

#### Note:

384

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

Protocol: 200622 Page 31 of 32

Population: Intent-to-Treat

Table 2.23 Summary of Mean Daily Fatigue Severity - Worst Level of Fatigue in Past 24 Hours (BFI Item 3) (Treatment Policy Estimand)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 31	BFI Item 3	n Mean SD Median Min. Max.	47 4.08 2.915 4.14 0.0 9.2	51 3.62 2.547 2.75 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.24 1.932 0.00 -5.4	51 -1.04 2.467 -0.86 -6.5 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

Protocol: 200622 Page 32 of 32

Population: Intent-to-Treat

Table 2.23 Summary of Mean Daily Fatigue Severity - Worst Level of Fatigue in Past 24 Hours (BFI Item 3) (Treatment Policy Estimand)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	BFI Item 3	n Mean SD Median Min. Max.	47 3.98 2.947 3.83 0.0 9.5	50 3.51 2.644 3.00 0.0
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.30 1.955 0.00 -5.7 2.9	50 -1.12 2.384 -0.82 -6.2 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = No fatigue to 10 = As bad as you can imagine.

Protocol: 200622 Page 1 of 8

Population: Intent-to-Treat

Table 90.32 Analysis of Change from Baseline in Mean Daily Fatigue Severity -Worst Level of Fatique in Past 24 Hours (BFI Item 3)

(Mixed Model Repeated Measures)

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 54 3.71 (0.233) -0.79 (0.233)	54 54 3.64 (0.235) -0.86 (0.235)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.07 (-0.73, 0.59) 0.842
Corrected Hedges g [3] 95% CI		-0.04 (-0.42, 0.34)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 77 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 8

Population: Intent-to-Treat

Table 90.32

Analysis of Change from Baseline in Mean Daily Fatigue Severity - Worst Level of Fatigue in Past 24 Hours (BFI Item 3)
(Mixed Model Repeated Measures)

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 3.75 (0.249) -0.75 (0.249)	54 54 3.83 (0.248) -0.68 (0.248)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.08 (-0.63, 0.78) 0.832	
Corrected Hedges g [3] 95% CI		0.04 (-0.34, 0.42)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 78 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 8

Population: Intent-to-Treat

Table 90.32

Analysis of Change from Baseline in Mean Daily Fatigue Severity -Worst Level of Fatique in Past 24 Hours (BFI Item 3)

(Mixed Model Repeated Measures)

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 3.79 (0.259) -0.71 (0.259)	54 53 3.88 (0.256) -0.62 (0.256)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.09 (-0.63, 0.82) 0.801
Corrected Hedges g [3] 95% CI		0.05 (-0.34, 0.43)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 79 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 4 of 8

Population: Intent-to-Treat

Table 90.32

Analysis of Change from Baseline in Mean Daily Fatigue Severity -Worst Level of Fatique in Past 24 Hours (BFI Item 3) (Mixed Model Repeated Measures)

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 3.84 (0.262) -0.66 (0.262)	54 52 3.78 (0.260) -0.73 (0.260)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.06 (-0.80, 0.67) 0.862
Corrected Hedges g [3] 95% CI		-0.03 (-0.42, 0.35)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 80 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 5 of 8

Population: Intent-to-Treat

Table 90.32

Analysis of Change from Baseline in Mean Daily Fatigue Severity -Worst Level of Fatique in Past 24 Hours (BFI Item 3)

Manali

(Mixed Model Repeated Measures)

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 48 3.95 (0.276) -0.55 (0.276)	54 52 3.48 (0.272) -1.02 (0.272)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.47 (-1.24, 0.30) 0.232	
Corrected Hedges g [3] 95% CI		-0.24 (-0.63, 0.15)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 81 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 6 of 8

Population: Intent-to-Treat

Table 90.32

Analysis of Change from Baseline in Mean Daily Fatigue Severity -Worst Level of Fatique in Past 24 Hours (BFI Item 3)

Manali

(Mixed Model Repeated Measures)

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 47 3.96 (0.296) -0.54 (0.296)	54 48 3.46 (0.292) -1.05 (0.292)	•
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.51 (-1.33, 0.32) 0.228	
Corrected Hedges g [3] 95% CI		-0.25 (-0.65, 0.16)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 82 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 7 of 8

Population: Intent-to-Treat

Table 90.32

Analysis of Change from Baseline in Mean Daily Fatigue Severity -Worst Level of Fatique in Past 24 Hours (BFI Item 3)

(Mixed Model Repeated Measures)

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 48 4.34 (0.295) -0.16 (0.295)	54 50 3.61 (0.290) -0.89 (0.290)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.73 (-1.56, 0.09) 0.080	
Corrected Hedges g [3] 95% CI		-0.36 (-0.76, 0.04)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 83 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 8 of 8

Population: Intent-to-Treat

Table 90.32

Analysis of Change from Baseline in Mean Daily Fatigue Severity -Worst Level of Fatique in Past 24 Hours (BFI Item 3)

(Mixed Model Repeated Measures)

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 47 4.21 (0.288) -0.29 (0.288)	54 50 3.47 (0.283) -1.04 (0.283)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.75 (-1.55, 0.06) 0.068
Corrected Hedges g [3] 95% CI		-0.37 (-0.77, 0.03)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 84 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 1 of 32

Population: Intent-to-Treat

Table 2.35
Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Most Bothersome Symptom Score	n	54	54
	olwbeew agera	Mean SD Median Min. Max.	4.26 2.248 4.37 0.0 9.2	4.61 2.630 4.18 0.3 9.4
		Subjects with no reported symptoms	1 (2%)	0
Week 1	Most Bothersome Symptom Score	n	54	54
	12 1	Mean SD Median Min. Max.	3.52 2.117 3.73 0.0 9.5	4.01 2.442 3.65 0.1 9.7
		Subjects with no reported symptoms	2 (4%)	0

### Note:

433

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as the most bothersome symptom score. Subject PPD reported 4 most bothersome symptoms.

2. The mean of the available assessments on p to and including the date of each study visit

<sup>2.</sup> The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 2 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 1	Change from Baseline	n Mean SD Median Min. Max.	54 -0.74 1.117 -0.37 -4.2 1.4	54 -0.60 1.153 -0.46 -3.7 2.7
Week 2	Most Bothersome Symptom Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	3.48 2.039 3.56 0.0 9.3	3.42 2.293 2.60 0.0 9.1
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.78 1.118 -0.51 -4.2 1.0	54 -1.19 1.944 -0.88 -7.3 2.3

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 3 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 3	Most Bothersome Symptom Score	n	54	54
	- 1	Mean	3.36	3.25
		SD	2.136	2.317
		Median	3.31	2.46
		Min.	0.0	0.0
		Max.	9.3	8.3
		Subjects with no reported symptoms	2 (4%)	2 (4%)
	Change from Baseline	n	54	54
		Mean	-0.89	-1.36
		SD	1.218	2.270
		Median	-0.70	-0.96
		Min.	-4.5	-8.3
		Max.	0.9	2.5

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as the most bothersome symptom score. Subject PPD reported 4 most bothersome symptoms.

2. The mean of the available assessments on p to and including the date of each study visit

is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 4 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 4	Most Bothersome Symptom Score	n	54	54
	Symptom Deole	Mean SD Median Min. Max.	3.32 2.195 3.50 0.0 9.7	3.31 2.356 2.70 0.0 9.0
		Subjects with no reported symptoms	2 (4%)	1 (2%)
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.93 1.418 -0.73 -5.7 1.3	54 -1.30 2.338 -0.60 -8.3 1.7

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 5 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 5	Most Bothersome Symptom Score	n	47	50
	Symptom dedic	Mean SD Median Min. Max.	3.20 2.202 3.17 0.0 9.7	3.22 2.354 2.46 0.0 8.8
		Subjects with no reported symptoms	2 (4%)	2 (4%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -1.18 1.356 -0.98 -4.9 1.0	50 -1.57 2.319 -0.86 -8.3 2.3

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 6 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 6	Most Bothersome Symptom Score	n	51	54
	Symptom dedic	Mean SD Median Min. Max.	3.29 2.225 3.50 0.0 9.7	3.25 2.412 2.71 0.0 8.9
		Subjects with no reported symptoms	2 (4%)	1 (2%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.93 1.463 -0.71 -5.9 1.0	54 -1.35 2.598 -0.64 -8.4 3.7

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 7 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 7	Most Bothersome Symptom Score	n	52	54
	Symptom dedic	Mean SD Median Min. Max.	3.47 2.430 3.66 0.0 8.7	3.11 2.373 2.42 0.0 8.1
		Subjects with no reported symptoms	4 (7%)	3 (6%)
	Change from Baseline	n Mean SD Median Min. Max.	52 -0.79 1.757 -0.74 -5.9 5.0	54 -1.50 2.481 -0.80 -8.3 3.9

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 8 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Most Bothersome Symptom Score	n	52	54
	Symposia Socie	Mean	3.38	3.06
		SD	2.260	2.367
		Median	3.39	2.72
		Min.	0.0	0.0
		Max.	7.9	8.3
		Subjects with no reported symptoms	2 (4%)	2 (4%)
	Change from Baseline	n	52	54
	3	Mean	-0.88	-1.55
		SD	1.467	2.531
		Median	-1.00	-0.98
		Min.	-5.1	-8.3
		Max.	2.8	3.9
			0	O • 3

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 9 of 32

Population: Intent-to-Treat

Table 2.35
Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 9	Most Bothersome Symptom Score	n	47	50
	Symptom Score	Mean SD Median Min. Max.	3.24 2.528 2.71 0.0 8.5	2.87 2.284 2.34 0.0 8.4
		Subjects with no reported symptoms	4 (7%)	3 (6%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.87 1.558 -0.71 -5.5 2.3	50 -1.60 2.405 -1.00 -8.3 3.9

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as the most bothersome symptom score. Subject PPD reported 4 most bothersome symptoms.

2. The mean of the available assessments on p to and including the date of each study visit

<sup>2.</sup> The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 10 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 10	Most Bothersome Symptom Score	n	51	52
		Mean SD Median Min. Max. Subjects with no reported symptoms	3.25 2.293 3.14 0.0 8.8	3.11 2.201 2.55 0.1 8.4
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.97 1.691 -0.73 -5.7 1.8	52 -1.40 2.488 -0.76 -8.1 3.9

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit

is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 11 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 11	Most Bothersome Symptom Score	n	49	52
	Symptom Beele	Mean SD Median Min. Max.	3.28 2.244 3.00 0.0 9.0	3.14 2.399 2.13 0.0 9.1
		Subjects with no reported symptoms	2 (4%)	1 (2%)
	Change from Baseline	n Mean SD Median Min. Max.	49 -0.98 1.640 -0.78 -5.9 1.1	52 -1.42 2.596 -0.86 -8.3 3.9

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 12 of 32

Population: Intent-to-Treat

Table 2.35
Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 12	Most Bothersome Symptom Score	n	51	53
	Symptom Score	Mean SD Median Min. Max.	3.26 2.240 3.07 0.0 8.7	3.21 2.335 2.83 0.0 8.8
		Subjects with no reported symptoms	2 (4%)	1 (2%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.91 1.530 -0.52 -4.1 2.4	53 -1.36 2.637 -0.93 -7.9 3.7

### Note:

444

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as the most bothersome symptom score. Subject PPD reported 4 most bothersome symptoms.

2. The mean of the available assessments on p to and including the date of each study visit

<sup>2.</sup> The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 13 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 13	Most Bothersome Symptom Score	n	43	48
	Symptom Beele	Mean SD Median Min. Max.	3.15 2.129 3.05 0.0 8.4	3.26 2.273 2.87 0.0 8.6
		Subjects with no reported symptoms	2 (4%)	2 (4%)
	Change from Baseline	n Mean SD Median Min. Max.	43 -1.24 1.728 -1.02 -4.7 3.0	48 -1.42 2.500 -0.96 -7.9 3.4

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 14 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 14	Most Bothersome Symptom Score	n	50	53
	Symptom Score	Mean SD Median Min. Max. Subjects with no	2.97 2.166 2.81 0.0 8.7	3.07 2.172 2.81 0.0 8.4 3 (6%)
		reported symptoms	3 (00)	3 (0%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -1.21 1.732 -1.01 -6.7 1.9	53 -1.49 2.315 -0.86 -7.9 3.0

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

# 2019N406842 00 $200\overline{6}22$

## CONFIDENTIAL

Protocol: 200622 Page 15 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 15	Most Bothersome Symptom Score	n	50	53
	Symptom Score	Mean SD Median Min. Max.	3.03 2.101 3.12 0.0 8.5	3.16 2.303 2.67 0.0 8.0
		Subjects with no reported symptoms	3 (6%)	3 (6%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -1.15 1.641 -0.81 -6.6 1.9	53 -1.40 2.257 -0.92 -7.9 2.7

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 16 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Most Bothersome Symptom Score	n	51	52
	Symptom Scole	Mean SD Median Min. Max.	3.09 2.081 3.67 0.0 8.2	3.02 2.270 2.33 0.0 8.2
		Subjects with no reported symptoms	4 (7%)	2 (4%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -1.09 1.709 -0.76 -5.9 1.3	52 -1.54 2.233 -0.97 -7.8 2.9

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

# 2019N406842 00 $200\overline{6}22$

## CONFIDENTIAL

Protocol: 200622 Page 17 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 17	Most Bothersome Symptom Score	n	41	42
	Symptom Score	Mean SD Median Min. Max.	3.06 2.270 2.86 0.0 8.3	3.10 2.316 2.40 0.0 8.8
		Subjects with no reported symptoms	2 (4%)	1 (2%)
	Change from Baseline	n Mean SD Median Min. Max.	41 -1.10 1.849 -1.07 -6.4 3.2	42 -1.65 2.269 -0.98 -7.9 3.1

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 18 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 18	Most Bothersome Symptom Score	n	48	51
	Symptom Score	Mean SD Median Min. Max.	3.09 2.166 3.31 0.0 8.4	2.96 2.229 2.44 0.0 7.9
		Subjects with no reported symptoms	4 (7%)	1 (2%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -1.08 1.798 -0.81 -6.7 3.0	51 -1.54 2.284 -1.20 -7.3 4.2

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 19 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 19	Most Bothersome Symptom Score	n	48	51
	Symptom Score	Mean SD Median Min. Max.	3.14 2.207 3.38 0.0 8.1	2.94 2.241 2.29 0.0 8.6
		Subjects with no reported symptoms	6 (11%)	1 (2%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -1.03 1.775 -0.83 -6.9 2.7	51 -1.56 2.296 -1.33 -7.3 4.0

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 20 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 20	Most Bothersome Symptom Score	n	48	52
	Symptom Score	Mean SD Median Min. Max.	3.19 2.290 3.49 0.0 8.1	2.89 2.286 2.49 0.0 8.7
		Subjects with no reported symptoms	4 (7%)	3 (6%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.98 1.640 -0.96 -5.7 2.8	52 -1.59 2.394 -1.05 -7.6 2.9

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 21 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 21	Most Bothersome Symptom Score	n	46	46
	Symptom Score	Mean SD Median Min. Max.	3.11 2.283 3.17 0.0 8.3	2.85 2.304 2.18 0.0 8.5
		Subjects with no reported symptoms	4 (7%)	2 (4%)
	Change from Baseline	n Mean SD Median Min. Max.	46 -1.01 1.731 -0.89 -5.3 3.0	46 -1.86 2.403 -1.21 -7.9 2.9

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 22 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 22	Most Bothersome Symptom Score	n	47	51
	Symptom Score	Mean SD Median Min. Max. Subjects with no	3.09 2.228 3.28 0.0 8.2	2.67 2.092 2.17 0.0 7.9
	Change from Baseline	reported symptoms  n Mean SD Median Min. Max.	47 -1.10 1.563 -1.03 -5.9 1.4	51 -1.87 2.227 -1.40 -7.9 2.9

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as the most bothersome symptom score. Subject PPD reported 4 most bothersome symptoms.

2. The mean of the available assessments on p to and including the date of each study visit

is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 23 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 23	Most Bothersome Symptom Score	n	47	49
	of mr com contra	Mean	3.14	2.79
		SD	2.292	2.258
		Median	3.00	2.08
		Min.	0.0	0.0
		Max.	8.4	7.9
		Subjects with no reported symptoms	4 (7%)	3 (6%)
	Change from Baseline	n	47	49
		Mean	-1.11	-1.80
		SD	1.847	2.418
		Median	-0.86	-1.33
		Min.	-6.9	-7 <b>.</b> 9
		Max.	2.8	3.3

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as the most bothersome symptom score. Subject PPD reported 4 most bothersome symptoms.

2. The mean of the available assessments on p to and including the date of each study visit

is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

# 2019N406842 00 $200\overline{6}22$

## CONFIDENTIAL

Protocol: 200622 Page 24 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Most Bothersome Symptom Score	n	47	48
	Symptom dedic	Mean SD Median Min. Max.	3.02 2.306 2.90 0.0 8.3	2.83 2.236 2.24 0.0 7.8
		Subjects with no reported symptoms	5 (9%)	3 (6%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -1.12 1.886 -0.80 -6.9 1.5	48 -1.77 2.577 -1.46 -7.9 4.1

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 25 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 25	Most Bothersome Symptom Score	n	45	44
	Symptom Beele	Mean SD Median Min. Max.	3.00 2.221 2.90 0.0 8.8	2.74 1.995 2.18 0.0 7.1
		Subjects with no reported symptoms	4 (7%)	3 (6%)
	Change from Baseline	n Mean SD Median Min. Max.	45 -1.39 1.884 -0.86 -6.9 1.4	44 -1.51 2.370 -1.05 -7.9 4.4

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 26 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 26	Most Bothersome Symptom Score	n	49	50
	Symptom Score	Mean SD Median Min. Max.	2.96 2.214 2.64 0.0 9.3	2.94 2.246 2.05 0.0 8.7
		Subjects with no reported symptoms	5 (9%)	2 (4%)
	Change from Baseline	n Mean SD Median Min. Max.	49 -1.30 1.851 -0.90 -6.9 1.3	50 -1.59 2.477 -1.06 -7.9 6.7

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as the most bothersome symptom score. Subject PPD reported 4 most bothersome symptoms.

2. The mean of the available assessments on p to and including the date of each study visit

is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 27 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 27	Most Bothersome Symptom Score	n	50	50
	Symptom Score	Mean SD Median Min. Max.	3.11 2.282 3.15 0.0 9.2	3.06 2.326 2.14 0.0 9.1
		Subjects with no reported symptoms	6 (11%)	2 (4%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -1.14 1.864 -0.66 -6.9 1.2	50 -1.47 2.495 -1.23 -7.9 7.1

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 28 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 28	Most Bothersome Symptom Score	n	48	50
	Symptom Beele	Mean SD Median Min. Max.	3.13 2.395 3.04 0.0 9.3	2.94 2.268 2.17 0.0 7.9
		Subjects with no reported symptoms	5 (9%)	3 (6%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -1.00 1.966 -0.54 -6.9 2.5	50 -1.59 2.330 -1.27 -7.9 4.1

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 29 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 29	Most Bothersome Symptom Score	n	44	40
	Symptom Beore	Mean SD Median Min. Max.	2.87 2.194 2.53 0.0 7.9	2.51 2.022 1.93 0.0 7.2
		Subjects with no reported symptoms	6 (11%)	1 (2%)
	Change from Baseline	n Mean SD Median Min. Max.	44 -1.10 1.923 -0.79 -6.9 1.8	40 -2.26 2.591 -1.36 -7.6 2.5

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 30 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 30	Most Bothersome Symptom Score	n	47	51
	Symptom Beole	Mean SD Median Min. Max.	2.96 2.304 2.67 0.0 9.2	2.51 2.131 1.86 0.0 8.3
		Subjects with no reported symptoms	5 (9%)	2 (4%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -1.23 1.849 -1.03 -6.9 1.9	51 -1.99 2.435 -1.24 -7.8 2.2

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 31 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 31	Most Bothersome Symptom Score	n	47	51
	Symptom Score	Mean SD Median Min. Max.	3.08 2.350 2.83 0.0 9.5	2.59 2.124 1.86 0.0 7.7
		Subjects with no reported symptoms	5 (9%)	3 (6%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -1.10 1.831 -0.71 -6.6 1.7	51 -1.91 2.349 -1.24 -7.9 1.9

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as

the most bothersome symptom score. Subject

The mean of the available assessments on p to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 32 of 32

Population: Intent-to-Treat

Table 2.35 Summary of Most Bothersome HES Symptom Severity Score (HES-DS)

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Most Bothersome Symptom Score	n	47	50
		Mean SD Median Min. Max. Subjects with no reported symptoms	3.25 2.360 3.08 0.0 9.4 4 (7%)	2.70 2.174 2.25 0.0 7.7
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.88 1.899 -0.28 -6.5 2.2	50 -1.80 2.392 -1.27 -7.9 1.9

<sup>1.</sup> The mean of up to 3 most bothersome symptoms identified by subjects at Visit 2 (Week 0) is used as the most bothersome symptom score. Subject PPD reported 4 most bothersome symptoms.

2. The mean of the available assessments on p to and including the date of each study visit

is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>3.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 1 of 8

Population: Intent-to-Treat

Table 90.40

Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) (Mixed Model Repeated Measures)

Mara a 1 d - . . . . . . la

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 54 3.43 (0.232) -0.95 (0.232)	54 54 3.11 (0.233) -1.27 (0.233)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.32 (-0.97, 0.34) 0.337	
Corrected Hedges g [3] 95% CI		-0.19 (-0.56, 0.19)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 117 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 8

Population: Intent-to-Treat

Table 90.40

Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) (Mixed Model Repeated Measures)

Mana 1 - - - - - la

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 3.50 (0.252) -0.87 (0.252)	54 54 2.86 (0.251) -1.51 (0.251)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.64 (-1.35, 0.07) 0.078	
Corrected Hedges g [3] 95% CI		-0.35 (-0.73, 0.04)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 118 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 8

Population: Intent-to-Treat

Table 90.40

Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) (Mixed Model Repeated Measures)

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 3.43 (0.257) -0.95 (0.257)	54 53 3.09 (0.256) -1.28 (0.256)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.33 (-1.06, 0.39) 0.360	
Corrected Hedges g [3] 95% CI		-0.18 (-0.56, 0.21)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 119 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 4 of 8

Population: Intent-to-Treat

Table 90.40

Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) (Mixed Model Repeated Measures)

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 3.25 (0.229) -1.12 (0.229)	54 52 2.91 (0.227) -1.46 (0.227)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.34 (-0.98, 0.31) 0.304
Corrected Hedges g [3] 95% CI		-0.20 (-0.59, 0.18)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 120 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 5 of 8

Population: Intent-to-Treat

Table 90.40

Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) (Mixed Model Repeated Measures)

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 48 3.36 (0.251) -1.01 (0.251)	54 52 2.85 (0.247) -1.52 (0.247)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.51 (-1.21, 0.20) 0.155
Corrected Hedges g [3] 95% CI		-0.29 (-0.68, 0.11)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 121 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 6 of 8

Population: Intent-to-Treat

Table 90.40

Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) (Mixed Model Repeated Measures)

Mara a 1 d - . . . . . . la

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 47 3.25 (0.268) -1.12 (0.268)	54 48 2.81 (0.265) -1.56 (0.265)	_
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.44 (-1.19, 0.31) 0.248	
Corrected Hedges g [3] 95% CI		-0.24 (-0.64, 0.17)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 122 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 7 of 8

Population: Intent-to-Treat

Table 90.40

Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) (Mixed Model Repeated Measures)

Visit: Week 28

X 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 48 3.38 (0.267) -0.99 (0.267)	54 50 2.89 (0.263) -1.48 (0.263)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.49 (-1.24, 0.26) 0.195
Corrected Hedges g [3] 95% CI		-0.26 (-0.66, 0.13)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 123 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 8 of 8

Population: Intent-to-Treat

Table 90.40

Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) (Mixed Model Repeated Measures)

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 47 3.37 (0.259) -1.01 (0.259)	54 50 2.68 (0.255) -1.70 (0.255)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.69 (-1.42, 0.03) 0.062
Corrected Hedges g [3] 95% CI		-0.38 (-0.78, 0.02)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 124 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

## CONFIDENTIAL

Protocol: 200622 Page 1 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Symptom Severity Score	n Mean SD Median Min. Max.	54 3.08 2.682 2.37 0.0 9.0	54 3.86 2.486 3.48 0.0 9.1
		Subjects with no reported symptoms	11 (20%)	2 (4%)
Week 1	Symptom Severity Score	n Mean SD Median Min. Max.	54 2.75 2.394 2.17 0.0 8.9	54 3.41 2.588 2.69 0.0 9.6
		Subjects with no reported symptoms	10 (19%)	5 (9%)

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

.. . . . .

## CONFIDENTIAL

Protocol: 200622 Page 2 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 1	Change from Baseline	n Mean SD Median Min. Max.	54 -0.33 1.161 -0.15 -4.8 1.6	54 -0.45 1.269 -0.21 -3.3 2.3
Week 2	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	54 2.61 2.371 2.00 0.0 9.0	54 3.25 2.591 2.64 0.0 9.6
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.47 1.350 -0.05 -4.8 2.4	54 -0.62 1.391 -0.27 -3.8 2.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 3 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 3	Symptom Severity Score	n Mean SD Median Min. Max.	54 2.51 2.434 1.85 0.0 9.0	54 3.06 2.550 2.39 0.0 9.3
		Subjects with no reported symptoms	10 (19%)	6 (11%)
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.58 1.272 -0.15 -4.0 2.3	54 -0.80 1.597 -0.83 -6.1 2.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

## CONFIDENTIAL

Protocol: 200622 Page 4 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 4	Symptom Severity Score	n Mean SD Median Min. Max.	54 2.63 2.575 2.21 0.0 9.4	54 3.04 2.477 2.63 0.0 9.9
		Subjects with no reported symptoms	14 (26%)	7 (13%)
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.45 1.411 -0.04 -4.7 3.0	54 -0.83 1.777 -0.14 -6.3 2.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 5 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 5	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.74 2.665 2.00 0.0 9.4	50 2.95 2.433 2.54 0.0 8.6
		Subjects with no reported symptoms	10 (19%)	8 (15%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.42 1.597 0.00 -5.1 3.1	50 -0.96 1.602 -0.66 -6.8 1.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 6 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 6	Symptom Severity Score	n Mean SD Median Min. Max.	51 2.93 2.581 2.80 0.0 9.3	54 3.03 2.491 2.52 0.0 8.3
		Subjects with no reported symptoms	9 (17%)	6 (11%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.08 1.751 0.00 -3.9 6.3	54 -0.83 1.843 -0.75 -7.2 2.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 7 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 7	Symptom Severity Score	n Mean SD Median Min. Max.	52 2.80 2.530 2.20 0.0 8.4	54 2.93 2.407 2.27 0.0 7.8
		Subjects with no reported symptoms	8 (15%)	8 (15%)
	Change from Baseline	n Mean SD Median Min. Max.	52 -0.27 1.734 0.00 -3.5 7.0	54 -0.93 1.840 -0.79 -7.4 1.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

### 2019N406842 00 CONFIDENTIAL

Protocol: 200622 Page 8 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Symptom: Worst Level of Muscle/Joint Pain Summary

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Symptom Severity Score	n Mean SD Median Min. Max.	52 2.80 2.581 2.42 0.0 8.7	54 2.93 2.483 2.14 0.0 8.3
		Subjects with no reported symptoms	10 (19%)	9 (17%)
	Change from Baseline	n Mean SD Median Min. Max.	52 -0.28 1.446 0.00 -3.2 3.6	54 -0.94 1.863 -0.71 -6.7 2.9

 $200\overline{6}22$ 

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

## CONFIDENTIAL

Protocol: 200622 Page 9 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 9	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.67 2.561 2.20 0.0 8.0	50 2.85 2.456 2.54 0.0 8.3
		Subjects with no reported symptoms	11 (20%)	8 (15%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.20 1.519 0.00 -3.5 4.0	50 -0.93 1.912 -0.43 -6.5 2.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

CONFIDENTIAL

Protocol: 200622 Page 10 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 10	Symptom Severity Score	n Mean SD Median Min. Max.	51 2.66 2.610 2.00 0.0 8.3	52 2.82 2.375 2.38 0.0 8.0
		Subjects with no reported symptoms	11 (20%)	9 (17%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.36 1.495 0.00 -4.0 2.9	52 -0.93 2.105 -0.85 -7.1 3.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

## CONFIDENTIAL

Protocol: 200622 Page 11 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 11	Symptom Severity Score	n Mean SD Median Min. Max.	49 2.85 2.532 2.20 0.0 9.1	52 3.08 2.593 2.36 0.0 8.9
		Subjects with no reported symptoms	8 (15%)	7 (13%)
	Change from Baseline	n Mean SD Median Min. Max.	49 -0.25 1.573 0.00 -3.9 2.7	52 -0.71 2.168 -0.81 -7.3 6.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 12 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 12	Symptom Severity Score	n Mean SD Median Min. Max.	51 2.64 2.643 2.00 0.0 9.9	53 3.20 2.599 2.71 0.0 8.9
		Subjects with no reported symptoms	11 (20%)	9 (17%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.38 1.553 0.00 -3.7 3.0	53 -0.62 2.208 -0.67 -7.3 6.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

## CONFIDENTIAL

Protocol: 200622 Page 13 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 13	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no	43 2.74 2.655 2.00 0.0 9.6	48 3.00 2.557 2.58 0.0 8.1 8 (15%)
	Change from Baseline	reported symptoms  n Mean SD Median Min. Max.	43 -0.56 1.679 -0.29 -3.9 3.5	48 -0.85 2.270 -0.83 -7.5 3.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

## CONFIDENTIAL

Protocol: 200622 Page 14 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 14	Symptom Severity Score	n Mean SD Median Min. Max.	50 2.51 2.621 2.07 0.0 9.0	53 2.82 2.510 2.29 0.0 8.3
		Subjects with no reported symptoms	13 (24%)	11 (20%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.56 1.597 -0.19 -3.8 2.2	53 -1.00 2.176 -0.83 -7.2 3.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00 CONFIDENTIAL  $200\overline{6}22$ 

Protocol: 200622 Page 15 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 15	Symptom Severity Score	n Mean SD Median Min. Max.	50 2.47 2.601 1.86 0.0 8.8	53 3.17 2.516 3.17 0.0 8.7
		Subjects with no reported symptoms	13 (24%)	9 (17%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.59 1.690 -0.18 -5.0 2.6	53 -0.65 2.033 -0.80 -6.3 3.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 16 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Symptom Severity Score	n Mean SD Median Min. Max.	51 2.61 2.632 2.00 0.0 8.1	52 2.90 2.402 2.39 0.0 7.9
		Subjects with no reported symptoms	14 (26%)	10 (19%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.41 1.701 0.00 -5.3 2.9	52 -0.89 1.976 -0.67 -6.8 4.5

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

### 2019N406842 00 CONFIDENTIAL $200\overline{6}22$

Protocol: 200622 Page 17 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 17	Symptom Severity Score	n Mean SD Median Min. Max.	41 2.45 2.788 1.40 0.0 9.0	42 2.79 2.426 2.37 0.0 8.0
		Subjects with no reported symptoms	11 (20%)	10 (19%)
	Change from Baseline	n Mean SD Median Min. Max.	41 -0.51 1.657 0.00 -4.6 1.6	42 -0.94 1.767 -0.70 -4.7 2.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

## CONFIDENTIAL

Protocol: 200622 Page 18 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 18	Symptom Severity Score	n Mean SD Median Min. Max.	48 2.60 2.505 2.08 0.0 8.7	51 2.62 2.346 2.29 0.0 8.0
		Subjects with no reported symptoms	12 (22%)	9 (17%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.48 1.603 0.00 -3.8 2.5	51 -1.12 2.034 -0.80 -7.3 2.4

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00 CONFIDENTIAL  $200\overline{6}22$ 

Population: Intent-to-Treat

Protocol: 200622

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Symptom: Worst Level of Muscle/Joint Pain Summary

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 19	Symptom Severity Score	n Mean SD Median Min. Max.	48 2.62 2.665 2.23 0.0 8.4	51 2.63 2.514 2.00 0.0 8.5
		Subjects with no reported symptoms	11 (20%)	8 (15%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.45 1.643 0.00 -4.0 2.7	51 -1.10 2.285 -1.00 -7.1 4.9

Page 19 of 192

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

## CONFIDENTIAL

Protocol: 200622 Page 20 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 20	Symptom Severity Score	n Mean SD Median Min. Max.	48 2.62 2.580 2.17 0.0 8.8	52 2.58 2.489 2.00 0.0 8.7
		Subjects with no reported symptoms	11 (20%)	10 (19%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.46 1.453 -0.14 -3.7 2.5	52 -1.17 2.083 -0.86 -7.3 3.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 21 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 21	Symptom Severity Score	n Mean SD Median Min. Max.	46 2.74 2.757 2.38 0.0 9.0	46 2.68 2.386 2.00 0.0 8.0
		Subjects with no reported symptoms	11 (20%)	7 (13%)
	Change from Baseline	n Mean SD Median Min. Max.	46 -0.32 1.572 0.00 -4.1 3.6	46 -1.27 2.067 -1.17 -6.3 3.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 22 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 22	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.38 2.473 2.00 0.0 9.0	51 2.53 2.280 2.17 0.0 8.0
		Subjects with no reported symptoms	13 (24%)	10 (19%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.60 1.564 0.00 -4.6 2.1	51 -1.28 1.958 -1.37 -6.5 2.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 23 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint	ind y	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 23	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	47 2.54 2.664 2.14 0.0 9.0	49 2.68 2.623 1.71 0.0 8.6
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.60 1.710 0.00 -5.6 2.4	49 -1.12 2.245 -1.17 -6.9 4.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 24 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.57 2.572 2.29 0.0 9.0	48 2.59 2.401 2.00 0.0 8.0
		Subjects with no reported symptoms	14 (26%)	9 (17%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.46 1.846 0.00 -5.6 3.6	48 -1.17 2.244 -1.14 -7.0 2.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 25 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 25	Symptom Severity Score	n Mean SD Median Min. Max.	45 2.41 2.422 2.33 0.0 9.0	44 2.40 2.280 2.00 0.0 8.4
		Subjects with no reported symptoms	12 (22%)	9 (17%)
	Change from Baseline	n Mean SD Median Min. Max.	45 -0.58 1.903 0.00 -5.3 3.3	44 -0.95 2.050 -0.92 -6.6 3.4

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 26 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 26	Symptom Severity Score	n Mean SD Median Min. Max.	49 2.32 2.593 1.71 0.0 9.3	50 2.62 2.417 2.00 0.0 8.0
		Subjects with no reported symptoms	15 (28%)	9 (17%)
	Change from Baseline	n Mean SD Median Min. Max.	49 -0.82 1.724 -0.05 -5.3 2.1	50 -1.11 2.230 -1.00 -7.7 3.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 27 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 27	Symptom Severity Score	n Mean SD Median Min. Max.	50 2.48 2.641 1.79 0.0 9.0	50 2.66 2.434 2.00 0.0 8.0
		Subjects with no reported symptoms	15 (28%)	7 (13%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.60 1.737 0.00 -5.0 3.4	50 -1.07 2.320 -0.93 -8.8 2.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 28 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 28	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	48 2.48 2.632 2.00 0.0 9.0	50 2.68 2.306 2.00 0.0 8.2 8 (15%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.51 1.755 0.00 -4.6 3.8	50 -1.05 2.171 -0.86 -7.0 2.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 29 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 29	Symptom Severity Score	n Mean SD Median Min. Max.	44 2.43 2.451 1.82 0.0 8.0	40 2.57 2.363 1.83 0.0 8.0
		Subjects with no reported symptoms	12 (22%)	7 (13%)
	Change from Baseline	n Mean SD Median Min. Max.	44 -0.46 1.877 0.00 -4.7 2.4	40 -1.44 2.423 -1.07 -7.3 2.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 30 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 30	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.40 2.573 1.60 0.0 9.4	51 2.69 2.327 2.00 0.0 8.0
		Subjects with no reported symptoms	12 (22%)	9 (17%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.58 1.718 0.00 -4.9 2.4	51 -1.04 2.179 -1.00 -7.0 2.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 31 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 31	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.77 2.729 1.86 0.0 9.2	51 2.71 2.364 2.00 0.0 8.0
		Subjects with no reported symptoms	12 (22%)	7 (13%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.37 1.777 0.00 -4.6 4.3	51 -1.02 2.378 -0.71 -7.2 2.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 32 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.87 2.910 2.00 0.0 9.3	50 2.45 2.276 2.00 0.0 8.0
		Subjects with no reported symptoms	12 (22%)	9 (17%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.15 1.730 0.00 -4.0 4.0	50 -1.24 2.216 -0.96 -7.3 2.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

.. . . . .

Protocol: 200622 Page 33 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Symptom Severity Score	n Mean SD Median Min. Max.	54 1.98 2.371 1.14 0.0 10.0	54 2.65 2.820 1.38 0.0 8.9
		Subjects with no reported symptoms	15 (28%)	11 (20%)
Week 1	Symptom Severity Score	n Mean SD Median Min. Max.	54 1.66 2.237 1.00 0.0	54 2.27 2.529 1.50 0.0 8.4
		Subjects with no reported symptoms	19 (35%)	17 (31%)

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 34 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint	-	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 1	Change from Baseline	n Mean SD Median Min. Max.	54 -0.32 0.816 -0.06 -2.8 1.6	54 -0.38 1.527 -0.21 -5.1 5.0
Week 2	Symptom Severity Score	n Mean SD Median Min. Max.	54 1.68 2.185 1.07 0.0 10.0	54 2.03 2.473 1.00 0.0 8.4
		Subjects with no reported symptoms	20 (37%)	15 (28%)
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.29 0.930 0.00 -2.8 2.1	54 -0.62 1.735 -0.13 -7.0 4.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 35 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint	ar i	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 3	Symptom Severity Score	n Mean SD Median Min. Max.	54 1.65 2.185 1.00 0.0 10.0	54 2.04 2.299 1.00 0.0 8.8
		Subjects with no reported symptoms	19 (35%)	15 (28%)
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.33 1.006 0.00 -3.0 1.6	54 -0.61 2.071 -0.07 -7.0 4.5

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 36 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 4	Symptom Severity Score	n Mean SD Median Min. Max.	54 1.54 2.227 0.64 0.0 10.0	54 1.90 2.188 1.00 0.0 7.8
		Subjects with no reported symptoms	21 (39%)	17 (31%)
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.44 1.018 0.00 -3.3 1.6	54 -0.75 1.902 -0.14 -7.0 2.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 37 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint	ar i	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 5	Symptom Severity Score	n Mean SD Median Min. Max.	47 1.66 2.277 0.71 0.0 10.0	50 1.93 2.246 0.92 0.0 7.6
		Subjects with no reported symptoms	18 (33%)	15 (28%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.48 1.532 0.00 -4.9 3.4	50 -0.87 1.925 -0.30 -7.0 2.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

## CONFIDENTIAL

Protocol: 200622 Page 38 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 6	Symptom Severity Score	n Mean SD Median Min. Max.	51 1.58 2.163 1.00 0.0 10.0	54 2.02 2.288 1.17 0.0 8.2
		Subjects with no reported symptoms	19 (35%)	19 (35%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.39 1.433 0.00 -3.7 2.5	54 -0.63 2.109 -0.15 -6.9 5.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

## CONFIDENTIAL

Protocol: 200622 Page 39 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 7	Symptom Severity Score	n Mean SD Median Min. Max.	52 1.56 2.189 0.50 0.0 10.0	54 1.94 2.026 1.29 0.0 6.9
		Subjects with no reported symptoms	23 (43%)	15 (28%)
	Change from Baseline	n Mean SD Median Min. Max.	52 -0.39 1.666 0.00 -4.6 3.3	54 -0.71 2.235 -0.31 -6.9 4.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 40 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Symptom Severity Score	n Mean SD Median Min. Max.	52 1.43 2.091 0.79 0.0	54 1.89 2.055 1.10 0.0 7.1
		Subjects with no reported symptoms	21 (39%)	17 (31%)
	Change from Baseline	n Mean SD Median Min. Max.	52 -0.52 1.721 0.00 -5.7 3.1	54 -0.76 2.202 -0.29 -6.8 5.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 41 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint	ar y	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 9	Symptom Severity Score	n Mean SD Median Min. Max.	47 1.41 2.151 0.17 0.0 10.0	50 1.55 2.120 0.64 0.0 7.2
		Subjects with no reported symptoms	20 (37%)	18 (33%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.50 1.772 0.00 -7.0 1.9	50 -0.91 2.002 -0.29 -6.7 2.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 42 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint	ar i	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 10	Symptom Severity Score	n Mean SD Median Min. Max.	51 1.59 2.187 0.86 0.0 10.0	52 1.57 2.012 0.62 0.0 7.3
		Subjects with no reported symptoms	16 (30%)	19 (35%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.40 1.817 0.00 -5.9 2.7	52 -0.97 2.030 -0.29 -7.1 1.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 43 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 11	Symptom Severity Score	n Mean SD Median Min. Max.	49 1.57 2.168 0.86 0.0 10.0	52 1.63 2.174 0.46 0.0 7.8
		Subjects with no reported symptoms	16 (30%)	19 (35%)
	Change from Baseline	n Mean SD Median Min. Max.	49 -0.38 1.826 0.00 -6.3 4.0	52 -0.93 2.102 -0.29 -7.1 3.2

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 44 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 12	Symptom Severity Score	n Mean SD Median Min. Max.	51 1.54 2.147 0.75 0.0 9.9	53 1.73 2.121 0.50 0.0 6.5
		Subjects with no reported symptoms	17 (31%)	24 (44%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.35 1.733 0.00 -6.3 4.0	53 -0.89 2.188 -0.29 -7.3 3.4

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 45 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint	~~ <u>1</u>	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 13	Symptom Severity Score	n Mean SD Median Min. Max.	43 1.60 2.275 1.00 0.0 9.8	48 1.71 2.052 0.92 0.0 6.0
		Subjects with no reported symptoms	15 (28%)	19 (35%)
	Change from Baseline	n Mean SD Median Min. Max.	43 -0.55 1.942 0.00 -7.7 4.1	48 -0.96 2.385 -0.15 -7.5 3.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 46 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint	al j	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 14	Symptom Severity Score	n Mean SD Median Min. Max.	50 1.46 2.048 0.79 0.0 9.0	53 1.71 2.084 1.00 0.0 7.1
		Subjects with no reported symptoms	16 (30%)	19 (35%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.46 1.918 0.00 -7.0 4.4	53 -0.91 2.244 -0.20 -7.7 2.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 47 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint	<u>1</u>	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 15	Symptom Severity Score	n Mean SD Median Min. Max.	50 1.57 2.087 1.00 0.0 8.8	53 1.72 2.168 1.00 0.0 7.2
		Subjects with no reported symptoms	21 (39%)	22 (41%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.34 1.812 0.00 -5.4 3.9	53 -0.90 2.266 -0.29 -7.0 4.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 48 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Symptom Severity Score	n Mean SD Median Min. Max.	51 1.46 2.033 0.57 0.0 8.6	52 1.49 1.925 0.44 0.0 6.5
		Subjects with no reported symptoms	22 (41%)	23 (43%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.42 1.945 0.00 -7.1 4.3	52 -1.08 2.238 -0.29 -7.0 2.4

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 49 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 17	Symptom Severity Score	n Mean SD Median Min. Max.	41 1.56 2.329 0.67 0.0 9.0	42 1.36 1.815 0.34 0.0 6.6
		Subjects with no reported symptoms	18 (33%)	17 (31%)
	Change from Baseline	n Mean SD Median Min. Max.	41 -0.47 2.189 0.00 -7.7 4.3	42 -1.43 2.443 -0.43 -7.9 2.4

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

Protocol: 200622 Page 50 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 18	Symptom Severity Score	n Mean SD Median Min. Max.	48 1.41 2.044 0.79 0.0 9.0	51 1.23 1.633 0.40 0.0 5.5
		Subjects with no reported symptoms	21 (39%)	20 (37%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.58 1.797 0.00 -6.9 1.9	51 -1.34 2.444 -0.33 -8.3 3.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

Protocol: 200622 Page 51 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 19	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	48 1.43 2.104 0.50 0.0 8.5	51 1.46 1.718 1.00 0.0 6.4 18 (33%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.56 1.931 0.00 -6.0 3.1	51 -1.10 2.235 -0.29 -7.9 2.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 52 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint	ar y	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 20	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no	48 1.62 2.271 0.83 0.0 9.0	52 1.38 1.796 0.82 0.0 7.2
	Change from Baseline	reported symptoms  n Mean SD Median Min. Max.	48 -0.38 2.331 0.00 -6.6 7.0	52 -1.16 2.330 -0.29 -8.0 2.5

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 53 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 21	Symptom Severity Score	n Mean SD Median Min. Max.	46 1.64 2.268 0.70 0.0 9.0	46 1.31 1.750 1.00 0.0 7.0
		Subjects with no reported symptoms	16 (30%)	19 (35%)
	Change from Baseline	n Mean SD Median Min. Max.	46 -0.26 2.113 0.00 -5.0 5.7	46 -1.53 2.491 -0.38 -7.9 2.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 54 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint	~-1	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 22	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	47 1.57 2.220 0.43 0.0 9.0	51 1.16 1.606 0.40 0.0 6.2
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.45 1.979 0.00 -7.7 3.4	51 -1.41 2.420 -0.33 -7.9 3.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 55 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint	~~ <i>Y</i>	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 23	Symptom Severity Score	n Mean SD	47 1.76 2.437	49 1.20 1.663
		Median Min. Max.	1.00 0.0 9.0	0.50 0.0 6.7
		Subjects with no reported symptoms	18 (33%)	19 (35%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.17 2.242 0.00 -6.3 7.3	49 -1.44 2.527 -0.33 -7.9 2.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

## CONFIDENTIAL

Protocol: 200622 Page 56 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Symptom Severity Score	n Mean SD Median Min. Max.	47 1.63 2.366 0.29 0.0 8.9	48 1.23 1.753 0.45 0.0 7.0
		Subjects with no reported symptoms	19 (35%)	21 (39%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.34 2.292 0.00 -7.4 4.9	48 -1.35 2.644 -0.35 -7.9 2.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 57 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 25	Symptom Severity Score	n Mean SD Median Min. Max.	45 1.57 2.323 0.29 0.0 9.0	44 1.03 1.404 0.36 0.0 5.3
		Subjects with no reported symptoms	21 (39%)	21 (39%)
	Change from Baseline	n Mean SD Median Min. Max.	45 -0.60 2.267 0.00 -7.4 4.1	44 -1.24 2.574 -0.23 -8.3 2.2

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

### CONFIDENTIAL

Protocol: 200622 Page 58 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 26	Symptom Severity Score	n Mean SD Median Min. Max.	49 1.59 2.433 0.20 0.0 9.3	50 1.30 1.606 0.63 0.0 5.6
		Subjects with no reported symptoms	22 (41%)	20 (37%)
	Change from Baseline	n Mean SD Median Min. Max.	49 -0.48 2.318 0.00 -7.6 6.3	50 -1.31 2.704 -0.31 -8.3 3.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 59 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 27	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	50 1.84 2.501 0.80 0.0 9.3	50 1.24 1.632 0.53 0.0 6.3
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.19 2.312 0.00 -7.7 6.0	50 -1.37 2.632 -0.29 -8.3 2.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

### CONFIDENTIAL

Protocol: 200622 Page 60 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 28	Symptom Severity Score	n Mean SD Median Min. Max.	48 1.76 2.667 0.36 0.0 10.0	50 1.19 1.610 0.50 0.0 6.8
		Subjects with no reported symptoms	22 (41%)	20 (37%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.18 2.602 0.00 -7.7 9.0	50 -1.42 2.590 -0.35 -8.3 3.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 61 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint	1	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 29	Symptom Severity Score	n Mean SD Median Min. Max.	44 1.42 2.118 0.00 0.0 8.5 24 (44%)	40 1.03 1.570 0.25 0.0 6.5
	Change from Baseline	reported symptoms  n Mean SD Median Min. Max.	44 -0.50 2.199 0.00 -7.2 3.3	40 -1.80 2.790 -0.38 -8.3 1.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

### CONFIDENTIAL

Protocol: 200622 Page 62 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 30	Symptom Severity Score	n Mean SD Median Min. Max.	47 1.50 2.343 0.00 0.0 9.6	51 1.20 1.712 0.20 0.0 5.8
		Subjects with no reported symptoms	24 (44%)	25 (46%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.52 2.061 0.00 -6.4 2.7	51 -1.36 2.503 -0.29 -7.9 2.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 63 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint	ar i	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 31	Symptom Severity Score	n Mean SD Median Min. Max.	47 1.67 2.518 0.29 0.0 9.8	51 1.21 1.695 0.33 0.0 5.9
		Subjects with no reported symptoms	21 (39%)	22 (41%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.37 2.329 0.00 -7.1 4.7	51 -1.36 2.457 -0.33 -7.4 2.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

### CONFIDENTIAL

Protocol: 200622 Page 64 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Symptom Severity Score	n Mean SD Median Min. Max.	47 1.75 2.440 0.50 0.0	50 1.21 1.686 0.00 0.0 5.4
		Subjects with no reported symptoms	20 (37%)	26 (48%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.28 2.044 0.00 -5.0 2.9	50 -1.29 2.422 -0.31 -7.4 3.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00 CONFIDENTIAL  $200\overline{6}22$ 

Protocol: 200622 Page 65 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Symptom Severity Score	n Mean SD Median Min. Max.	54 2.63 2.412 2.27 0.0 8.6	54 3.12 2.836 2.79 0.0 10.0
		Subjects with no reported symptoms	12 (22%)	11 (20%)
Week 1	Symptom Severity Score	n Mean SD Median Min. Max.	54 2.37 2.295 1.43 0.0 9.0	54 2.91 2.826 1.93 0.0 10.0
		Subjects with no reported symptoms	11 (20%)	12 (22%)

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

.. . . . .

### CONFIDENTIAL

Protocol: 200622 Page 66 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 1	Change from Baseline	n Mean SD Median Min. Max.	54 -0.26 1.254 0.00 -3.0 4.7	54 -0.21 1.231 0.00 -2.4 4.8
Week 2	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no	54 2.34 2.389 1.62 0.0 8.8	54 2.73 2.699 2.27 0.0 10.0
	Change from Baseline	reported symptoms  n Mean SD Median Min. Max.	54 -0.29 1.522 0.00 -3.2 6.5	54 -0.39 1.428 -0.07 -6.0 4.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 67 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 3	Symptom Severity Score	n Mean SD Median Min. Max.	54 2.35 2.311 1.64 0.0 8.8	54 2.67 2.627 2.14 0.0 10.0
		Subjects with no reported symptoms	14 (26%)	11 (20%)
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.28 1.583 0.00 -4.8 5.9	54 -0.45 1.685 -0.05 -6.9 3.2

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 68 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 4	Symptom Severity Score	n Mean SD Median Min. Max.	54 2.31 2.369 1.61 0.0 9.0	54 2.63 2.629 1.79 0.0 10.0
		Subjects with no reported symptoms	14 (26%)	9 (17%)
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.33 1.570 -0.07 -3.9 5.7	54 -0.49 1.635 -0.14 -7.1 2.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 69 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 5	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.28 2.448 1.43 0.0 9.0	50 2.71 2.700 2.00 0.0 10.0
		Subjects with no reported symptoms	13 (24%)	12 (22%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.33 1.837 -0.14 -5.1 6.1	50 -0.50 1.583 0.00 -5.9 2.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

### CONFIDENTIAL

Protocol: 200622 Page 70 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 6	Symptom Severity Score	n Mean SD Median Min. Max.	51 2.15 2.338 1.29 0.0 9.2	54 2.74 2.686 2.07 0.0 10.0
		Subjects with no reported symptoms	13 (24%)	12 (22%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.40 1.726 -0.14 -5.3 5.1	54 -0.38 1.926 0.00 -7.1 4.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 71 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 7	Symptom Severity Score	n Mean SD Median Min. Max.	52 2.40 2.534 1.36 0.0 7.9	54 2.53 2.623 1.66 0.0
		Subjects with no reported symptoms	15 (28%)	13 (24%)
	Change from Baseline	n Mean SD Median Min. Max.	52 -0.21 1.847 0.00 -6.3 5.7	54 -0.60 1.777 -0.15 -7.6 4.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

### CONFIDENTIAL

Protocol: 200622 Page 72 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Symptom Severity Score	n Mean SD Median Min. Max.	52 2.42 2.519 1.43 0.0 8.4	54 2.58 2.570 1.77 0.0
		Subjects with no reported symptoms	15 (28%)	12 (22%)
	Change from Baseline	n Mean SD Median Min. Max.	52 -0.19 1.981 0.00 -6.3 7.3	54 -0.54 1.813 0.00 -7.1 4.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

### CONFIDENTIAL

Protocol: 200622 Page 73 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 9	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.50 2.676 1.17 0.0 8.0	50 2.40 2.631 1.18 0.0 10.0
		Subjects with no reported symptoms	13 (24%)	10 (19%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.14 1.815 -0.14 -6.3 6.5	50 -0.65 1.869 -0.24 -6.9 3.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

### CONFIDENTIAL

Protocol: 200622 Page 74 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 10	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	51 2.54 2.653 1.43 0.0 8.4	52 2.51 2.665 1.51 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.08 1.860 0.00 -6.3 6.3	52 -0.51 1.748 -0.07 -6.3 3.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

### CONFIDENTIAL

Protocol: 200622 Page 75 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 11	Symptom Severity Score	n Mean SD Median Min. Max.	49 2.48 2.680 1.29 0.0 8.9	52 2.55 2.571 1.64 0.0 10.0
		Subjects with no reported symptoms	13 (24%)	13 (24%)
	Change from Baseline	n Mean SD Median Min. Max.	49 -0.13 1.849 0.00 -6.3 5.9	52 -0.43 1.930 0.00 -7.1 4.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 76 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 12	Symptom Severity Score	n Mean SD Median Min. Max.	51 2.30 2.600 1.25 0.0 8.6	53 2.58 2.569 1.83 0.0
		Subjects with no reported symptoms	15 (28%)	12 (22%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.24 1.787 0.00 -6.3 5.4	53 -0.50 1.943 0.00 -7.0 2.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

### CONFIDENTIAL

Protocol: 200622 Page 77 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 13	Symptom Severity Score	n Mean SD Median Min. Max.	43 2.31 2.421 1.86 0.0 8.5	48 2.65 2.671 1.83 0.0 10.0
		Subjects with no reported symptoms	12 (22%)	8 (15%)
	Change from Baseline	n Mean SD Median Min. Max.	43 -0.49 1.937 -0.07 -6.3 4.8	48 -0.44 1.747 0.00 -5.9 2.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

### CONFIDENTIAL

Protocol: 200622 Page 78 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 14	Symptom Severity Score	n Mean SD Median Min. Max.	50 2.33 2.492 1.75 0.0 8.3	53 2.58 2.668 1.86 0.0 10.0
		Subjects with no reported symptoms	17 (31%)	15 (28%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.20 1.849 0.00 -6.3 5.2	53 -0.51 1.946 0.00 -6.1 5.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 79 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 15	Symptom Severity Score	n Mean SD Median Min. Max.	50 2.28 2.700 1.07 0.0 8.4	53 2.62 2.717 2.00 0.0
		Subjects with no reported symptoms	17 (31%)	14 (26%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.25 1.906 0.00 -6.3 5.4	53 -0.47 1.641 -0.14 -6.4 2.2

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 80 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Symptom Severity Score	n Mean SD Median Min. Max.	51 2.23 2.408 1.83 0.0 8.1	52 2.41 2.566 2.00 0.0 10.0
		Subjects with no reported symptoms	17 (31%)	12 (22%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.31 1.915 0.00 -6.3 4.7	52 -0.57 1.707 0.00 -6.7 2.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 81 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 17	Symptom Severity Score	n Mean SD Median Min. Max.	41 2.37 2.578 1.80 0.0 8.3	42 2.52 2.740 1.70 0.0 10.0
		Subjects with no reported symptoms	13 (24%)	11 (20%)
	Change from Baseline	n Mean SD Median Min. Max.	41 -0.13 1.759 0.00 -6.3 6.1	42 -0.95 1.946 -0.28 -7.9 1.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 82 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 18	Symptom Severity Score	n Mean SD Median Min. Max.	48 2.52 2.600 2.29 0.0 8.7	51 2.24 2.594 1.67 0.0
		Subjects with no reported symptoms	14 (26%)	14 (26%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.10 2.004 0.00 -6.3 5.7	51 -0.80 1.743 0.00 -6.3 2.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

### CONFIDENTIAL

Protocol: 200622 Page 83 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 19	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	48 2.51 2.657 2.29 0.0 8.7	51 2.35 2.599 1.86 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.12 2.050 0.00 -6.1 5.9	51 -0.70 1.683 -0.43 -6.6 2.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 84 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 20	Symptom Severity Score	n Mean SD Median Min. Max.	48 2.43 2.729 1.27 0.0 8.8	52 2.35 2.647 1.63 0.0 10.0
		Subjects with no reported symptoms	16 (30%)	16 (30%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.20 2.094 0.00 -6.0 5.7	52 -0.70 1.784 -0.25 -6.5 3.5

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 85 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 21	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	46 2.46 2.783 1.50 0.0 8.8	46 2.44 2.678 1.71 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	46 -0.21 2.037 0.00 -4.9 6.1	46 -0.72 1.710 -0.15 -6.8 1.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

### CONFIDENTIAL

Protocol: 200622 Page 86 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 22	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.33 2.690 1.14 0.0 9.5	51 2.09 2.474 1.57 0.0 10.0
		Subjects with no reported symptoms	16 (30%)	17 (31%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.20 1.942 0.00 -5.6 5.0	51 -0.96 1.732 -0.27 -6.3 1.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00 CONFIDENTIAL

Protocol: 200622 Page 87 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Symptom: Worst Level of Abdominal Pain/Bloating Summary

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 23	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.48 2.741 1.86 0.0 8.8	49 2.33 2.651 1.40 0.0 10.0
		Subjects with no reported symptoms	16 (30%)	14 (26%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.19 2.004 0.00 -6.3 5.9	49 -0.70 1.683 -0.33 -6.6 2.3

 $200\overline{6}22$ 

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

### CONFIDENTIAL

Protocol: 200622 Page 88 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.41 2.803 1.00 0.0 8.5	48 2.18 2.583 1.07 0.0
		Subjects with no reported symptoms	16 (30%)	16 (30%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.21 2.080 0.00 -5.9 5.9	48 -0.73 1.731 0.00 -5.9 2.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 89 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 25	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	45 2.36 2.572 1.57 0.0 8.8	44 1.75 2.178 1.00 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	45 -0.36 1.989 0.00 -5.7 5.9	44 -0.78 1.548 -0.33 -5.6 2.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 90 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 26	Symptom Severity Score	n Mean SD Median Min. Max.	49 2.45 2.794 1.43 0.0 9.3	50 2.25 2.535 1.43 0.0 10.0
		Subjects with no reported symptoms	15 (28%)	16 (30%)
	Change from Baseline	n Mean SD Median Min. Max.	49 -0.25 2.002 0.00 -6.0 6.7	50 -0.78 1.657 -0.18 -5.6 2.2

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

CONFIDENTIAL

Protocol: 200622 Page 91 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 27	Symptom Severity Score	n Mean SD Median Min. Max.	50 2.50 2.790 1.79 0.0 9.2	50 2.38 2.536 1.86 0.0 10.0
		Subjects with no reported symptoms	16 (30%)	15 (28%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.21 2.122 0.00 -6.3 5.6	50 -0.64 1.619 -0.14 -5.6 2.4

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

### CONFIDENTIAL

Protocol: 200622 Page 92 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 28	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	48 2.44 2.758 1.54 0.0 8.8	50 2.28 2.684 1.41 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.19 2.060 0.00 -6.3 6.4	50 -0.75 1.548 -0.21 -5.6 1.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 93 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 29	Symptom Severity Score	n Mean SD Median Min. Max.	44 2.36 2.697 1.08 0.0 9.0	40 2.45 2.874 1.33 0.0 10.0
		Subjects with no reported symptoms	14 (26%)	12 (22%)
	Change from Baseline	n Mean SD Median Min. Max.	44 -0.03 2.153 0.00 -6.3 7.4	40 -0.61 1.729 -0.14 -6.3 2.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

### CONFIDENTIAL

Protocol: 200622 Page 94 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 30	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.45 2.693 1.71 0.0 8.8	51 2.15 2.549 1.40 0.0 10.0
		Subjects with no reported symptoms	17 (31%)	15 (28%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.08 2.029 0.00 -6.3 6.9	51 -0.89 1.747 -0.29 -6.4 1.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

### CONFIDENTIAL

Protocol: 200622 Page 95 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 31	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.66 2.844 2.14 0.0 9.5	51 2.18 2.543 1.29 0.0 10.0
		Subjects with no reported symptoms	15 (28%)	15 (28%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.02 2.017 0.00 -6.3 7.2	51 -0.86 1.680 -0.14 -6.6 1.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 96 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint	ng Samuely	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	47 2.65 2.732 1.83 0.0 9.2	50 2.06 2.453 1.42 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	47 0.02 2.031 0.00 -6.3 6.9	50 -0.86 1.752 -0.14 -6.0 2.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 97 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Symptom Severity Score	n Mean SD Median Min. Max.	54 3.23 2.795 2.75 0.0 9.1	54 4.08 3.217 3.21 0.0 10.0
		Subjects with no reported symptoms	11 (20%)	6 (11%)
Week 1	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no	54 2.90 2.658 2.75 0.0 9.4	54 3.41 2.740 2.77 0.0 10.0
		reported symptoms	(200)	(100)

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Population: Intent-to-Treat

Protocol: 200622

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Symptom: Worst Level of Breathing Symptoms Summary

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 1	Change from Baseline	n Mean SD Median Min. Max.	54 -0.33 1.145 -0.05 -3.6 2.8	54 -0.67 1.569 -0.33 -6.1 5.4
Week 2	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	54 2.79 2.677 2.03 0.0 9.0	54 2.81 2.626 2.00 0.0 10.0 8 (15%)
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.44 1.048 0.00 -3.2 1.7	54 -1.27 2.154 -0.87 -8.2 5.5

Page 98 of 192

.. . . . .

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 99 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 3	Symptom Severity Score	n Mean SD Median Min. Max.	54 2.76 2.579 2.33 0.0 9.2	54 2.64 2.559 1.93 0.0 10.0
		Subjects with no reported symptoms	12 (22%)	11 (20%)
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.47 1.001 -0.19 -3.5 1.7	54 -1.44 2.441 -0.57 -8.3 4.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 100 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 4	Symptom Severity Score	n Mean SD Median Min. Max.	54 2.56 2.582 1.71 0.0 10.0	54 2.56 2.524 1.86 0.0 10.0
		Subjects with no reported symptoms	12 (22%)	9 (17%)
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.67 1.527 -0.21 -6.4 1.6	54 -1.52 2.533 -0.98 -8.5 4.4

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 101 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 5	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.76 2.469 2.50 0.0 10.0	50 2.54 2.584 2.07 0.0 10.0
		Subjects with no reported symptoms	8 (15%)	10 (19%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.69 1.443 -0.14 -4.6 1.3	50 -1.74 2.823 -1.14 -8.9 3.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 102 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 6	Symptom Severity Score	n Mean SD Median Min. Max.	51 2.90 2.476 2.50 0.0 10.0	54 2.40 2.628 1.46 0.0 10.0
		Subjects with no reported symptoms	9 (17%)	13 (24%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.41 1.540 -0.03 -5.9 2.3	54 -1.68 2.898 -0.85 -8.9 5.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 103 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 7	Symptom Severity Score	n Mean SD Median Min. Max.	52 2.84 2.889 2.07 0.0	54 2.35 2.552 1.59 0.0 10.0
		Subjects with no reported symptoms	12 (22%)	16 (30%)
	Change from Baseline	n Mean SD Median Min. Max.	52 -0.43 1.803 0.00 -5.9 5.1	54 -1.73 2.851 -1.13 -8.8 4.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 104 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Symptom Severity Score	n Mean SD Median Min. Max.	52 2.77 2.729 2.54 0.0 9.8	54 2.44 2.578 1.66 0.0
		Subjects with no reported symptoms	13 (24%)	13 (24%)
	Change from Baseline	n Mean SD Median Min. Max.	52 -0.50 1.684 0.00 -5.1 4.3	54 -1.64 2.956 -0.87 -8.8 5.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 105 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 9	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.74 2.911 2.00 0.0 9.7	50 2.04 2.445 1.15 0.0
		Subjects with no reported symptoms	12 (22%)	18 (33%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.40 1.620 0.00 -5.5 4.0	50 -1.85 3.004 -1.07 -8.8 4.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 106 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 10	Symptom Severity Score	n Mean SD Median Min. Max.	51 2.64 2.660 1.80 0.0 9.7	52 2.30 2.538 1.00 0.0 10.0
		Subjects with no reported symptoms	12 (22%)	12 (22%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.56 1.749 0.00 -5.7 2.9	52 -1.65 3.047 -0.90 -8.8 4.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 107 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 11	Symptom Severity Score	n Mean SD Median Min. Max.	49 2.60 2.664 2.00 0.0 10.0	52 2.40 2.716 1.41 0.0 10.0
		Subjects with no reported symptoms	10 (19%)	15 (28%)
	Change from Baseline	n Mean SD Median Min. Max.	49 -0.74 1.870 -0.14 -7.0 2.0	52 -1.55 2.859 -0.75 -8.8 3.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 108 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 12	Symptom Severity Score	n Mean SD Median Min. Max.	51 2.67 2.663 2.00 0.0 9.6	53 2.31 2.645 1.33 0.0
		Subjects with no reported symptoms	11 (20%)	16 (30%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.56 1.837 0.00 -7.1 2.4	53 -1.71 2.928 -1.00 -8.8 2.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 109 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 13	Symptom Severity Score	n Mean SD Median Min. Max.	43 2.74 2.744 2.14 0.0 10.0	48 2.22 2.607 1.23 0.0 10.0
		Subjects with no reported symptoms	11 (20%)	18 (33%)
	Change from Baseline	n Mean SD Median Min. Max.	43 -0.76 2.189 0.00 -7.1 3.3	48 -1.96 2.975 -1.10 -8.9 2.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 110 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 14	Symptom Severity Score	n Mean SD Median Min. Max.	50 2.54 2.687 1.85 0.0 9.4	53 2.21 2.521 1.57 0.0 10.0
		Subjects with no reported symptoms	12 (22%)	17 (31%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.73 2.187 0.00 -7.1 3.5	53 -1.82 2.880 -0.98 -8.9 3.5

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 111 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 15	Symptom Severity Score	n Mean SD Median Min. Max.	50 2.38 2.545 2.00 0.0 9.0	53 2.32 2.541 1.20 0.0 10.0
		Subjects with no reported symptoms	14 (26%)	17 (31%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.89 1.962 -0.15 -7.1 3.1	53 -1.70 2.850 -1.00 -8.9 4.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 112 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Symptom Severity Score	n Mean SD Median Min. Max.	51 2.42 2.484 1.86 0.0 8.9	52 2.18 2.473 1.31 0.0 10.0
	Change from Baseline	reported symptoms  n Mean SD Median Min. Max.	51 -0.82 2.005 0.00 -6.6 2.8	52 -1.77 2.808 -1.12 -8.8 4.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 113 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 17	Symptom Severity Score	n Mean SD Median Min. Max.	41 2.42 2.769 1.29 0.0 9.8	42 2.17 2.528 1.14 0.0 10.0
		Subjects with no reported symptoms	11 (20%)	11 (20%)
	Change from Baseline	n Mean SD Median Min. Max.	41 -0.86 2.328 -0.29 -6.8 4.9	42 -2.12 2.717 -1.14 -8.8 2.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 114 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 18	Symptom Severity Score	n Mean SD Median Min. Max.	48 2.62 2.655 2.00 0.0 9.3	51 1.92 2.246 1.14 0.0 10.0
		Subjects with no reported symptoms	11 (20%)	14 (26%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.73 2.251 0.00 -7.1 4.4	51 -2.08 2.754 -1.29 -8.8 4.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

### CONFIDENTIAL

Protocol: 200622 Page 115 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 19	Symptom Severity Score	n Mean SD Median Min. Max.	48 2.71 2.733 2.14 0.0 9.7	51 2.01 2.178 1.17 0.0 9.0
		Subjects with no reported symptoms	13 (24%)	15 (28%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.63 2.315 0.00 -7.1 4.8	51 -1.99 2.760 -1.29 -8.8 4.5

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 116 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 20	Symptom Severity Score	n Mean SD Median Min. Max.	48 2.71 2.749 2.07 0.0 9.5	52 1.88 2.197 1.14 0.0
		Subjects with no reported symptoms	13 (24%)	16 (30%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.63 2.110 -0.10 -7.1 4.6	52 -2.11 2.634 -1.20 -8.8 2.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 117 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 21	Symptom Severity Score	n Mean SD Median Min. Max.	46 2.57 2.542 1.92 0.0 9.3	46 1.87 2.306 1.14 0.0
		Subjects with no reported symptoms	10 (19%)	16 (30%)
	Change from Baseline	n Mean SD Median Min. Max.	46 -0.60 1.908 -0.14 -5.3 4.5	46 -2.44 2.762 -1.45 -8.9 2.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

### CONFIDENTIAL

Protocol: 200622 Page 118 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 22	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.56 2.591 2.00 0.0 8.7	51 1.75 2.152 1.00 0.0 10.0
		Subjects with no reported symptoms	12 (22%)	13 (24%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.75 1.920 0.00 -7.1 2.3	51 -2.32 2.655 -1.29 -8.9 1.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

### 2019N406842 00 CONFIDENTIAL

Protocol: 200622 Page 119 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Symptom: Worst Level of Breathing Symptoms Summary

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 23	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.66 2.853 2.14 0.0 9.7	49 1.69 2.109 1.00 0.0
		Subjects with no reported symptoms	15 (28%)	12 (22%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.76 2.275 0.00 -7.1 4.8	49 -2.46 2.652 -1.50 -8.9 1.0

 $200\overline{6}22$ 

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 120 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.50 2.791 2.00 0.0 9.0	48 1.79 2.138 1.14 0.0 10.0
		Subjects with no reported symptoms	16 (30%)	12 (22%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.83 2.163 0.00 -7.1 2.9	48 -2.29 2.726 -1.48 -8.9 1.4

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 121 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 25	Symptom Severity Score	n Mean SD Median Min. Max.	45 2.55 2.596 2.00 0.0 9.0	44 1.61 1.675 1.15 0.0 6.0
		Subjects with no reported symptoms	12 (22%)	11 (20%)
	Change from Baseline	n Mean SD Median Min. Max.	45 -0.80 2.132 0.00 -7.1 2.5	44 -2.11 2.841 -1.36 -8.9 5.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 122 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 26	Symptom Severity Score	n Mean SD Median Min. Max.	49 2.50 2.659 2.00 0.0 9.0	50 1.94 2.113 1.14 0.0 10.0
		Subjects with no reported symptoms	17 (31%)	11 (20%)
	Change from Baseline	n Mean SD Median Min. Max.	49 -0.88 2.062 -0.14 -7.1 2.3	50 -2.13 2.865 -1.20 -8.9 4.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 123 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 27	Symptom Severity Score	n Mean SD Median Min. Max.	50 2.65 2.780 2.23 0.0 9.0	50 1.94 2.186 1.15 0.0 10.0
		Subjects with no reported symptoms	18 (33%)	13 (24%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.68 2.270 -0.07 -7.1 5.9	50 -2.12 2.621 -1.20 -8.9 3.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 124 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 28	Symptom Severity Score	n Mean SD Median Min. Max.	48 2.78 3.042 2.00 0.0 10.0	50 1.91 2.204 1.17 0.0 10.0
		Subjects with no reported symptoms	16 (30%)	13 (24%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.51 2.451 0.00 -7.0 5.1	50 -2.15 2.793 -1.24 -8.9 1.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 125 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 29	Symptom Severity Score	n Mean SD Median Min. Max.	44 2.25 2.384 2.00 0.0 7.8	40 1.69 2.118 1.00 0.0 8.0
		Subjects with no reported symptoms	15 (28%)	12 (22%)
	Change from Baseline	n Mean SD Median Min. Max.	44 -0.91 2.171 -0.04 -6.9 3.1	40 -2.59 3.066 -1.27 -9.0 1.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 126 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 30	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.44 2.569 2.00 0.0 9.0	51 1.82 2.194 1.00 0.0 9.9
		Subjects with no reported symptoms	16 (30%)	14 (26%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.87 2.010 -0.14 -6.9 3.3	51 -2.18 2.810 -1.14 -9.3 2.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 127 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 31	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.53 2.646 2.00 0.0 9.0	51 1.86 2.252 1.00 0.0 10.0
		Subjects with no reported symptoms	14 (26%)	18 (33%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.83 2.065 0.00 -6.6 2.9	51 -2.14 2.786 -1.33 -9.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 128 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.59 2.641 1.67 0.0 9.0	50 2.03 2.375 1.18 0.0 10.0
		Subjects with no reported symptoms	14 (26%)	17 (31%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.69 2.311 0.00 -6.8 3.0	50 -1.89 2.823 -1.13 -10.0 4.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 129 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	54 2.90 2.827 2.21 0.0 10.0	54 3.51 3.043 3.00 0.0 10.0 4 (7%)
Week 1	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	54 2.66 2.570 2.00 0.0 10.0	54 2.95 2.732 2.62 0.0 10.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 130 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 1	Change from Baseline	n Mean SD Median Min. Max.	54 -0.24 1.298 0.00 -3.2 3.7	54 -0.56 1.269 -0.14 -5.1 2.7
Week 2	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	54 2.72 2.701 2.00 0.0 10.0	54 2.64 2.569 2.00 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.18 1.622 0.00 -4.1 5.7	54 -0.87 1.890 -0.15 -8.0 2.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

## CONFIDENTIAL

Protocol: 200622 Page 131 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 3	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	54 2.68 2.658 2.00 0.0 10.0	54 2.41 2.378 1.64 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.22 1.704 -0.04 -5.0 5.0	54 -1.10 2.238 -0.23 -8.6 2.5

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 132 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 4	Symptom Severity Score	n Mean SD Median Min. Max.	54 2.72 2.655 1.96 0.0 10.0	54 2.41 2.357 1.73 0.0 10.0
		Subjects with no reported symptoms	12 (22%)	9 (17%)
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.18 1.823 0.00 -6.0 7.3	54 -1.11 2.277 -0.37 -8.8 3.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 133 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint	mo Sammar <sub>i</sub>	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 5	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.64 2.526 2.43 0.0 10.0	50 2.44 2.479 1.67 0.0
		Subjects with no reported symptoms	10 (19%)	10 (19%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.35 1.720 0.00 -4.3 5.6	50 -1.23 2.372 -0.34 -7.5 2.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

### 2019N406842 00 CONFIDENTIAL $200\overline{6}22$

Protocol: 200622 Page 134 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 6	Symptom Severity Score	n Mean SD Median Min. Max.	51 2.52 2.538 2.00 0.0 9.8	54 2.33 2.276 1.76 0.0 10.0
		Subjects with no reported symptoms	14 (26%)	9 (17%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.38 1.534 0.00 -5.3 4.3	54 -1.18 2.360 -0.31 -7.1 3.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 135 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 7	Symptom Severity Score	n Mean SD Median Min. Max.	52 2.42 2.612 1.54 0.0 9.7	54 2.53 2.254 1.71 0.0 9.8
		Subjects with no reported symptoms	14 (26%)	7 (13%)
	Change from Baseline	n Mean SD Median Min. Max.	52 -0.45 1.769 -0.14 -5.7 5.3	54 -0.98 2.415 -0.50 -7.0 4.4

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 136 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Symptom Severity Score	n Mean SD Median Min. Max.	52 2.43 2.549 1.67 0.0 8.8	54 2.44 2.213 2.00 0.0 9.6
		Subjects with no reported symptoms	13 (24%)	8 (15%)
	Change from Baseline	n Mean SD Median Min. Max.	52 -0.44 1.769 -0.15 -5.7 4.4	54 -1.07 2.387 -0.39 -7.0 2.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 137 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 9	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.63 2.868 1.50 0.0 8.7	50 2.06 2.132 1.27 0.0 8.6
		Subjects with no reported symptoms	14 (26%)	9 (17%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.18 1.689 0.00 -5.7 4.3	50 -1.38 2.533 -0.31 -7.6 2.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 138 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 10	Symptom Severity Score	n Mean SD Median Min. Max.	51 2.31 2.573 1.33 0.0 8.8	52 2.02 2.038 1.45 0.0 8.0
		Subjects with no reported symptoms	14 (26%)	11 (20%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.48 1.816 0.00 -6.5 3.0	52 -1.36 2.469 -0.64 -7.6 3.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 139 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint	one of animal y	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
 Week 11	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	49 2.28 2.578 1.40 0.0 8.8	52 2.33 2.289 2.00 0.0 8.8
	Change from Baseline	n Mean SD Median Min. Max.	49 -0.67 1.720 -0.20 -5.9 2.9	52 -1.06 2.519 -0.58 -8.1 6.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

## CONFIDENTIAL

Protocol: 200622 Page 140 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 12	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	51 2.23 2.539 1.33 0.0 8.7	53 2.43 2.352 1.57 0.0 9.0
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.63 1.737 -0.29 -5.9 3.8	53 -1.02 2.663 -0.57 -7.8 6.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 141 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 13	Symptom Severity Score	n Mean SD Median Min. Max.	43 2.34 2.332 1.14 0.0 8.3	48 2.32 2.345 1.85 0.0 10.0
		Subjects with no reported symptoms	8 (15%)	8 (15%)
	Change from Baseline	n Mean SD Median Min. Max.	43 -0.77 1.825 -0.57 -5.9 2.8	48 -1.21 2.533 -0.24 -7.6 4.4

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 142 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 14	Symptom Severity Score	n Mean SD Median Min. Max.	50 2.33 2.595 1.35 0.0 9.0	53 2.14 2.305 1.43 0.0 9.6
		Subjects with no reported symptoms	14 (26%)	12 (22%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.59 2.014 -0.14 -6.5 6.1	53 -1.30 2.334 -0.71 -8.0 3.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## 2019N406842 00 CONFIDENTIAL

Protocol: 200622 Page 143 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Symptom: Worst Level of Nasal or Sinus Symptoms Summary

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 15	Symptom Severity Score	n Mean SD Median Min. Max.	50 2.39 2.573 1.14 0.0 8.3	53 2.27 2.241 1.43 0.0 9.9
		Subjects with no reported symptoms	15 (28%)	9 (17%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.53 1.783 -0.15 -6.7 3.6	53 -1.17 2.223 -0.86 -8.0 2.9

 $200\overline{6}22$ 

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 144 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Symptom Severity Score	n Mean SD Median Min. Max.	51 2.35 2.439 1.43 0.0 8.8	52 2.21 2.213 1.46 0.0 10.0
		Subjects with no reported symptoms	16 (30%)	9 (17%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.51 1.716 0.00 -6.5 2.7	52 -1.18 2.219 -0.43 -8.0 3.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 145 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 17	Symptom Severity Score	n Mean SD Median Min. Max.	41 2.23 2.694 1.00 0.0 9.5	42 2.48 2.300 2.00 0.0 10.0
		Subjects with no reported symptoms	12 (22%)	6 (11%)
	Change from Baseline	n Mean SD Median Min. Max.	41 -0.60 2.206 0.00 -6.0 5.1	42 -1.39 2.361 -0.43 -7.6 3.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## 2019N406842 00 CONFIDENTIAL

Protocol: 200622 Page 146 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Symptom: Worst Level of Nasal or Sinus Symptoms Summary

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 18	Symptom Severity Score	n Mean SD Median Min. Max.	48 2.47 2.607 1.76 0.0 9.3	51 2.20 2.091 1.57 0.0 8.8
		Subjects with no reported symptoms	13 (24%)	10 (19%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.54 2.035 -0.07 -6.4 4.8	51 -1.24 2.262 -0.69 -7.6 3.4

 $200\overline{6}22$ 

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

## CONFIDENTIAL

Protocol: 200622 Page 147 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 19	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	48 2.40 2.554 1.53 0.0 8.3	51 2.33 2.276 2.00 0.0 10.0
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.62 1.843 -0.14 -6.7 3.6	51 -1.11 2.621 -0.71 -6.7 7.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 148 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint	one samuely	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 20	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	48 2.57 2.545 1.86 0.0 8.8	52 2.36 2.330 1.75 0.0 9.0
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.44 1.895 0.00 -6.7 3.6	52 -1.06 2.632 -0.29 -7.9 4.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 149 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 21	Symptom Severity Score	n Mean SD Median Min. Max.	46 2.46 2.562 1.83 0.0 9.0	46 2.43 2.187 1.90 0.0 8.6
		Subjects with no reported symptoms	12 (22%)	6 (11%)
	Change from Baseline	n Mean SD Median Min. Max.	46 -0.64 2.069 -0.29 -6.5 4.2	46 -1.21 2.583 -0.43 -8.1 3.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 150 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 22	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.43 2.457 2.00 0.0 9.0	51 2.28 2.075 1.86 0.0 8.0
		Subjects with no reported symptoms	12 (22%)	9 (17%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.56 1.746 0.00 -6.7 3.1	51 -1.21 2.475 -0.40 -8.1 3.5

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 151 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 23	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.36 2.477 2.00 0.0 9.0	49 2.29 2.049 2.00 0.0 7.0
		Subjects with no reported symptoms	14 (26%)	10 (19%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.72 2.033 0.00 -6.7 4.4	49 -1.29 2.438 -0.43 -8.1 2.4

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 152 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	47 2.31 2.519 1.71 0.0 8.7	48 2.29 1.967 1.83 0.0 6.7
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.74 1.990 0.00 -6.7 3.3	48 -1.23 2.477 -0.23 -8.1 2.4

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 153 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 25	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	45 2.22 2.161 2.00 0.0 8.9	44 2.16 1.852 1.73 0.0 6.1 8 (15%)
	Change from Baseline	n Mean SD Median Min. Max.	45 -0.74 2.078 0.00 -6.7 3.5	44 -0.93 1.990 -0.15 -7.6 1.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 154 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 26	Symptom Severity Score	n Mean SD Median Min. Max.	49 2.30 2.429 2.00 0.0 9.5	50 2.36 2.077 2.00 0.0 8.8
		Subjects with no reported symptoms	14 (26%)	8 (15%)
	Change from Baseline	n Mean SD Median Min. Max.	49 -0.72 2.174 0.00 -6.7 3.9	50 -1.15 2.554 -0.44 -8.1 5.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 155 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 27	Symptom Severity Score	n Mean SD Median Min. Max.	50 2.35 2.546 2.00 0.0 9.5	50 2.42 2.253 1.83 0.0 8.2
		Subjects with no reported symptoms	17 (31%)	10 (19%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.61 2.410 0.00 -6.7 8.0	50 -1.09 2.428 -0.15 -8.1 5.2

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 156 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 28	Symptom Severity Score	n Mean SD Median Min. Max.	48 2.59 2.671 2.07 0.0 10.0	50 2.29 2.042 1.92 0.0 7.3
		Subjects with no reported symptoms	14 (26%)	10 (19%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.41 2.271 0.00 -6.7 5.5	50 -1.22 2.298 -0.47 -8.1 4.4

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

. . . . .

## CONFIDENTIAL

Protocol: 200622 Page 157 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 29	Symptom Severity Score	n Mean SD Median Min. Max.	44 2.41 2.301 2.00 0.0 8.8	40 2.38 2.074 1.67 0.0 8.0
		Subjects with no reported symptoms	11 (20%)	6 (11%)
	Change from Baseline	n Mean SD Median Min. Max.	44 -0.55 2.347 -0.07 -6.7 4.0	40 -1.30 2.610 -0.73 -8.1 4.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## 2019N406842 00 CONFIDENTIAL

Protocol: 200622 Page 158 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Symptom: Worst Level of Nasal or Sinus Symptoms Summary

Analysis Time Point	Endpoint	and Schulder y	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 30	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	47 2.32 2.682 1.67 0.0 9.8	51 2.14 2.022 1.60 0.0 8.5
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.66 2.401 0.00 -6.7 4.8	51 -1.30 2.207 -0.57 -8.1 1.7

 $200\overline{6}22$ 

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 159 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 31	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.34 2.700 1.43 0.0 10.0	51 2.10 2.058 1.20 0.0 7.6
		Subjects with no reported symptoms	15 (28%)	10 (19%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.62 2.254 0.00 -6.7 4.7	51 -1.35 2.210 -0.57 -8.1 1.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

## CONFIDENTIAL

Protocol: 200622 Page 160 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.68 2.901 2.00 0.0 10.0	50 2.19 2.218 1.63 0.0 8.0
		Subjects with no reported symptoms	15 (28%)	11 (20%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.25 2.407 0.00 -6.7 7.5	50 -1.19 2.310 -0.23 -8.1 2.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 161 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Symptom Severity Score	n Mean SD Median Min. Max.	54 3.37 3.143 2.50 0.0 9.0	54 2.94 2.800 2.14 0.0 9.3
		Subjects with no reported symptoms	11 (20%)	12 (22%)
Week 1	Symptom Severity Score	n Mean SD Median Min. Max.	54 3.11 2.878 2.33 0.0 9.2	54 2.36 2.521 1.54 0.0 8.1
		Subjects with no reported symptoms	14 (26%)	13 (24%)

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 162 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 1	Change from Baseline	n Mean SD Median Min. Max.	54 -0.26 1.329 0.00 -4.2 3.4	54 -0.58 1.408 -0.08 -6.6 1.4
Week 2	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	54 3.17 2.832 2.24 0.0 9.5	54 2.33 2.307 1.71 0.0 8.0
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.20 1.327 -0.14 -4.2 3.2	54 -0.60 1.661 0.00 -7.3 1.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 163 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 3	Symptom Severity Score	n Mean SD Median Min. Max.	54 2.93 2.880 1.79 0.0	54 2.14 2.391 1.50 0.0 8.3
		Subjects with no reported symptoms	15 (28%)	15 (28%)
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.44 1.415 -0.15 -4.5 2.7	54 -0.80 1.782 -0.21 -8.3 3.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 164 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 4	Symptom Severity Score	n Mean SD Median Min. Max.	54 2.96 2.933 2.10 0.0 9.5	54 2.07 2.387 1.07 0.0 8.3
		Subjects with no reported symptoms	16 (30%)	14 (26%)
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.41 1.651 -0.29 -3.9 4.7	54 -0.86 1.834 -0.27 -8.3 2.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 165 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 5	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.87 2.889 2.00 0.0 9.3	50 1.94 2.448 1.00 0.0 8.3
		Subjects with no reported symptoms	13 (24%)	20 (37%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.49 1.916 -0.17 -4.7 4.9	50 -1.11 1.966 -0.54 -8.3 2.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

### CONFIDENTIAL

Protocol: 200622 Page 166 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 6	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no	51 2.77 2.748 1.57 0.0 9.0 13 (24%)	54 2.14 2.325 1.31 0.0 8.7
	Change from Baseline	reported symptoms  n Mean SD Median Min. Max.	51 -0.42 1.799 0.00 -5.1 3.9	54 -0.80 2.119 -0.23 -8.4 3.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 167 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 7	Symptom Severity Score	n Mean SD Median Min. Max.	52 2.96 2.757 2.57 0.0 8.6	54 2.06 2.305 1.31 0.0 8.1
		Subjects with no reported symptoms	14 (26%)	13 (24%)
	Change from Baseline	n Mean SD Median Min. Max.	52 -0.29 2.063 0.00 -4.7 5.0	54 -0.87 2.068 -0.43 -8.3 3.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 168 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no	52 2.76 2.548 2.37 0.0 8.0	54 1.98 2.168 1.21 0.0 8.3
	Change from Baseline	reported symptoms  n Mean SD Median Min. Max.	52 -0.49 1.996 -0.23 -5.7 4.1	54 -0.96 2.107 -0.54 -8.3 3.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 169 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 9	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	47 2.49 2.598 1.67 0.0 8.3	50 2.08 2.420 1.10 0.0 8.4 17 (31%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.59 2.187 -0.14 -6.4 5.5	50 -0.74 2.296 -0.42 -8.3 3.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 170 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 10	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	51 2.48 2.656 1.33 0.0 8.6	52 1.97 2.445 1.00 0.0 8.6
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.74 2.292 -0.29 -6.4 5.4	52 -0.81 2.248 -0.40 -8.1 4.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 171 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 11	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no	49 2.61 2.684 1.60 0.0 10.0	52 2.12 2.506 1.27 0.0 9.2
	Change from Baseline	reported symptoms  n Mean SD Median Min. Max.	49 -0.58 2.176 -0.29 -5.9 5.7	52 -0.82 2.371 -0.20 -8.3 3.9

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 172 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 12	Symptom Severity Score	n Mean SD Median Min. Max.	51 2.55 2.559 1.71 0.0 10.0	53 2.12 2.360 1.33 0.0 8.8
		Subjects with no reported symptoms	14 (26%)	14 (26%)
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.60 2.216 0.00 -6.1 5.7	53 -0.76 2.426 -0.14 -7.9 4.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 173 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 13	Symptom Severity Score	n Mean SD Median Min. Max.	43 2.36 2.543 1.14 0.0 10.0	48 2.44 2.441 2.17 0.0 8.2
		Subjects with no reported symptoms	13 (24%)	15 (28%)
	Change from Baseline	n Mean SD Median Min. Max.	43 -0.92 2.245 -0.67 -5.5 4.1	48 -0.39 2.483 0.00 -7.0 5.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 174 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 14	Symptom Severity Score	n Mean SD Median Min. Max.	50 2.38 2.519 1.27 0.0 10.0	53 2.27 2.318 1.50 0.0 8.0
		Subjects with no reported symptoms	16 (30%)	13 (24%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.71 2.255 -0.23 -5.5 4.7	53 -0.61 2.286 -0.25 -7.0 5.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 175 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 15	Symptom Severity Score	n Mean SD Median Min. Max.	50 2.48 2.535 1.68 0.0 10.0	53 2.28 2.356 1.50 0.0 8.0
		Subjects with no reported symptoms	14 (26%)	14 (26%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.61 2.088 -0.14 -6.3 4.0	53 -0.60 2.416 -0.17 -7.0 7.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 176 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no	51 2.50 2.629 1.60 0.0 10.0	52 2.24 2.415 1.29 0.0 8.2
	Change from Baseline	reported symptoms  n Mean SD Median Min. Max.	51 -0.65 2.245 -0.14 -7.1 4.6	52 -0.69 2.377 -0.21 -6.9 7.4

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 177 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 17	Symptom Severity Score	n Mean SD Median Min. Max.	41 2.44 2.635 1.33 0.0 9.4	42 2.23 2.336 1.75 0.0 8.5
		Subjects with no reported symptoms	13 (24%)	10 (19%)
	Change from Baseline	n Mean SD Median Min. Max.	41 -0.57 2.106 -0.17 -6.4 4.1	42 -0.67 2.244 -0.14 -7.0 3.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 178 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 18	Symptom Severity Score	n Mean SD Median Min. Max.	48 2.44 2.427 2.15 0.0 9.0	51 2.36 2.607 1.43 0.0 8.7
	Change from Baseline	reported symptoms  n Mean SD Median Min. Max.	48 -0.58 2.190 -0.15 -5.9 4.0	51 -0.39 2.445 -0.17 -7.0 7.7

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 179 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 19	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no reported symptoms	48 2.45 2.465 1.69 0.0 9.0	51 2.11 2.363 1.20 0.0 8.6
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.58 2.143 0.00 -6.1 3.6	51 -0.64 2.291 -0.25 -6.9 7.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

### CONFIDENTIAL

Protocol: 200622 Page 180 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 20	Symptom Severity Score	n Mean SD Median Min. Max.	48 2.50 2.566 1.71 0.0 10.0	52 2.03 2.288 1.42 0.0 8.7
		Subjects with no reported symptoms	14 (26%)	16 (30%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.53 2.013 -0.07 -5.1 5.0	52 -0.74 2.080 -0.30 -7.2 3.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 181 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 21	Symptom Severity Score	n Mean SD Median Min. Max.	46 2.59 2.643 2.08 0.0 9.8	46 2.08 2.424 1.00 0.0 9.3
		Subjects with no reported symptoms	13 (24%)	15 (28%)
	Change from Baseline	n Mean SD Median Min. Max.	46 -0.40 2.001 0.00 -5.1 3.9	46 -0.81 2.143 -0.35 -7.6 3.3

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 182 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 22	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.51 2.531 2.00 0.0 9.2	51 2.15 2.334 1.40 0.0 9.0
		Subjects with no reported symptoms	15 (28%)	14 (26%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.55 2.129 0.00 -5.1 4.3	51 -0.67 2.109 -0.25 -6.0 4.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 183 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 23	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.60 2.680 2.00 0.0 9.5	49 2.24 2.526 1.33 0.0 8.0
		Subjects with no reported symptoms	12 (22%)	17 (31%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.49 2.286 0.00 -5.6 5.1	49 -0.63 2.611 -0.17 -7.1 6.5

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 184 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.48 2.567 1.67 0.0 9.0	48 2.39 2.655 1.29 0.0 9.4
		Subjects with no reported symptoms	11 (20%)	14 (26%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.44 2.295 0.00 -6.0 4.1	48 -0.53 2.720 -0.37 -7.2 8.4

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 185 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 25	Symptom Severity Score	n Mean SD Median Min. Max.	45 2.60 2.619 2.00 0.0 9.0	44 2.58 2.785 1.71 0.0 9.8
		Subjects with no reported symptoms	13 (24%)	14 (26%)
	Change from Baseline	n Mean SD Median Min. Max.	45 -0.83 2.472 0.00 -6.1 3.7	44 -0.11 2.637 0.00 -5.8 8.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

### CONFIDENTIAL

Protocol: 200622 Page 186 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 26	Symptom Severity Score	n Mean SD Median Min. Max.	49 2.50 2.506 1.67 0.0 9.0	50 2.39 2.618 1.36 0.0 8.5
		Subjects with no reported symptoms	12 (22%)	14 (26%)
	Change from Baseline	n Mean SD Median Min. Max.	49 -0.64 2.248 0.00 -6.6 4.7	50 -0.42 2.409 -0.17 -5.5 7.5

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 187 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 27	Symptom Severity Score	n Mean SD Median Min. Max.	50 2.47 2.662 1.55 0.0 9.0	50 2.40 2.662 1.63 0.0 10.0
		Subjects with no reported symptoms	14 (26%)	16 (30%)
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.74 2.177 -0.15 -7.0 3.5	50 -0.41 2.535 -0.17 -6.4 9.0

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 188 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 28	Symptom Severity Score	n Mean SD Median Min. Max.	48 2.42 2.560 1.50 0.0 9.0	50 2.38 2.603 1.62 0.0 9.6
		Subjects with no reported symptoms	11 (20%)	14 (26%)
	Change from Baseline	n Mean SD Median Min. Max.	48 -0.57 2.348 0.00 -7.0 4.9	50 -0.43 2.464 -0.14 -6.9 8.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 189 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 29	Symptom Severity Score	n Mean SD Median Min. Max.	44 2.58 2.543 2.00 0.0 9.0	40 1.90 2.172 1.00 0.0 6.8
		Subjects with no reported symptoms	11 (20%)	13 (24%)
	Change from Baseline	n Mean SD Median Min. Max.	44 -0.31 2.162 0.00 -6.1 5.7	40 -1.03 2.720 -0.15 -7.6 5.1

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

. . . . .

Protocol: 200622 Page 190 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 30	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.67 2.742 2.00 0.0 9.6	51 2.00 2.452 1.00 0.0 9.0
		Subjects with no reported symptoms	12 (22%)	19 (35%)
	Change from Baseline	n Mean SD Median Min. Max.	47 -0.40 2.227 0.00 -6.1 4.4	51 -0.75 2.461 -0.29 -7.6 5.5

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

CONFIDENTIAL

Protocol: 200622 Page 191 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 31	Symptom Severity Score	n Mean SD Median Min. Max. Subjects with no	47 2.67 2.773 1.86 0.0 9.2	51 2.00 2.309 1.14 0.0 7.9
	Change from Baseline	reported symptoms  n Mean SD Median Min. Max.	47 -0.42 2.163 0.00 -6.1 6.0	51 -0.75 2.317 -0.43 -6.7 5.6

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

2019N406842 00  $200\overline{6}22$ 

Protocol: 200622 Page 192 of 192

Population: Intent-to-Treat

Table 2.38

Summary of HES Symptom Severity Score (HES-DS) by Symptom

Analysis Time Point	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Symptom Severity Score	n Mean SD Median Min. Max.	47 2.68 2.685 2.17 0.0 8.7	50 2.17 2.403 1.20 0.0 8.7
	Change from Baseline	reported symptoms  n Mean SD Median Min. Max.	47 -0.31 2.104 0.00 -5.8 5.7	50 -0.64 2.519 -0.17 -7.1 5.8

<sup>1.</sup> The mean of the available assessments on the 7 days up to and including the date of each study visit is used as the value for that visit. For time points between visits i.e week 1, 2, 3, 5, 6, 7, 9, 10, 11, 13, 14, 15, 17, 18, 19, 21, 22, 23, 25, 26, 27, 29, 30, 31, the number of available assessments depends on the elapsed time between visits.

<sup>2.</sup> Scale 0 = None to 10 = As bad as you can imagine.

Protocol: 200622 Page 2 of 2

Population: Intent-to-Treat

Table 90.44

Subgroup Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) at Week 32 by Duration of Disease (Mixed Model Repeated Measures)

Duration of disease: >=2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	22	32	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	22 18 3.82 (0.402) -0.76 (0.402)	32 30 2.50 (0.314) -2.08 (0.314)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-1.32 (-2.35, -0.29) 0.013	
Corrected Hedges g [3] 95% CI		-0.76 (-1.36, -0.15)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 317 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 1 of 2

Population: Intent-to-Treat

Table 90.45

Subgroup Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) at Week 32 by Baseline Blood Eosinophils (Mixed Model Repeated Measures)

Baseline blood eosinophils: <1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	30	26	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	30 29 3.24 (0.302) -1.21 (0.302)	26 24 3.08 (0.331) -1.37 (0.331)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.16 (-1.07, 0.74) 0.722	
Corrected Hedges g [3] 95% CI		-0.10 (-0.64, 0.44)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 318 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 2

Population: Intent-to-Treat

Table 90.45

Subgroup Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) at Week 32 by Baseline Blood Eosinophils (Mixed Model Repeated Measures)

Baseline blood eosinophils: >=1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	24	28
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	24 18 3.62 (0.431) -0.67 (0.431)	28 26 2.25 (0.381) -2.04 (0.381)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-1.37 (-2.54, -0.21) 0.022
Corrected Hedges g [3] 95% CI		-0.71 (-1.33, -0.09)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 319 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 1 of 1

Population: Intent-to-Treat

Table 90.46

Subgroup Analysis of Change from Baseline in

Most Bothersome HES Symptom Severity Score (HES-DS) at Week 32

p-values for Subgroup-by-Treatment Interactions

Subgroup	Treatment by subgroup interaction p-value
Age (12-<18, 18-64, >=65 Years) Gender (Male, Female) Region (Europe, Rest of World) Duration of disease (<2.76, >=2.76 Years) [1] Baseline blood eosinophils (<1.5, >=1.5 10^9/L)	0.420 0.018 0.464 0.242 0.191

### [1] 2.76 is the median in the ITT population.

Note: Interaction p-values obtained from separate mixed models repeated measures with covariates of treatment, region, baseline, baseline OCS dose, visit, subgroup plus interaction terms for visit-by-baseline, visit-by-treatment and subgroup-by-treatment. Region covariate is categorised as Argentina, Mexico and Brazil; USA; Rest of World; except for the region subgroup model where region is categorised as Europe; Rest of World.

Mepolizumab (Nucala) - HES Seite 320 von 1069

Protocol: 200622 Page 1 of 1

Population: Intent-to-Treat

Table 90.47
Analysis of Proportion of Subjects with an Improvement of >=1.5 in Most Bothersome HES Symptom Severity Score (HES-DS) at Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	54 15 (28%) 39 (72%) 7 (13%)	,
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		0.60 (0.24,1.51) 0.279 0.56 (0.23,1.35) 0.68 (0.36,1.17) -0.13 (-0.31,0.05) 0.224

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

Mepolizumab (Nucala) - HES Seite 321 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Protocol: 200622 Page 1 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Muscle/Joint Pain Summary

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 54 2.89 (0.210) -0.53 (0.210)	54 54 2.69 (0.211) -0.73 (0.211)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.20 (-0.80, 0.40) 0.506	
Corrected Hedges g [3] 95% CI		-0.13 (-0.51, 0.25)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 322 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Muscle/Joint Pain Summary

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 3.04 (0.220) -0.38 (0.220)	54 54 2.59 (0.219) -0.83 (0.219)	•
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.45 (-1.07, 0.17) 0.157	
Corrected Hedges g [3] 95% CI		-0.28 (-0.66, 0.11)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 323 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Muscle/Joint Pain Summary

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 2.87 (0.257) -0.55 (0.257)	54 53 2.96 (0.255) -0.46 (0.255)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.09 (-0.63, 0.81) 0.805	
Corrected Hedges g [3] 95% CI		0.05 (-0.34, 0.43)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 324 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 4 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Muscle/Joint Pain Summary

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 2.84 (0.243) -0.58 (0.243)	54 52 2.70 (0.241) -0.72 (0.241)	•
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.14 (-0.83, 0.54) 0.684	
Corrected Hedges g [3] 95% CI		-0.08 (-0.47, 0.31)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 325 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 5 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Muscle/Joint Pain Summary

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 48 2.91 (0.243) -0.51 (0.243)	54 52 2.41 (0.239) -1.01 (0.239)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.50 (-1.18, 0.18) 0.149	
Corrected Hedges g [3] 95% CI		-0.29 (-0.69, 0.10)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 326 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 6 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Muscle/Joint Pain Summary

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 47 2.96 (0.268) -0.45 (0.268)	54 48 2.50 (0.265) -0.91 (0.265)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.46 (-1.21, 0.29) 0.228	
Corrected Hedges g [3] 95% CI		-0.25 (-0.65, 0.15)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 327 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 7 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Muscle/Joint Pain Summary

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 48 2.86 (0.259) -0.55 (0.259)	54 50 2.52 (0.255) -0.90 (0.255)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.34 (-1.07, 0.39) 0.355
Corrected Hedges g [3] 95% CI		-0.19 (-0.58, 0.21)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 328 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 8 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Muscle/Joint Pain Summary

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 47 3.15 (0.273) -0.27 (0.273)	54 50 2.39 (0.268) -1.03 (0.268)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.76 (-1.52, 0.01) 0.052	
Corrected Hedges g [3] 95% CI		-0.40 (-0.80, 0.00)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 329 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 9 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Chills or Sweats Summary

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 54 1.77 (0.176) -0.51 (0.176)	54 54 1.60 (0.176) -0.68 (0.176)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.17 (-0.67, 0.33) 0.505	
Corrected Hedges g [3] 95% CI		-0.13 (-0.51, 0.25)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 330 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 10 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Chills or Sweats Summary

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 1.65 (0.219) -0.63 (0.219)	54 54 1.65 (0.218) -0.63 (0.218)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.00 (-0.61, 0.62) 0.994	
Corrected Hedges g [3] 95% CI		0.00 (-0.38, 0.38)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 331 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 11 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Chills or Sweats Summary

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 1.78 (0.221) -0.50 (0.221)	54 53 1.51 (0.219) -0.77 (0.219)	_
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.26 (-0.88, 0.36) 0.403	
Corrected Hedges g [3] 95% CI		-0.16 (-0.55, 0.22)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 332 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 12 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Chills or Sweats Summary

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 1.66 (0.221) -0.61 (0.221)	54 52 1.32 (0.220) -0.95 (0.220)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.34 (-0.96, 0.28) 0.282	
Corrected Hedges g [3] 95% CI		-0.21 (-0.60, 0.17)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 333 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 13 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Chills or Sweats Summary

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 48 1.77 (0.249) -0.51 (0.249)	54 52 1.28 (0.245) -1.00 (0.245)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.49 (-1.19, 0.21) 0.165	
Corrected Hedges g [3] 95% CI		-0.28 (-0.67, 0.12)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 334 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 14 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Chills or Sweats Summary

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 47 1.82 (0.263) -0.46 (0.263)	54 48 1.08 (0.260) -1.20 (0.260)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.74 (-1.47, 0.00) 0.051	
Corrected Hedges g [3] 95% CI		-0.41 (-0.81, 0.00)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 335 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 15 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Chills or Sweats Summary

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 48 1.92 (0.283) -0.36 (0.283)	54 50 1.05 (0.279) -1.23 (0.279)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.87 (-1.67, -0.08) 0.031	
Corrected Hedges g [3] 95% CI		-0.44 (-0.84, -0.04)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 336 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 16 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Chills or Sweats Summary

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 47 1.87 (0.245) -0.41 (0.245)	54 50 1.09 (0.242) -1.19 (0.242)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.78 (-1.47, -0.09) 0.026	
Corrected Hedges g [3] 95% CI		-0.46 (-0.86, -0.05)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 337 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 17 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Abdominal Pain/Bloating Summary

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 54 2.47 (0.200) -0.35 (0.200)	54 54 2.37 (0.201) -0.45 (0.201)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.10 (-0.67, 0.47) 0.727	
Corrected Hedges g [3] 95% CI		-0.07 (-0.44, 0.31)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 338 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 18 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Abdominal Pain/Bloating Summary

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 2.61 (0.237) -0.21 (0.237)	54 54 2.34 (0.236) -0.49 (0.236)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.28 (-0.94, 0.39) 0.414	
Corrected Hedges g [3] 95% CI		-0.16 (-0.54, 0.22)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 339 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 19 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Abdominal Pain/Bloating Summary

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 2.55 (0.231) -0.27 (0.231)	54 53 2.37 (0.230) -0.46 (0.230)	_
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.19 (-0.84, 0.46) 0.565	
Corrected Hedges g [3] 95% CI		-0.11 (-0.50, 0.27)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 340 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 20 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Abdominal Pain/Bloating Summary

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 2.47 (0.220) -0.35 (0.220)	54 52 2.28 (0.219) -0.54 (0.219)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.19 (-0.82, 0.43) 0.535
Corrected Hedges g [3] 95% CI		-0.12 (-0.51, 0.26)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 341 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 21 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Abdominal Pain/Bloating Summary

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 48 2.60 (0.245) -0.22 (0.245)	54 52 2.19 (0.242) -0.64 (0.242)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.41 (-1.10, 0.27) 0.236
Corrected Hedges g [3] 95% CI		-0.24 (-0.63, 0.16)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 342 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 22 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Menolizumah

Symptom: Worst Level of Abdominal Pain/Bloating Summary

Visit: Week 24

	Placebo (N=54)	300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 47 2.66 (0.250) -0.16 (0.250)	54 48 2.17 (0.248) -0.65 (0.248)	_
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.50 (-1.20, 0.21) 0.164	
Corrected Hedges g [3] 95% CI		-0.29 (-0.69, 0.12)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 343 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 23 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Abdominal Pain/Bloating Summary

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 48 2.72 (0.246) -0.10 (0.246)	54 50 2.11 (0.243) -0.71 (0.243)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.61 (-1.29, 0.08) 0.084
Corrected Hedges g [3] 95% CI		-0.35 (-0.75, 0.05)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 344 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 24 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Abdominal Pain/Bloating Summary

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 47 2.77 (0.247) -0.05 (0.247)	54 50 2.07 (0.244) -0.75 (0.244)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.70 (-1.39, 0.00) 0.049	
Corrected Hedges g [3] 95% CI		-0.40 (-0.81, 0.00)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 345 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 25 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Breathing Symptoms Summary

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 54 2.85 (0.238) -0.81 (0.238)	54 54 2.24 (0.239) -1.41 (0.239)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.60 (-1.28, 0.07) 0.079
Corrected Hedges g [3] 95% CI		-0.34 (-0.72, 0.04)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 346 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 26 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Breathing Symptoms Summary

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 3.00 (0.278) -0.65 (0.278)	54 54 2.14 (0.277) -1.52 (0.277)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.86 (-1.65, -0.08) 0.031
Corrected Hedges g [3] 95% CI		-0.42 (-0.81, -0.04)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 347 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 27 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Breathing Symptoms Summary

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 2.90 (0.279) -0.75 (0.279)	54 53 2.10 (0.277) -1.55 (0.277)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.80 (-1.58, -0.01) 0.046	
Corrected Hedges g [3] 95% CI		-0.40 (-0.78, -0.01)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 348 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 28 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Breathing Symptoms Summary

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 2.63 (0.262) -1.03 (0.262)	54 52 2.00 (0.261) -1.66 (0.261)	_
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.63 (-1.37, 0.11) 0.094	
Corrected Hedges g [3] 95% CI		-0.33 (-0.72, 0.06)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 349 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 29 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Breathing Symptoms Summary

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 48 2.88 (0.254) -0.77 (0.254)	54 52 1.74 (0.251) -1.92 (0.251)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-1.15 (-1.86, -0.43) 0.002	
Corrected Hedges g [3] 95% CI		-0.64 (-1.04, -0.23)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 350 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 30 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Breathing Symptoms Summary

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 47 2.76 (0.272) -0.90 (0.272)	54 48 1.69 (0.269) -1.97 (0.269)	•
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-1.07 (-1.83, -0.30) 0.007	
Corrected Hedges g [3] 95% CI		-0.57 (-0.98, -0.16)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 351 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 31 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Breathing Symptoms Summary

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 48 3.03 (0.298) -0.62 (0.298)	54 50 1.84 (0.294) -1.82 (0.294)	_
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-1.20 (-2.03, -0.36) 0.005	
Corrected Hedges g [3] 95% CI		-0.57 (-0.98, -0.17)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 352 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 32 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Breathing Symptoms Summary

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 47 2.83 (0.276) -0.82 (0.276)	54 50 1.92 (0.272) -1.73 (0.272)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.91 (-1.68, -0.13) 0.022
Corrected Hedges g [3] 95% CI		-0.47 (-0.88, -0.07)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 353 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 33 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Nasal or Sinus Symptoms Summary

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 54 2.92 (0.239) -0.29 (0.239)	54 54 2.19 (0.240) -1.01 (0.240)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.72 (-1.40, -0.05) 0.036
Corrected Hedges g [3] 95% CI		-0.41 (-0.79, -0.03)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 354 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 34 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Nasal or Sinus Symptoms Summary

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 2.66 (0.238) -0.54 (0.238)	54 54 2.24 (0.236) -0.96 (0.236)	_
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.41 (-1.08, 0.26) 0.222	
Corrected Hedges g [3] 95% CI		-0.24 (-0.62, 0.14)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Seite 355 von 1069 Mepolizumab (Nucala) - HES

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 35 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Nasal or Sinus Symptoms Summary

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 2.45 (0.257) -0.76 (0.257)	54 53 2.30 (0.254) -0.90 (0.254)	_
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.14 (-0.86, 0.58) 0.699	
Corrected Hedges g [3] 95% CI		-0.08 (-0.46, 0.31)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 356 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 36 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Nasal or Sinus Symptoms Summary

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 2.57 (0.218) -0.63 (0.218)	54 52 2.09 (0.216) -1.11 (0.216)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.48 (-1.09, 0.13) 0.123
Corrected Hedges g [3] 95% CI		-0.31 (-0.69, 0.08)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 357 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 37 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Nasal or Sinus Symptoms Summary

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 48 2.70 (0.264) -0.51 (0.264)	54 52 2.31 (0.258) -0.90 (0.258)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.39 (-1.12, 0.35) 0.296	
Corrected Hedges g [3] 95% CI		-0.21 (-0.60, 0.18)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 358 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 38 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Nasal or Sinus Symptoms Summary

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 47 2.53 (0.243) -0.67 (0.243)	54 48 2.16 (0.240) -1.04 (0.240)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.37 (-1.06, 0.31) 0.278	
Corrected Hedges g [3] 95% CI		-0.22 (-0.63, 0.18)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 359 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 39 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Nasal or Sinus Symptoms Summary

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 48 2.82 (0.257) -0.38 (0.257)	54 50 2.14 (0.253) -1.06 (0.253)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.68 (-1.40, 0.04) 0.064
Corrected Hedges g [3] 95% CI		-0.38 (-0.78, 0.02)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 360 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 40 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Nasal or Sinus Symptoms Summary

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 47 2.88 (0.280) -0.32 (0.280)	54 50 2.13 (0.273) -1.07 (0.273)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.75 (-1.53, 0.03) 0.059
Corrected Hedges g [3] 95% CI		-0.39 (-0.79, 0.01)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 361 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 41 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Skin Symptoms Summary

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 54 2.68 (0.215) -0.32 (0.215)	54 54 2.13 (0.215) -0.86 (0.215)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.54 (-1.15, 0.07) 0.080	
Corrected Hedges g [3] 95% CI		-0.34 (-0.72, 0.04)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 362 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 42 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Skin Symptoms Summary

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 2.63 (0.229) -0.37 (0.229)	54 54 2.03 (0.226) -0.96 (0.226)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.59 (-1.24, 0.05) 0.070	
Corrected Hedges g [3] 95% CI		-0.36 (-0.74, 0.03)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 363 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 43 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Skin Symptoms Summary

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 2.48 (0.265) -0.51 (0.265)	54 53 2.22 (0.262) -0.77 (0.262)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.26 (-1.01, 0.48) 0.481	
Corrected Hedges g [3] 95% CI		-0.14 (-0.52, 0.25)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 364 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 44 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Skin Symptoms Summary

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 2.42 (0.271) -0.57 (0.271)	54 52 2.34 (0.268) -0.65 (0.268)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.09 (-0.84, 0.67) 0.824	
Corrected Hedges g [3] 95% CI		-0.04 (-0.43, 0.34)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 365 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 45 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Skin Symptoms Summary

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 48 2.53 (0.242) -0.46 (0.242)	54 52 2.25 (0.237) -0.75 (0.237)	•
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.29 (-0.96, 0.39) 0.402	
Corrected Hedges g [3] 95% CI		-0.17 (-0.56, 0.23)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 366 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 46 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Skin Symptoms Summary

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 47 2.53 (0.298) -0.47 (0.298)	54 48 2.50 (0.294) -0.49 (0.294)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.02 (-0.86, 0.81) 0.956	
Corrected Hedges g [3] 95% CI		-0.01 (-0.41, 0.39)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 367 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 47 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Skin Symptoms Summary

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 48 2.45 (0.289) -0.55 (0.289)	54 50 2.56 (0.283) -0.43 (0.283)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.11 (-0.69, 0.92) 0.782	
Corrected Hedges g [3] 95% CI		0.06 (-0.34, 0.45)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 368 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 48 of 48

Population: Intent-to-Treat

Table 90.48

Analysis of Change from Baseline in HES Symptom Severity Score (HES-DS) by Symptom (Mixed Model Repeated Measures)

Symptom: Worst Level of Skin Symptoms Summary

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 47 2.58 (0.280) -0.41 (0.280)	54 50 2.33 (0.275) -0.66 (0.275)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.25 (-1.04, 0.53) 0.522	
Corrected Hedges g [3] 95% CI		-0.13 (-0.53, 0.27)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 369 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

# CONFIDENTIAL 2019N406842\_00 200622

Protocol: 200622 Page 1 of 3

Population: Intent-to-Treat

Table 2.44

Summary of Clinician-Rated Overall Response to Therapy

Visit		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 4	n Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	51 2 (4%) 8 (16%) 8 (16%) 26 (51%) 5 (10%) 2 (4%)	51 10 (20%) 9 (18%) 10 (20%) 18 (35%) 1 (2%) 2 (4%) 1 (2%)
Week 8	n Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	49 6 (12%) 6 (12%) 10 (20%) 20 (41%) 4 (8%) 3 (6%) 0	47 12 (26%) 6 (13%) 7 (15%) 17 (36%) 3 (6%) 1 (2%) 1 (2%)
Week 12	n Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	46 5 (11%) 9 (20%) 6 (13%) 17 (37%) 7 (15%) 2 (4%) 0	45 13 (29%) 6 (13%) 11 (24%) 11 (24%) 4 (9%) 0

Protocol: 200622 Page 2 of 3

Population: Intent-to-Treat

Table 2.44

Summary of Clinician-Rated Overall Response to Therapy

Visit		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	n Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	44 5 (11%) 4 (9%) 11 (25%) 15 (34%) 5 (11%) 4 (9%)	43 15 (35%) 7 (16%) 11 (26%) 7 (16%) 3 (7%) 0
Week 20	n Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	41 5 (12%) 5 (12%) 8 (20%) 16 (39%) 5 (12%) 2 (5%)	42 12 (29%) 10 (24%) 8 (19%) 9 (21%) 3 (7%) 0
Week 24	n Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	42 3 (7%) 11 (26%) 6 (14%) 14 (33%) 6 (14%) 2 (5%)	42 13 (31%) 7 (17%) 8 (19%) 9 (21%) 4 (10%) 0 1 (2%)

### 2019N406842<u>00</u> 200<del>6</del>22

### CONFIDENTIAL

Protocol: 200622 Page 3 of 3

Population: Intent-to-Treat

Table 2.44 Summary of Clinician-Rated Overall Response to Therapy

Visit		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 28	n Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	42 8 (19%) 4 (10%) 8 (19%) 17 (40%) 4 (10%) 1 (2%)	43 16 (37%) 8 (19%) 5 (12%) 8 (19%) 3 (7%) 3 (7%)
Week 32	n Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	41 3 (7%) 8 (20%) 11 (27%) 12 (29%) 6 (15%) 0 1 (2%)	41 18 (44%) 3 (7%) 7 (17%) 7 (17%) 3 (7%) 3 (7%) 0

Protocol: 200622 Page 1 of 3

Population: Intent-to-Treat
Table

Table 2.46
Summary of Subject-Rated Overall Response to Therapy

Visit		Placebo (N=54)	Mepolizumab 300mg SC (N=54)		
Week 4	n Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	51 2 (4%) 9 (18%) 16 (31%) 18 (35%) 3 (6%) 1 (2%) 2 (4%)	51 12 (24%) 5 (10%) 11 (22%) 17 (33%) 4 (8%) 2 (4%)		
Week 8	n Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	49 6 (12%) 9 (18%) 8 (16%) 22 (45%) 3 (6%) 1 (2%)	47 13 (28%) 6 (13%) 8 (17%) 17 (36%) 1 (2%) 1 (2%)		
Week 12	n Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	46 7 (15%) 5 (11%) 12 (26%) 16 (35%) 4 (9%) 1 (2%) 1 (2%)	45 13 (29%) 7 (16%) 8 (18%) 13 (29%) 2 (4%) 1 (2%) 1 (2%)		

# CONFIDENTIAL 2019N406842\_00 200622

Protocol: 200622 Page 2 of 3

Population: Intent-to-Treat

Table 2.46
Summary of Subject-Rated Overall Response to Therapy

Visit		Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Week 16	n Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	44 5 (11%) 13 (30%) 6 (14%) 19 (43%) 1 (2%) 0	44 12 (27%) 5 (11%) 16 (36%) 9 (20%) 2 (5%) 0	
Week 20	n Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	44 5 (11%) 10 (23%) 12 (27%) 14 (32%) 1 (2%) 2 (5%) 0	42 13 (31%) 6 (14%) 13 (31%) 8 (19%) 2 (5%) 0	
Week 24	n Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	43 5 (12%) 11 (26%) 7 (16%) 16 (37%) 2 (5%) 2 (5%) 0	42 15 (36%) 7 (17%) 7 (17%) 12 (29%) 1 (2%) 0	

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 3 of 3

Population: Intent-to-Treat

Table 2.46
Summary of Subject-Rated Overall Response to Therapy

Visit		Placebo (N=54)		$ \begin{array}{c} {\tt Mepolizumab 300mg} \\ {\tt SC} \\ {\tt (N=54)} \end{array} $	
Week 28	n Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	43 3 8 9 20 1 2	(7%) (19%) (21%) (47%) (2%) (5%)	43 13 11 7 9 1 1	(30%) (26%) (16%) (21%) (2%) (2%) (2%)
Week 32	n Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	41 7 7 9 13 4 1	(17%) (17%) (22%) (32%) (10%) (2%)	42 12 9 12 8 1 0	(29%) (21%) (29%) (19%) (2%)

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 1 of 8

Population: Intent-to-Treat

Table 2.48
Summary of Subject-Rated Symptom Severity

Visit				cebo 54)	_	olizumab 300mg SC:54)
Baseline	SSR Score	n None (0) Mild (1) Moderate (2) Severe (3) Very severe (4)	54 5 12 19 16 2	(9%) (22%) (35%) (30%) (4%)	54 4 11 21 15 3	(7%) (20%) (39%) (28%) (6%)
Week 4	SSR Score	n None (0) Mild (1) Moderate (2) Severe (3) Very severe (4)	51 8 12 23 5 3	(16%) (24%) (45%) (10%) (6%)	51 5 21 18 7 0	•
	Change from Baseline	n 4 point improvement (-4) 3 point improvement (-3) 2 point improvement (-2) 1 point improvement (-1) No change (0) 1 point worsening (1) 2 point worsening (2) 3 point worsening (3) 4 point worsening (4)	51 0 0 6 14 21 9 1 0	(12%) (27%) (41%) (18%) (2%)	51 0 1 7 16 20 6 1 0	(2%) (14%) (31%) (39%) (12%) (2%)

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 2 of 8

Population: Intent-to-Treat

Table 2.48
Summary of Subject-Rated Symptom Severity

Visit		Placebo (N=54)			Mepolizumab 300mg SC (N=54)	
Week 8	SSR Score	n	49		47	
		None (0)	4	(8%)	9	(19%)
		Mild (1)	13	(27%)	16	(34%)
		Moderate (2)	26	(53%)	14	(30%)
		Severe (3)	6	(12%)	6	(13%)
		Very severe (4)	0		2	(4%)
	Change from Baseline	n	49		47	
		4 point improvement (-4)	0		1	(2%)
		3 point improvement (-3)	0		3	(6%)
		2 point improvement (-2)	3	(6%)	7	(15%)
		1 point improvement (-1)	19	(39%)	11	(23%)
		No change (0)	18	(37%)	17	(36%)
		1 point worsening (1)	8	(16%)	4	(9%)
		2 point worsening (2)	1	(2%)	2	(4%)
		3 point worsening (3)	0	. ,	2	(4%)
		4 point worsening (4)	0		0	` '

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 3 of 8

Population: Intent-to-Treat

Table 2.48
Summary of Subject-Rated Symptom Severity

Visit				cebo 54)	_	oolizumab 300mg SC 54)
Week 12	SSR Score	n Narra (0)	46	(200)	45	(100)
		None (0) Mild (1)	9 10	(20%) (22%)	8 14	(18%) (31%)
		Moderate (2)	20	(43%)	17	(38%)
		Severe (3)	6	(13%)	4	(9%)
		Very severe (4)	1	(2%)	2	(4%)
	Change from Baseline	n	46		45	
		4 point improvement (-4)	0		0	
		3 point improvement (-3)	1	(2%)	4	(9%)
		2 point improvement (-2)	5	(11%)	4	(9%)
		1 point improvement (-1)	16	(35%)	14	(31%)
		No change (0)	19	(41%)	15	(33%)
		1 point worsening (1)	3	(7%)	6	(13%)
		2 point worsening (2)	2	(4%)	1	(2%)
		3 point worsening (3)	0		0	
		4 point worsening (4)	0		1	(2%)

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 4 of 8

Population: Intent-to-Treat

Table 2.48
Summary of Subject-Rated Symptom Severity

Visit				.cebo :54)	_	oolizumab 300mg SC:54)
Week 16	SSR Score	n None (0) Mild (1) Moderate (2) Severe (3) Very severe (4)	45 8 12 18 7 0	(18%) (27%) (40%) (16%)	44 7 15 17 5	(16%) (34%) (39%) (11%)
	Change from Baseline	n 4 point improvement (-4) 3 point improvement (-3) 2 point improvement (-2) 1 point improvement (-1) No change (0) 1 point worsening (1) 2 point worsening (2) 3 point worsening (3) 4 point worsening (4)	45 0 2 4 18 11 8 2	(4%) (9%) (40%) (24%) (18%) (4%)	44 0 3 7 13 13 6 0 2	(7%) (16%) (30%) (30%) (14%)

# CONFIDENTIAL 2019N406842\_00 200622

Protocol: 200622 Page 5 of 8

Population: Intent-to-Treat

Table 2.48
Summary of Subject-Rated Symptom Severity

Visit				cebo 54)	_	Mepolizumab 300mg SC (N=54)	
Week 20	SSR Score	n None (0) Mild (1)	45 10 14	(22%) (31%)	42 7 17	(17%) (40%)	
		Moderate (2) Severe (3) Very severe (4)	15 5 1	(33%) (11%) (2%)	15 3 0	(36%) (7%)	
	Change from Baseline	n 4 point improvement (-4) 3 point improvement (-3) 2 point improvement (-2) 1 point improvement (-1) No change (0) 1 point worsening (1) 2 point worsening (2) 3 point worsening (3) 4 point worsening (4)	45 0 0 7 18 15 2 3 0	(16%) (40%) (33%) (4%) (7%)	42 1 2 8 10 15 4 2 0	(2%) (5%) (19%) (24%) (36%) (10%) (5%)	

# CONFIDENTIAL 2019N406842\_00 200622

Protocol: 200622 Page 6 of 8

Population: Intent-to-Treat

Table 2.48
Summary of Subject-Rated Symptom Severity

Visit				cebo :54)	_	oolizumab 300mg SC 54)
Week 24	SSR Score	n	43		42	
		None (0)	6	(14%)	4	(10%)
		Mild (1)	18	(42%)	21	(50%)
		Moderate (2)	11	(26%)	10	(24%)
		Severe (3)	7	(16%)	6	(14%)
		Very severe (4)	1	(2%)	1	(2%)
	Change from Baseline	n	43		42	
		4 point improvement (-4)	0		0	
		3 point improvement (-3)	1	(2%)	2	(5%)
		2 point improvement (-2)	8	(19%)	7	(17%)
		1 point improvement (-1)	10	(23%)	10	(24%)
		No change (0)	17	(40%)	17	(40%)
		1 point worsening (1)	5	(12%)	4	(10%)
		2 point worsening (2)	2	(5%)	2	(5%)
		3 point worsening (3)	0		0	
		4 point worsening (4)	0		0	

2019N406842\_00 200<del>6</del>22

Protocol: 200622 Page 7 of 8

Population: Intent-to-Treat

Table 2.48
Summary of Subject-Rated Symptom Severity

Visit				cebo 54)	_	oolizumab 300mg SC:54)
Week 28	SSR Score	n	43		43	
		None (0)	6	(14%)	6	(14%)
		Mild (1)	16	(37%)	14	(33%)
		Moderate (2)	14	(33%)	17	(40%)
		Severe (3)	5	(12%)	4	(9%)
		Very severe (4)	2	(5%)	2	(5%)
	Change from Baseline	n	43		43	
		4 point improvement (-4)	0		0	
		3 point improvement (-3)	0		4	(9%)
		2 point improvement (-2)	7	(16%)	5	(12%)
		1 point improvement (-1)	12	(28%)	9	(21%)
		No change (0)	18	(42%)	16	(37%)
		1 point worsening (1)	4	(9%)	6	(14%)
		2 point worsening (2)	2	(5%)	2	(5%)
		3 point worsening (3)	0		0	
		4 point worsening (4)	0		1	(2%)

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 8 of 8

Population: Intent-to-Treat

Table 2.48
Summary of Subject-Rated Symptom Severity

Visit			Placebo (N=54)		Mepolizumab 300mg SC (N=54)	
Week 32	SSR Score	n None (0) Mild (1) Moderate (2)	41 6 14 16	(15%) (34%) (39%)	42 8 15 16	(19%) (36%) (38%)
		Severe (3) Very severe (4)	5 0	(12%)	2 1	(5%) (2%)
	Change from Baseline	n 4 point improvement (-4) 3 point improvement (-3) 2 point improvement (-2) 1 point improvement (-1) No change (0) 1 point worsening (1) 2 point worsening (2) 3 point worsening (3) 4 point worsening (4)	41 0 1 5 16 13 4 2 0	(2%) (12%) (39%) (32%) (10%) (5%)	42 0 7 1 14 10 9 1 0	(17%) (2%) (33%) (24%) (21%) (2%)

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 1 of 12

Population: Intent-to-Treat

Table 2.50 Summary of MSAS-SF Total and Subscale Scores

Endpoint: Total Score

Visit	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Total Score	n Mean SD Median Min. Max.	54 0.97 0.614 0.95 0.0 2.5	54 1.03 0.552 1.00 0.1 2.5
Week 4	Total Score	n Mean SD Median Min. Max.	51 0.79 0.660 0.68 0.0 2.9	51 0.73 0.535 0.63 0.0 2.3
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.16 0.394 -0.14 -1.2 0.5	51 -0.28 0.466 -0.15 -1.5 0.6
Week 8	Total Score	n Mean SD Median Min. Max.	49 0.79 0.638 0.69 0.0 2.7	47 0.76 0.505 0.74 0.1 2.2

# CONFIDENTIAL 2019N406842\_00 200622

Protocol: 200622 Page 2 of 12

Population: Intent-to-Treat

Table 2.50 Summary of MSAS-SF Total and Subscale Scores

Endpoint: Total Score

Visit	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Change from Baseline	n Mean SD Median Min. Max.	49 -0.17 0.396 -0.13 -1.0 0.7	47 -0.25 0.489 -0.25 -1.3 1.4
Week 16	Total Score	n Mean SD Median Min. Max.	46 0.75 0.578 0.72 0.0 2.4	44 0.65 0.474 0.62 0.0 1.8
	Change from Baseline	n Mean SD Median Min. Max.	46 -0.21 0.449 -0.16 -1.7 0.8	44 -0.34 0.406 -0.23 -1.4 0.2
Week 24	Total Score	n Mean SD Median Min. Max.	45 0.81 0.658 0.61 0.0 2.6	42 0.63 0.484 0.54 0.0 1.8

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 3 of 12

Population: Intent-to-Treat

Table 2.50 Summary of MSAS-SF Total and Subscale Scores

Endpoint: Total Score

Visit	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Change from Baseline	n Mean SD Median Min. Max.	45 -0.14 0.467 -0.11 -1.1	42 -0.37 0.484 -0.34 -1.7 0.4
Week 32	Total Score	n Mean SD Median Min. Max.	41 0.82 0.679 0.60 0.0 2.6	42 0.61 0.550 0.54 0.0 2.5
	Change from Baseline	n Mean SD Median Min. Max.	41 -0.17 0.476 -0.09 -1.2 0.8	42 -0.35 0.469 -0.31 -1.2 1.0

#### 2019N406842 00 CONFIDENTIAL

Protocol: 200622 Page 4 of 12

Population: Intent-to-Treat

Table 2.50

Summary of MSAS-SF Total and Subscale Scores

Endpoint: Global Distress Index

Visit	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Global Distress Index	n Mean SD Median Min. Max.	54 1.21 0.743 1.27 0.0 3.0	54 1.36 0.764 1.30 0.0 3.4
Week 4	Global Distress Index	n Mean SD Median Min. Max.	51 1.03 0.837 0.80 0.0 3.1	51 1.00 0.781 0.94 0.0 3.2
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.16 0.505 -0.10 -1.4 0.8	51 -0.35 0.719 -0.18 -2.0 0.7
Week 8	Global Distress Index	n Mean SD Median Min. Max.	49 0.99 0.789 0.96 0.0 2.9	47 1.00 0.757 0.96 0.0 3.0

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

 $200\overline{6}22$ 

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 5 of 12

Population: Intent-to-Treat

Table 2.50

Summary of MSAS-SF Total and Subscale Scores

Endpoint: Global Distress Index

Visit	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Change from Baseline	n Mean SD Median Min. Max.	49 -0.20 0.584 -0.10 -1.3 1.2	47 -0.35 0.645 -0.24 -1.7 1.4
Week 16	Global Distress Index	n Mean SD Median Min. Max.	46 0.94 0.716 0.84 0.0 2.6	44 0.85 0.723 0.86 0.0 2.9
	Change from Baseline	n Mean SD Median Min. Max.	46 -0.25 0.606 -0.20 -1.8 1.3	44 -0.47 0.505 -0.32 -1.7 0.4
Week 24	Global Distress Index	n Mean SD Median Min. Max.	45 1.01 0.787 0.84 0.0 2.8	42 0.83 0.766 0.68 0.0 2.8

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 6 of 12

Population: Intent-to-Treat

Table 2.50

Summary of MSAS-SF Total and Subscale Scores

Endpoint: Global Distress Index

Visit	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Change from Baseline	n Mean SD Median Min. Max.	45 -0.20 0.642 -0.22 -1.4 1.3	42 -0.48 0.612 -0.41 -1.8 0.9
Week 32	Global Distress Index	n Mean SD Median Min. Max.	41 1.03 0.829 0.96 0.0 2.9	42 0.84 0.791 0.62 0.0 3.2
	Change from Baseline	n Mean SD Median Min. Max.	41 -0.22 0.640 -0.24 -1.4 1.3	42 -0.45 0.609 -0.45 -1.7 1.1

# CONFIDENTIAL 2019N406842\_00 200622

Protocol: 200622 Page 7 of 12

Population: Intent-to-Treat

Table 2.50 Summary of MSAS-SF Total and Subscale Scores

Endpoint: Physical Symptom Subscale Score

Visit	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Physical Symptom Subscale Score	n Mean SD Median Min. Max.	54 0.89 0.641 0.87 0.0 2.5	54 0.98 0.603 0.93 0.0 2.7
Week 4	Physical Symptom Subscale Score	n Mean SD Median Min. Max.	51 0.75 0.647 0.60 0.0 2.7	51 0.71 0.547 0.73 0.0 2.4
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.12 0.434 -0.07 -1.1 0.9	51 -0.24 0.483 -0.13 -1.8 0.7
Week 8	Physical Symptom Subscale Score	n Mean SD Median Min. Max.	49 0.70 0.609 0.60 0.0 2.5	47 0.71 0.582 0.60 0.0 2.4

2019N406842<u>00</u> 200622

Protocol: 200622 Page 8 of 12

Population: Intent-to-Treat

Table 2.50

Summary of MSAS-SF Total and Subscale Scores

Endpoint: Physical Symptom Subscale Score

Visit	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Change from Baseline	n Mean SD Median Min. Max.	49 -0.16 0.395 -0.13 -1.0 0.7	47 -0.23 0.648 -0.20 -1.5 1.3
Week 16	Physical Symptom Subscale Score	n Mean SD Median Min. Max.	46 0.67 0.551 0.63 0.0 2.1	44 0.57 0.493 0.47 0.0 2.0
	Change from Baseline	n Mean SD Median Min. Max.	46 -0.22 0.480 -0.20 -1.8 0.6	44 -0.36 0.444 -0.30 -1.5 0.4
Week 24	Physical Symptom Subscale Score	n Mean SD Median Min. Max.	45 0.70 0.633 0.67 0.0 2.3	42 0.57 0.503 0.43 0.0

2019N406842\_00 200622

Protocol: 200622 Page 9 of 12

Population: Intent-to-Treat

Table 2.50

Summary of MSAS-SF Total and Subscale Scores

Endpoint: Physical Symptom Subscale Score

Visit	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Change from Baseline	n Mean SD Median Min. Max.	45 -0.19 0.582 -0.20 -1.5	42 -0.35 0.532 -0.30 -1.7 0.7
Week 32	Physical Symptom Subscale Score	n Mean SD Median Min. Max.	41 0.77 0.669 0.67 0.0 2.3	42 0.56 0.534 0.47 0.0 2.3
	Change from Baseline	n Mean SD Median Min. Max.	41 -0.16 0.539 -0.00 -1.3 0.9	42 -0.37 0.591 -0.27 -1.9 1.1

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 10 of 12

Population: Intent-to-Treat

Table 2.50

Summary of MSAS-SF Total and Subscale Scores

Endpoint: Psychological Symptom Subscale Score

Visit	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Psychological Symptom Subscale Score	n Mean SD Median Min. Max.	54 1.33 0.938 1.20 0.0 3.7	54 1.42 0.934 1.37 0.0 3.9
Week 4	Psychological Symptom Subscale Score	n Mean SD Median Min. Max.	51 1.11 1.016 0.93 0.0 3.3	51 1.06 0.911 1.00 0.0 3.2
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.19 0.653 -0.17 -2.1	51 -0.33 0.787 -0.13 -2.3 1.1
Week 8	Psychological Symptom Subscale Score	n Mean SD Median Min. Max.	49 1.06 1.038 0.60 0.0 3.2	47 1.12 0.894 1.00 0.0 3.2

2019N406842<u>00</u> 200622

Protocol: 200622 Page 11 of 12

Population: Intent-to-Treat

Table 2.50

Summary of MSAS-SF Total and Subscale Scores

Endpoint: Psychological Symptom Subscale Score

Visit	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Change from Baseline	n Mean SD Median Min. Max.	49 -0.24 0.792 -0.17 -2.6 1.5	47 -0.28 0.624 -0.20 -1.7 1.6
Week 16	Psychological Symptom Subscale Score	n Mean SD Median Min. Max.	46 1.05 0.950 0.78 0.0 3.2	44 1.00 0.910 1.00 0.0 3.4
	Change from Baseline	n Mean SD Median Min. Max.	46 -0.25 0.727 -0.27 -2.0 1.4	44 -0.38 0.715 -0.33 -1.9
Week 24	Psychological Symptom Subscale Score	n Mean SD Median Min. Max.	45 1.16 1.047 0.87 0.0 3.5	42 0.93 0.882 0.78 0.0 3.4

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 12 of 12

Population: Intent-to-Treat

Table 2.50

Summary of MSAS-SF Total and Subscale Scores

Endpoint: Psychological Symptom Subscale Score

Visit	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Change from Baseline	n Mean SD Median Min. Max.	45 -0.16 0.876 -0.17 -2.1 2.5	42 -0.45 0.790 -0.33 -2.0
Week 32	Psychological Symptom Subscale Score	n Mean SD Median Min. Max.	41 1.13 1.029 0.67 0.0 3.6	42 0.92 0.971 0.73 0.0 3.4
	Change from Baseline	n Mean SD Median Min. Max.	41 -0.23 0.777 -0.17 -1.6 2.0	42 -0.40 0.830 -0.45 -1.9 1.3

Protocol: 200622 Page 1 of 20

Population: Intent-to-Treat

Table 90.76 Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores (Mixed Model Repeated Measures)

Endpoint: Total Score

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 51 0.81 (0.059) -0.17 (0.059)	51 51 0.71 (0.059) -0.27 (0.059)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.10 (-0.27, 0.06) 0.223	
Corrected Hedges g [3] 95% CI		-0.24 (-0.63, 0.15)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 396 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 20

Population: Intent-to-Treat

Table 90.76 Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores (Mixed Model Repeated Measures)

Endpoint: Total Score

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 49 0.81 (0.058) -0.17 (0.058)	51 47 0.74 (0.059) -0.23 (0.059)	_
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.06 (-0.23, 0.10) 0.453	
Corrected Hedges g [3] 95% CI		-0.15 (-0.55, 0.25)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 397 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 20

Population: Intent-to-Treat

Table 90.76
Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores (Mixed Model Repeated Measures)

Endpoint: Total Score

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 46 0.76 (0.056) -0.22 (0.056)	51 44 0.66 (0.057) -0.32 (0.057)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.10 (-0.26, 0.06) 0.204	
Corrected Hedges g [3] 95% CI		-0.27 (-0.68, 0.15)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or

bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 398 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 4 of 20

Population: Intent-to-Treat

Table 90.76
Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores (Mixed Model Repeated Measures)

Endpoint: Total Score

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 45 0.82 (0.064) -0.16 (0.064)	51 42 0.66 (0.066) -0.32 (0.066)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.16 (-0.34, 0.03) 0.095	
Corrected Hedges g [3] 95% CI		-0.36 (-0.78, 0.06)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or

bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 399 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 5 of 20

Population: Intent-to-Treat

Table 90.76 Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores (Mixed Model Repeated Measures)

Endpoint: Total Score

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 41 0.80 (0.069) -0.17 (0.069)	51 42 0.64 (0.070) -0.34 (0.070)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.16 (-0.36, 0.03) 0.104	
Corrected Hedges g [3] 95% CI		-0.36 (-0.79, 0.08)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 400 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 6 of 20

Population: Intent-to-Treat

Table 90.76 Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores (Mixed Model Repeated Measures)

Endpoint: Global Distress Index

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 51 1.08 (0.084) -0.18 (0.084)	51 51 0.94 (0.084) -0.33 (0.084)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.15 (-0.38, 0.09) 0.219	
Corrected Hedges g [3] 95% CI		-0.24 (-0.63, 0.15)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 401 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 7 of 20

Population: Intent-to-Treat

Table 90.76 Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores (Mixed Model Repeated Measures)

Endpoint: Global Distress Index

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 49 1.04 (0.083) -0.22 (0.083)	51 47 0.96 (0.085) -0.31 (0.085)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.09 (-0.32, 0.15) 0.463
Corrected Hedges g [3] 95% CI		-0.15 (-0.55, 0.25)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 402 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 8 of 20

Population: Intent-to-Treat

Table 90.76
Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores (Mixed Model Repeated Measures)

Endpoint: Global Distress Index

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 46 0.99 (0.076) -0.27 (0.076)	51 44 0.84 (0.078) -0.42 (0.078)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.15 (-0.37, 0.07) 0.172
Corrected Hedges g [3] 95% CI		-0.29 (-0.71, 0.13)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or

bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 403 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 9 of 20

Population: Intent-to-Treat

Table 90.76
Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores (Mixed Model Repeated Measures)

Endpoint: Global Distress Index

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 45 1.04 (0.086) -0.22 (0.086)	51 42 0.84 (0.088) -0.42 (0.088)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.20 (-0.44, 0.05) 0.113	
Corrected Hedges g [3] 95% CI		-0.34 (-0.77, 0.08)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or

bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 404 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 10 of 20

Population: Intent-to-Treat

Table 90.76

Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores (Mixed Model Repeated Measures)

Endpoint: Global Distress Index

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 41 1.03 (0.091) -0.23 (0.091)	51 42 0.85 (0.091) -0.41 (0.091)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.18 (-0.44, 0.08) 0.166	
Corrected Hedges g [3] 95% CI		-0.31 (-0.74, 0.13)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or

bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 405 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 11 of 20

Population: Intent-to-Treat

Table 90.76

Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores (Mixed Model Repeated Measures)

Endpoint: Physical Symptom Subscale Score

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 51 0.78 (0.060) -0.13 (0.060)	51 51 0.68 (0.060) -0.23 (0.060)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.10 (-0.27, 0.07) 0.262	
Corrected Hedges g [3] 95% CI		-0.22 (-0.61, 0.17)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 406 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 12 of 20

Population: Intent-to-Treat

Table 90.76

Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores (Mixed Model Repeated Measures)

Endpoint: Physical Symptom Subscale Score

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 49 0.73 (0.068) -0.17 (0.068)	51 47 0.69 (0.069) -0.22 (0.069)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.04 (-0.23, 0.15) 0.673
Corrected Hedges g [3] 95% CI		-0.09 (-0.49, 0.31)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or

bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 407 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 13 of 20

Population: Intent-to-Treat

Table 90.76

Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores (Mixed Model Repeated Measures)

Endpoint: Physical Symptom Subscale Score

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 46 0.68 (0.056) -0.23 (0.056)	51 44 0.56 (0.057) -0.35 (0.057)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.12 (-0.28, 0.04) 0.142	
Corrected Hedges g [3] 95% CI		-0.31 (-0.73, 0.10)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 408 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 14 of 20

Population: Intent-to-Treat

Table 90.76

Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores (Mixed Model Repeated Measures)

(1121104 110401 110404 110404

Endpoint: Physical Symptom Subscale Score

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 45 0.71 (0.069) -0.20 (0.069)	51 42 0.60 (0.071) -0.31 (0.071)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.11 (-0.31, 0.09) 0.263
Corrected Hedges g [3] 95% CI		-0.24 (-0.66, 0.18)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or

bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 409 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 15 of 20

Population: Intent-to-Treat

Table 90.76

Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores (Mixed Model Repeated Measures)

Endpoint: Physical Symptom Subscale Score

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 41 0.77 (0.073) -0.14 (0.073)	51 42 0.57 (0.074) -0.34 (0.074)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.20 (-0.41, 0.01) 0.057	
Corrected Hedges g [3] 95% CI		-0.42 (-0.86, 0.02)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or

bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 410 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 16 of 20

Population: Intent-to-Treat

Table 90.76

Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores

(Mixed Model Repeated Measures)

Endpoint: Psychological Symptom Subscale Score

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 51 1.14 (0.094) -0.21 (0.094)	51 51 1.03 (0.094) -0.32 (0.094)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.11 (-0.38, 0.15) 0.410
Corrected Hedges g [3] 95% CI		-0.16 (-0.55, 0.23)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 411 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 17 of 20

Population: Intent-to-Treat

Table 90.76

Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores

(Mixed Model Repeated Measures)

Endpoint: Psychological Symptom Subscale Score

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 49 1.09 (0.098) -0.26 (0.098)	51 47 1.09 (0.101) -0.26 (0.101)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.00 (-0.29, 0.28) 0.977	
Corrected Hedges g [3] 95% CI		-0.01 (-0.41, 0.39)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or

bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 412 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 18 of 20

Population: Intent-to-Treat

Table 90.76 Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores

(Mixed Model Repeated Measures)

Endpoint: Psychological Symptom Subscale Score

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 46 1.05 (0.102) -0.29 (0.102)	51 44 1.00 (0.105) -0.34 (0.105)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.05 (-0.34, 0.24) 0.733
Corrected Hedges g [3] 95% CI		-0.07 (-0.49, 0.34)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 413 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 19 of 20

Population: Intent-to-Treat

Table 90.76

Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores

(Mixed Model Repeated Measures)

Endpoint: Psychological Symptom Subscale Score

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 45 1.15 (0.115) -0.19 (0.115)	51 42 0.97 (0.119) -0.38 (0.119)	_
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.18 (-0.51, 0.15) 0.277	
Corrected Hedges g [3] 95% CI		-0.23 (-0.66, 0.19)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or

bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 414 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 20 of 20

Population: Intent-to-Treat

Table 90.76

Analysis of Change from Baseline in MSAS-SF Total and Subscale Scores

(Mixed Model Repeated Measures)

Endpoint: Psychological Symptom Subscale Score

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 41 1.06 (0.119) -0.29 (0.119)	51 42 0.96 (0.120) -0.38 (0.120)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.10 (-0.43, 0.24) 0.570	
Corrected Hedges g [3] 95% CI		-0.12 (-0.56, 0.31)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 415 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 1 of 3

Population: Intent-To-Treat

Table 2.53

Summary of PROMIS Physical Function Score

Visit	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Physical Function Score	n Mean SD Median Min. Max.	54 3.59 1.018 3.79 1.4 5.0	54 3.49 1.124 3.42 1.3 5.0
Week 4	Physical Function Score	n Mean SD Median Min. Max.	51 3.74 1.047 3.92 1.4 5.0	51 3.90 1.009 4.08 1.3 5.0
	Change from Baseline	n Mean SD Median Min. Max.	51 0.17 0.564 0.00 -1.2 1.9	51 0.39 0.685 0.25 -0.8 2.3

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

Protocol: 200622
Population: Intent-To-Treat

Table 2.53
Summary of PROMIS Physical Function Score

Visit	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Physical Function Score		1.4	47 4.02 1.077 4.42 1.3 5.0
	Change from Baseline	SD	49 0.28 0.501 0.17 -0.8 1.6	47 0.47 0.850 0.25 -2.1 2.4
Week 16	Physical Function Score		44 3.91 0.959 3.92 1.4 5.0	44 4.10 1.038 4.42 1.3 5.0
	Change from Baseline	SD	44 0.45 0.606 0.33 -1.2 1.8	44 0.50 0.748 0.42 -1.2 2.8

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

Protocol: 200622
Population: Intent-To-Treat

Table 2.53
Summary of PROMIS Physical Function Score

Visit	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Physical Function Score	n Mean SD Median Min. Max.	43 3.75 1.087 3.75 1.3 5.0	42 4.06 1.055 4.46 1.4 5.0
	Change from Baseline	n Mean SD Median Min. Max.	43 0.30 0.742 0.17 -1.1 2.8	42 0.51 0.700 0.33 -1.0 2.5
Week 32	Physical Function Score	n Mean SD Median Min. Max.	41 3.78 1.091 4.00 1.3 5.0	42 4.11 1.008 4.50 1.3 5.0
	Change from Baseline	n Mean SD Median Min. Max.	41 0.36 0.653 0.17 -0.8 2.7	42 0.49 0.785 0.29 -0.9 3.3

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

Protocol: 200622 Page 1 of 5

Population: Intent-to-Treat

Table 90.84
Analysis of Change from Baseline in PROMIS Physical Function Score (Mixed Model Repeated Measures)

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	51 51 3.70 (0.083) 0.17 (0.083)	51 51 3.92 (0.083) 0.39 (0.083)	•
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.22 (-0.01, 0.45) 0.065	
Corrected Hedges g [3] 95% CI		0.37 (-0.02, 0.76)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

· · -

Mepolizumab (Nucala) - HES Seite 419 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 5

Population: Intent-to-Treat

Table 90.84
Analysis of Change from Baseline in PROMIS Physical Function Score (Mixed Model Repeated Measures)

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	51 49 3.80 (0.091) 0.27 (0.091)	51 47 4.03 (0.093) 0.50 (0.093)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.23 (-0.03, 0.49) 0.085
Corrected Hedges g [3] 95% CI		0.35 (-0.05, 0.76)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

Mepolizumab (Nucala) - HES Seite 420 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 5

Population: Intent-to-Treat

Table 90.84
Analysis of Change from Baseline in PROMIS Physical Function Score (Mixed Model Repeated Measures)

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	51 44 3.95 (0.089) 0.42 (0.089)	51 44 4.06 (0.089) 0.53 (0.089)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.10 (-0.15, 0.36) 0.416
Corrected Hedges g [3] 95% CI		0.17 (-0.25, 0.59)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

Mepolizumab (Nucala) - HES Seite 421 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 4 of 5

Population: Intent-to-Treat

Table 90.84 Analysis of Change from Baseline in PROMIS Physical Function Score (Mixed Model Repeated Measures)

Visit: Week 24

. 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	51 43 3.82 (0.100) 0.29 (0.100)	51 42 4.03 (0.101) 0.50 (0.101)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.21 (-0.08, 0.49) 0.147
Corrected Hedges g [3] 95% CI		0.32 (-0.11, 0.74)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

Mepolizumab (Nucala) - HES Seite 422 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 5 of 5

Population: Intent-to-Treat

Table 90.84
Analysis of Change from Baseline in PROMIS Physical Function Score (Mixed Model Repeated Measures)

Visit: Week 32

. 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	51 41 3.86 (0.101) 0.33 (0.101)	51 42 4.01 (0.101) 0.48 (0.101)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.15 (-0.13, 0.44) 0.287
Corrected Hedges g [3] 95% CI		0.23 (-0.20, 0.67)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

Mepolizumab (Nucala) - HES Seite 423 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

2019N406842 00  $200\overline{6}22$ 

Page 1 of 3 Protocol: 200622

Population: Intent-To-Treat

Table 2.56 Summary of PROMIS Sleep Score

Visit	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Sleep Score			54 2.44 1.097 2.00 1.0 5.0
Week 4	Sleep Score		51 2.41 1.219 2.00 1.0 5.0	51 2.37 1.104 2.00 1.0 5.0
	Change from Baseline	n Mean SD Median Min. Max.		51 -0.05 0.923 0.00 -2.0 2.5

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

PPD

Page 2 of 3 Protocol: 200622

Population: Intent-To-Treat

Table 2.56 Summary of PROMIS Sleep Score

Visit	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Sleep Score	n Mean SD Median Min. Max.	49 2.46 1.294 2.50 1.0 5.0	47 2.27 0.972 2.00 1.0 4.5
	Change from Baseline	n Mean SD Median Min. Max.	49 -0.07 0.952 0.00 -2.0 3.0	47 -0.17 0.892 0.00 -2.0 2.0
Week 16	Sleep Score	n Mean SD Median Min. Max.	44 2.38 1.317 2.00 1.0 5.0	44 2.35 1.097 2.00 1.0 5.0
	Change from Baseline		44 -0.22 1.020 0.00 -2.5 2.0	44 -0.07 1.038 0.00 -2.0 3.0

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

PPD

Protocol: 200622 Page 3 of 3

Population: Intent-To-Treat

Table 2.56
Summary of PROMIS Sleep Score

Visit	Endpoint		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Sleep Score	n Mean SD Median Min. Max.	1.297	42 2.30 1.153 2.00 1.0 5.0
	Change from Baseline	n Mean SD Median Min. Max.	1.296	42 -0.11 1.107 0.00 -3.0 2.5
Week 32	Sleep Score		41 2.62 1.144 2.50 1.0 5.0	42 2.11 0.880 2.00 1.0 5.0
	Change from Baseline	n Mean SD Median Min. Max.	0.907	42 -0.23 0.864 0.00 -2.5 1.5

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

PPD

Table 90.92
Analysis of Change from Baseline in PROMIS Sleep Score

(Mixed Model Repeated Measures)

Mara a 1 d - . . . . . . la

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	51 51 2.37 (0.108) -0.13 (0.108)	51 51 2.43 (0.108) -0.06 (0.108)	_
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.07 (-0.24, 0.37) 0.667	
Corrected Hedges g [3] 95% CI		0.09 (-0.30, 0.47)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

Mepolizumab (Nucala) - HES Seite 427 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Table 90.92

Analysis of Change from Baseline in PROMIS Sleep Score

(Mixed Model Repeated Measures)

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	51 49 2.44 (0.120) -0.06 (0.120)	51 47 2.26 (0.122) -0.23 (0.122)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.17 (-0.52, 0.17) 0.315
Corrected Hedges g [3] 95% CI		-0.21 (-0.61, 0.20)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

Mepolizumab (Nucala) - HES Seite 428 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Table 90.92
Analysis of Change from Baseline in PROMIS Sleep Score

(Mixed Model Repeated Measures)

Mara a 1 d - . . . . . . la

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	51 44 2.29 (0.139) -0.20 (0.139)	51 44 2.36 (0.139) -0.13 (0.139)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.07 (-0.32, 0.46) 0.734	
Corrected Hedges g [3] 95% CI		0.07 (-0.35, 0.49)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

Mepolizumab (Nucala) - HES Seite 429 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Table 90.92

Analysis of Change from Baseline in PROMIS Sleep Score

(Mixed Model Repeated Measures)

Visit: Week 24

. 21	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	51 43 2.32 (0.156) -0.18 (0.156)	51 42 2.28 (0.158) -0.22 (0.158)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.04 (-0.48, 0.40) 0.864
Corrected Hedges g [3] 95% CI		-0.04 (-0.46, 0.39)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

Mepolizumab (Nucala) - HES Seite 430 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Table 90.92
Analysis of Change from Baseline in PROMIS Sleep Score

(Mixed Model Repeated Measures)

Mara a 1 d - . . . . . . la

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	51 41 2.47 (0.111) -0.02 (0.111)	51 42 2.17 (0.110) -0.33 (0.110)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.30 (-0.62, 0.01) 0.058	
Corrected Hedges g [3] 95% CI		-0.42 (-0.86, 0.01)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

Mepolizumab (Nucala) - HES Seite 431 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

### 2019N406842\_00 200622

# CONFIDENTIAL

Protocol: 200622 Page 6 of 10

Population: Intent-to-Treat

Table 3.2

Summary of SF-36 Health Survey Component Summary Scores

Component: SF363-Physical Component Score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score	n Mean SD Median Min. Max.		54 39.87 10.338 38.99 17.2 58.1
Week 4	Score	n Mean SD Median Min. Max.		54 43.73 9.263 43.42 21.5 59.8
	Change from Baseline		54 2.75 5.832 1.83 -8.9 18.8	54 3.85 7.234 2.03 -8.4 31.1

# CONFIDENTIAL 2019N406842\_00 200622

Protocol: 200622 Page 7 of 10

Population: Intent-to-Treat

Table 3.2 Summary of SF-36 Health Survey Component Summary Scores

Component: SF363-Physical Component Score

Analysis Time Point	lent Score		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score	n Mean SD Median Min. Max.	53 43.47 10.249 44.63 23.7 60.6	54 45.32 10.225 45.87 23.9 61.0
	Change from Baseline	n Mean SD Median Min. Max.	53 3.27 5.756 2.17 -9.3 17.6	54 5.44 9.251 4.63 -19.9 35.4
Week 12	Score	n Mean SD Median Min. Max.	53 43.39 8.450 43.27 23.0 61.1	53 45.43 9.816 45.45 21.6 63.1
	Change from Baseline	n Mean SD Median Min. Max.	53 3.19 5.681 3.60 -10.6 13.0	53 5.46 8.890 3.40 -14.4 38.0

### 2019N406842\_00 200<del>6</del>22

## CONFIDENTIAL

Protocol: 200622 Page 8 of 10

Population: Intent-to-Treat

Table 3.2 Summary of SF-36 Health Survey Component Summary Scores

Component: SF363-Physical Component Score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score	SD Median Min.	53 44.61 9.391 47.73 23.4 61.2	45.94 20.0
	Change from Baseline	SD Median Min.	53 4.41 5.723 4.22 -10.0 15.0	9.348 3.05
Week 20	Score	SD Median	52 43.66 9.872 44.82 15.3 60.0	45.50
	Change from Baseline	n Mean SD Median Min. Max.	52 3.55 6.047 3.86 -11.0 18.3	

### 2019N406842\_00 200622

## CONFIDENTIAL

Protocol: 200622 Page 9 of 10

Population: Intent-to-Treat

Table 3.2 Summary of SF-36 Health Survey Component Summary Scores

Component: SF363-Physical Component Score

Analysis Time Point	lent score		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	n Mean SD Median Min. Max.	52 44.22 9.784 44.69 18.6 60.3	51 45.85 10.155 47.91 22.1 63.0
	Change from Baseline	n Mean SD Median Min. Max.	52 4.11 6.738 4.08 -8.8 19.4	51 6.04 8.853 3.63 -8.8 35.1
Week 28	Score	n Mean SD Median Min. Max.	51 44.47 9.169 45.15 24.3 61.5	51 45.19 9.188 47.24 20.4 62.1
	Change from Baseline	n Mean SD Median Min. Max.	51 4.35 6.015 4.94 -14.9 22.3	51 5.33 8.546 3.83 -6.5 35.0

#### 2019N406842 00 CONFIDENTIAL

Protocol: 200622 Page 10 of 10

Population: Intent-to-Treat

Table 3.2

Summary of SF-36 Health Survey Component Summary Scores

Component: SF363-Physical Component Score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 44.10 9.996 44.40 20.9 61.6	50 46.11 8.901 45.52 22.7 62.7
	Change from Baseline	n Mean SD Median Min. Max.	50 3.81 5.745 3.88 -6.0 25.2	50 6.33 9.466 3.87 -10.1 37.7

 $200\overline{6}22$ 

Protocol: 200622 Page 1 of 8

Population: Intent-to-Treat

Table 90.100 Analysis of Change from Baseline in SF-36 Physical Component Summary Score (Mixed Model Repeated Measures)

Visit: Week 4

<b>.</b> 1	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 54 42.77 (0.800) 2.75 (0.800)	54 54 43.93 (0.800) 3.90 (0.800)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		1.16 (-1.10, 3.41) 0.311
Corrected Hedges g [3] 95% CI		0.20 (-0.18, 0.57)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 437 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 8

Population: Intent-to-Treat

Table 90.100 Analysis of Change from Baseline in SF-36 Physical Component Summary Score (Mixed Model Repeated Measures)

Mana a 1 - - - - - la

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 43.11 (0.979) 3.09 (0.979)	54 54 45.52 (0.973) 5.50 (0.973)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		2.41 (-0.34, 5.16) 0.085
Corrected Hedges g [3] 95% CI		0.34 (-0.05, 0.72)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 438 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 8

Population: Intent-to-Treat

Table 90.100 Analysis of Change from Baseline in SF-36 Physical Component Summary Score

(Mixed Model Repeated Measures)

Mana a 1 - - - - - la

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 43.05 (0.911) 3.03 (0.911)	54 53 45.38 (0.909) 5.35 (0.909)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		2.33 (-0.24, 4.89) 0.075	
Corrected Hedges g [3] 95% CI		0.35 (-0.03, 0.73)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 439 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 4 of 8

Population: Intent-to-Treat

Table 90.100 Analysis of Change from Baseline in SF-36 Physical Component Summary Score (Mixed Model Repeated Measures)

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 44.27 (0.958) 4.24 (0.958)	54 53 44.74 (0.956) 4.71 (0.956)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.47 (-2.23, 3.16) 0.731
Corrected Hedges g [3] 95% CI		0.07 (-0.31, 0.45)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 440 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 5 of 8

Population: Intent-to-Treat

Table 90.100 Analysis of Change from Baseline in SF-36 Physical Component Summary Score (Mixed Model Repeated Measures)

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 43.31 (0.935) 3.28 (0.935)	54 52 45.65 (0.933) 5.62 (0.933)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		2.34 (-0.29, 4.98) 0.080
Corrected Hedges g [3] 95% CI		0.35 (-0.04, 0.73)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 441 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 6 of 8

Population: Intent-to-Treat

Table 90.100 Analysis of Change from Baseline in SF-36 Physical Component Summary Score (Mixed Model Repeated Measures)

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 43.88 (1.013) 3.86 (1.013)	54 51 45.57 (1.015) 5.54 (1.015)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		1.68 (-1.17, 4.54) 0.245
Corrected Hedges g [3] 95% CI		0.23 (-0.16, 0.62)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 442 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 7 of 8

Population: Intent-to-Treat

Table 90.100 Analysis of Change from Baseline in SF-36 Physical Component Summary Score (Mixed Model Repeated Measures)

Visit: Week 28

. 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 44.24 (0.907) 4.21 (0.907)	54 51 45.09 (0.906) 5.06 (0.906)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.85 (-1.71, 3.40) 0.513
Corrected Hedges g [3] 95% CI		0.13 (-0.26, 0.52)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 443 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 8 of 8

Population: Intent-to-Treat

Table 90.100 Analysis of Change from Baseline in SF-36 Physical Component Summary Score (Mixed Model Repeated Measures)

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 50 43.77 (0.955) 3.74 (0.955)	54 50 46.11 (0.954) 6.08 (0.954)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		2.34 (-0.35, 5.03) 0.088
Corrected Hedges g [3] 95% CI		0.34 (-0.05, 0.74)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 444 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

## CONFIDENTIAL 2019N406842\_00 200622

Protocol: 200622 Page 1 of 10

Population: Intent-to-Treat

Table 3.2

Summary of SF-36 Health Survey Component Summary Scores

Component: SF363-Mental Component Score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score	n Mean SD Median Min. Max.	54 44.78 10.885 47.68 19.3 66.8	54 43.52 11.077 46.23 18.8 61.7
Week 4	Score	n Mean SD Median Min. Max.	54 44.76 11.345 47.58 19.3 64.2	54 46.26 10.605 49.33 20.8 65.3
	Change from Baseline		54 -0.02 6.048 -0.33 -14.6 16.8	54 2.73 8.282 3.01 -15.7 26.6

# CONFIDENTIAL 2019N406842\_00 200622

Protocol: 200622 Page 2 of 10

Population: Intent-to-Treat

Table 3.2 Summary of SF-36 Health Survey Component Summary Scores

Component: SF363-Mental Component Score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score	SD Median Min.		54 45.83 10.382 47.96 20.0 60.5
	Change from Baseline	SD Median Min.	53 2.13 7.949 1.06 -13.8 32.1	1.25
Week 12	Score	SD	53 45.40 11.323 47.47 16.7 63.3	53 43.72 10.261 46.35 22.3 59.8
	Change from Baseline	SD	53 0.35 9.957 -0.73 -20.6 40.9	-0.04

### 2019N406842\_00 200622

## CONFIDENTIAL

Protocol: 200622 Page 3 of 10

Population: Intent-to-Treat

Table 3.2 Summary of SF-36 Health Survey Component Summary Scores

Component: SF363-Mental Component Score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score	SD Median Min.	53 46.14 11.340 48.54 17.2 62.1	47.28 24.0
	Change from Baseline	SD Median Min.	53 1.09 9.643 1.25 -17.4 27.4	7.632
Week 20	Score	SD Median	52 46.38 11.168 50.05 19.1 60.1	52 45.59 10.414 47.81 25.8 61.6
	Change from Baseline	n Mean SD Median Min. Max.	52 1.39 8.659 1.20 -16.9 28.4	

### 2019N406842\_00 200622

## CONFIDENTIAL

Protocol: 200622 Page 4 of 10

Population: Intent-to-Treat

Table 3.2 Summary of SF-36 Health Survey Component Summary Scores

Component: SF363-Mental Component Score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	SD Median	17.3	51 46.85 10.374 48.14 21.0 61.7
	Change from Baseline	SD Median Min.	52 1.09 10.162 2.29 -30.6 31.4	2.28
Week 28	Score	SD	11.740 45.56	51 45.73 11.254 47.30 16.9 62.9
	Change from Baseline	Median Min.		1.48

# CONFIDENTIAL 2019N406842\_00 200622

Protocol: 200622 Page 5 of 10

Population: Intent-to-Treat

Table 3.2

Summary of SF-36 Health Survey Component Summary Scores

Component: SF363-Mental Component Score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 45.94 12.777 47.97 17.5 63.8	50 47.67 10.098 49.18 22.4 64.7
	Change from Baseline	n Mean SD Median Min. Max.	50 1.46 8.765 0.96 -25.9 27.5	50 3.55 9.030 4.95 -14.3 20.4

Protocol: 200622 Page 1 of 8

Population: Intent-to-Treat

Table 90.109 Analysis of Change from Baseline in SF-36 Mental Component Summary Score (Mixed Model Repeated Measures)

Visit: Week 4

<b>.</b> 1	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 54 44.49 (0.938) 0.18 (0.938)	54 54 46.74 (0.939) 2.43 (0.939)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		2.25 (-0.39, 4.90) 0.094
Corrected Hedges g [3] 95% CI		0.32 (-0.06, 0.70)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 450 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 8

Population: Intent-to-Treat

Table 90.109 Analysis of Change from Baseline in SF-36 Mental Component Summary Score (Mixed Model Repeated Measures)

Mana 1 - - - - - la

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 46.65 (1.008) 2.34 (1.008)	54 54 46.24 (1.002) 1.93 (1.002)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.41 (-3.24, 2.42) 0.776
Corrected Hedges g [3] 95% CI		-0.06 (-0.43, 0.32)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 451 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 8

Population: Intent-to-Treat

Table 90.109 Analysis of Change from Baseline in SF-36 Mental Component Summary Score (Mixed Model Repeated Measures)

Mana all i muna ala

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 44.93 (1.164) 0.62 (1.164)	54 53 43.92 (1.160) -0.39 (1.160)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-1.01 (-4.29, 2.26) 0.540	
Corrected Hedges g [3] 95% CI		-0.12 (-0.50, 0.26)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 452 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 4 of 8

Population: Intent-to-Treat

Table 90.109 Analysis of Change from Baseline in SF-36 Mental Component Summary Score (Mixed Model Repeated Measures)

Mana all i muna ala

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 45.67 (1.087) 1.36 (1.087)	54 53 46.11 (1.084) 1.79 (1.084)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.43 (-2.62, 3.49) 0.779	
Corrected Hedges g [3] 95% CI		0.05 (-0.33, 0.44)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 453 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 5 of 8

Population: Intent-to-Treat

Table 90.109 Analysis of Change from Baseline in SF-36 Mental Component Summary Score (Mixed Model Repeated Measures)

Mana all i muna ala

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 45.91 (1.107) 1.60 (1.107)	54 52 45.55 (1.105) 1.24 (1.105)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.36 (-3.47, 2.75) 0.818	
Corrected Hedges g [3] 95% CI		-0.04 (-0.43, 0.34)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 454 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 6 of 8

Population: Intent-to-Treat

Table 90.109 Analysis of Change from Baseline in SF-36 Mental Component Summary Score (Mixed Model Repeated Measures)

Mana a 1 - - - - - la

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 45.63 (1.195) 1.32 (1.195)	54 51 46.64 (1.197) 2.33 (1.197)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		1.01 (-2.36, 4.38) 0.553	
Corrected Hedges g [3] 95% CI		0.12 (-0.27, 0.50)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 455 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 7 of 8

Population: Intent-to-Treat

Table 90.109 Analysis of Change from Baseline in SF-36 Mental Component Summary Score (Mixed Model Repeated Measures)

Mana 1 - - - - - la

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 44.94 (1.238) 0.63 (1.238)	54 51 45.84 (1.236) 1.53 (1.236)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.90 (-2.58, 4.38) 0.610	
Corrected Hedges g [3] 95% CI		0.10 (-0.29, 0.49)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 456 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 8 of 8

Population: Intent-to-Treat

Table 90.109 Analysis of Change from Baseline in SF-36 Mental Component Summary Score (Mixed Model Repeated Measures)

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 50 45.78 (1.176) 1.46 (1.176)	54 50 47.56 (1.175) 3.25 (1.175)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		1.78 (-1.52, 5.09) 0.287
Corrected Hedges g [3] 95% CI		0.21 (-0.18, 0.61)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 457 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 1 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Analysis Time Point	Score		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score	n Mean SD Median Min. Max.	54 52.22 28.199 51.00 0.0 100.0	54 50.56 24.605 46.50 0.0 100.0
Week 4	Score	n Mean SD Median Min. Max.	54 59.19 25.657 62.00 0.0 100.0	54 60.61 25.140 61.50 10.0
	Change from Baseline	n Mean SD Median Min. Max.	54 6.96 18.414 9.00 -38.0 58.0	54 10.06 20.100 4.50 -22.0 69.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 2 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Bodily Pain: 0-100 score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score		53 59.49 30.710 62.00 0.0 100.0	28.554 74.00 0.0
	Change from Baseline	n Mean SD Median Min. Max.	53 8.17 21.072 9.00 -40.0 62.0	27.863 14.00
Week 12	Score		25.131 61.00 10.0	62.00 0.0
	Change from Baseline	n Mean SD Median Min. Max.	53 6.75 20.571 9.00 -40.0 41.0	

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 3 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score	n Mean SD Median Min. Max.	62.00 10.0	26.273 62.00 10.0
	Change from Baseline	n Mean SD Median Min. Max.	53 11.92 19.550 16.00 -31.0 69.0	24.566
Week 20	Score	n Mean SD Median Min. Max.	63.00	52 62.21 23.804 62.00 22.0 100.0
	Change from Baseline	n Mean SD Median Min. Max.	52 11.48 21.128 12.00 -52.0 53.0	52 12.56 22.560 10.00 -29.0 78.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 4 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	n Mean SD Median Min. Max.	62.00 0.0	51 66.41 26.204 74.00 0.0 100.0
	Change from Baseline	n Mean SD Median Min. Max.	52 10.46 21.640 9.50 -49.0 69.0	26.090 16.00
Week 28	Score	n Mean SD Median Min. Max.	51 62.80 27.767 62.00 0.0	51 63.59 26.225 62.00 0.0 100.0
	Change from Baseline	n Mean SD Median Min. Max.	51 11.27 21.630 10.00 -40.0 69.0	51 13.39 24.997 10.00 -31.0 78.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 5 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Analysis Time H			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 62.78 28.490 62.00 0.0	50 66.70 28.134 72.00 0.0 100.0
	Change from Baseline	n Mean SD Median Min. Max.	50 11.08 19.013 5.00 -33.0 49.0	50 17.36 27.360 16.00 -41.0 78.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 6 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Bodily Pain: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score	n Mean SD Median Min. Max.	54 42.73 11.370 42.24 21.7 62.0	54 42.06 9.920 40.43 21.7 62.0
Week 4	Score	n Mean SD Median Min. Max.	54 45.54 10.345 46.68 21.7 62.0	
	Change from Baseline	n Mean SD Median Min. Max.	54 2.81 7.424 3.63 -15.3 23.4	54 4.05 8.104 1.82 -8.9 27.8

2019N406842<u>00</u> 200<del>6</del>22

Mepolizumab

62.0

4.07

10.593

4.03

-21.0

27.4

53

Protocol: 200622 Page 7 of 90

Population: Intent-to-Treat

Table 3.1
Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Bodily Pain: norm-based score

Analysis Time Point			Placebo (N=54)	300mg SC (N=54)
Week 8	Score	n Mean SD Median Min. Max.	53 45.67 12.383 46.68 21.7 62.0	54 48.90 11.514 51.51 21.7 62.0
	Change from Baseline	n Mean SD Median Min. Max.	53 3.29 8.496 3.63 -16.1 25.0	
Week 12	Score	n Mean SD Median Min.	53 45.09 10.133 46.27 25.7	

Change from Baseline

PPD

Max.

Mean

Min.

Max.

Median

SD

n

62.0

2.72

8.295

3.63

-16.1

16.5

53

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 8 of 90

Population: Intent-to-Treat

Table 3.1
Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Bodily Pain: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score	n Mean SD Median Min. Max.	53 47.18 10.529 46.68 25.7 62.0	10.594
	Change from Baseline	n Mean SD Median Min. Max.	53 4.81 7.883 6.45 -12.5 27.8	0.00
Week 20	Score	n Mean SD Median Min. Max.	52 47.00 11.075 47.08 21.7 62.0	
	Change from Baseline	n Mean SD Median Min. Max.	52 4.63 8.519 4.83 -21.0 21.4	

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 9 of 90

Population: Intent-to-Treat

Table 3.1
Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Bodily Pain: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	Median	52 46.59 11.136 46.68 21.7 62.0	10.566 51.51 21.7
	Change from Baseline	Median Min.	52 4.22 8.726 3.84 -19.8 27.8	6.45 -15.3
Week 28	Score	n Mean SD Median Min. Max.	51 47.00 11.196 46.68 21.7 62.0	10.574
	Change from Baseline	SD Median Min.	51 4.55 8.721 4.04 -16.1 27.8	10.078 4.03 -12.5

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 10 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Bodily Pain: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 46.99 11.487 46.68 21.7 62.0	50 48.57 11.344 50.71 21.7 62.0
	Change from Baseline	n Mean SD Median Min. Max.	50 4.47 7.666 2.01 -13.3 19.8	50 7.00 11.032 6.45 -16.5 31.5

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 11 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-General Health: 0-100 score

Analysis Time Poi			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score	n Mean SD Median Min. Max.	54 41.19 20.851 38.50 10.0 87.0	54 36.52 19.566 33.50 5.0 87.0
Week 4	Score	n Mean SD Median Min. Max.	54 45.22 21.802 41.00 10.0 87.0	54 43.63 18.587 40.00 10.0 87.0
	Change from Baseline	n Mean SD Median Min. Max.	54 4.04 12.977 0.00 -25.0 50.0	54 7.11 15.029 5.00 -25.0 42.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 12 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-General Health: 0-100 score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score	n Mean SD Median Min. Max.	53 48.25 21.517 47.00 10.0 92.0	20.405 43.50 5.0
	Change from Baseline	n Mean SD Median Min. Max.	53 6.75 15.024 5.00 -35.0 55.0	16.265 10.00
Week 12	Score	n Mean SD Median Min. Max.	53 46.17 20.386 45.00 10.0 92.0	
	Change from Baseline	n Mean SD Median Min. Max.	53 4.68 14.172 5.00 -35.0 37.0	53 10.55 19.244 10.00 -32.0 62.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 13 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-General Health: 0-100 score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score		5.0	22.372 42.00 5.0
	Change from Baseline	n Mean SD Median Min. Max.	53 3.49 15.611 0.00 -35.0 42.0	20.856 5.00
Week 20	Score		52 45.19 20.726 45.00 5.0 92.0	21.858 40.00 0.0
	Change from Baseline	n Mean SD Median Min. Max.	52 3.81 14.871 5.00 -35.0 55.0	52 10.00 21.775 5.00 -40.0 72.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 14 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-General Health: 0-100 score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	SD Median	52 44.79 22.492 40.00 5.0 97.0	23.040 42.00 0.0
	Change from Baseline	Median Min.	52 3.40 15.506 0.00 -35.0 50.0	10.00 -25.0
Week 28	Score	n Mean SD Median Min. Max.	51 44.47 21.742 40.00 5.0 97.0	23.543
	Change from Baseline	SD Median Min.	51 2.86 16.588 0.00 -35.0 62.0	23.760 5.00 -47.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 15 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-General Health: 0-100 score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 44.58 22.385 41.00 5.0 97.0	50 47.98 21.646 43.50 10.0
	Change from Baseline	n Mean SD Median Min. Max.	50 4.02 17.881 0.00 -35.0 67.0	50 11.12 21.098 5.00 -32.0 72.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 16 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-General Health: norm-based score

Analysis Time Point	TOTHE DASECT SCOTE		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score	n Mean SD Median Min. Max.	54 38.54 9.915 37.26 23.7 60.3	54 36.32 9.304 34.88 21.3 60.3
Week 4	Score	n Mean SD Median Min. Max.	54 40.45 10.367 38.45 23.7 60.3	
	Change from Baseline	n Mean SD Median Min. Max.	54 1.92 6.171 0.00 -11.9 23.8	54 3.38 7.146 2.38 -11.9 20.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 17 of 90

Population: Intent-to-Treat

Table 3.1
Summary of SF-36 Health Survey Domain Scores

Domain: SF363-General Health: norm-based score

Analysis Time Point	Jim-pased Scole		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score	n Mean SD Median Min. Max.	53 41.89 10.231 41.30 23.7 62.7	54 40.30 9.702 39.64 21.3 60.3
	Change from Baseline	n Mean SD Median Min. Max.	53 3.21 7.143 2.38 -16.6 26.2	54 3.98 7.733 4.75 -11.9 28.5
Week 12	Score	n Mean SD Median Min. Max.	53 40.91 9.693 40.35 23.7 62.7	53 41.52 9.781 41.30 23.7 60.3
	Change from Baseline	n Mean SD Median Min. Max.	53 2.22 6.738 2.37 -16.6 17.6	53 5.02 9.150 4.75 -15.2 29.5

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 18 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-General Health: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score		53 40.34 10.000 38.92 21.3 65.1	10.638 38.92 21.3
	Change from Baseline	n Mean SD Median Min. Max.	53 1.66 7.423 0.00 -16.6 20.0	9.917 2.38
Week 20	Score		52 40.44 9.854 40.35 21.3 62.7	10.393 37.97
	Change from Baseline	n Mean SD Median Min. Max.	52 1.81 7.070 2.38 -16.6 26.2	52 4.75 10.354 2.38 -19.0 34.2

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 19 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-General Health: norm-based score

Analysis Time Point	JIM-Dased Score		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	n Mean SD Median Min. Max.	52 40.25 10.695 37.97 21.3 65.1	51 41.92 10.955 38.92 19.0 64.1
	Change from Baseline	n Mean SD Median Min. Max.	52 1.62 7.373 0.00 -16.6 23.8	51 5.40 10.084 4.75 -11.9 34.2
Week 28	Score	n Mean SD Median Min. Max.	51 40.10 10.338 37.97 21.3 65.1	51 40.73 11.194 40.35 21.3 64.1
	Change from Baseline	n Mean SD Median Min. Max.	51 1.36 7.888 0.00 -16.6 29.5	51 4.11 11.297 2.38 -22.3 31.9

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 20 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-General Health: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 40.15 10.644 38.45 21.3 65.1	50 41.76 10.292 39.64 23.7 66.5
	Change from Baseline	n Mean SD Median Min. Max.	50 1.91 8.502 0.00 -16.6 31.9	50 5.29 10.032 2.38 -15.2 34.2

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 21 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Health Utility Index

Analysis Time Po	-		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score	n Mean SD Median Min. Max.	54 0.63 0.113 0.62 0.4 0.9	54 0.61 0.101 0.62 0.4 0.8
Week 4	Score	n Mean SD Median Min. Max.	54 0.65 0.123 0.64 0.3 1.0	54 0.67 0.116 0.64 0.5 0.9
	Change from Baseline	n Mean SD Median Min. Max.	54 0.02 0.061 0.00 -0.1 0.2	54 0.05 0.091 0.04 -0.1 0.3

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 22 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Health Utility Index

Analysis Time Point	lex		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score	n Mean SD Median Min. Max.	53 0.67 0.140 0.64 0.4 1.0	54 0.67 0.116 0.64 0.5 0.9
	Change from Baseline	n Mean SD Median Min. Max.	53 0.03 0.075 0.02 -0.1 0.3	54 0.06 0.087 0.06 -0.1 0.3
Week 12	Score	n Mean SD Median Min. Max.	53 0.66 0.122 0.63 0.4 0.9	53 0.65 0.123 0.62 0.4 1.0
	Change from Baseline	n Mean SD Median Min. Max.	53 0.03 0.084 0.02 -0.1 0.4	53 0.03 0.104 0.04 -0.2 0.3

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 23 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Health Utility Index

Analysis Time Point	uex		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score	n Mean SD Median Min. Max.	53 0.68 0.125 0.65 0.4 1.0	53 0.66 0.122 0.64 0.4 0.9
	Change from Baseline	n Mean SD Median Min. Max.	53 0.05 0.083 0.05 -0.1 0.3	53 0.05 0.087 0.04 -0.1 0.3
Week 20	Score	n Mean SD Median Min. Max.	52 0.67 0.142 0.64 0.4	52 0.67 0.110 0.65 0.4 0.9
	Change from Baseline	n Mean SD Median Min. Max.	52 0.04 0.090 0.02 -0.1 0.3	52 0.06 0.097 0.05 -0.2 0.3

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 24 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Health Utility Index

Analysis Time Point	lex		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	n Mean SD Median Min. Max.	52 0.67 0.146 0.65 0.3 1.0	51 0.68 0.122 0.64 0.4 0.9
	Change from Baseline	n Mean SD Median Min. Max.	52 0.04 0.094 0.04 -0.2 0.3	51 0.07 0.094 0.06 -0.1 0.3
Week 28	Score	n Mean SD Median Min. Max.	51 0.67 0.144 0.64 0.4 0.9	51 0.68 0.132 0.64 0.3
	Change from Baseline	n Mean SD Median Min. Max.	51 0.04 0.085 0.04 -0.1 0.2	51 0.07 0.098 0.06 -0.1 0.4

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 25 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Health Utility Index

Analysis Time	-		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 0.68 0.135 0.65 0.4 0.9	50 0.70 0.120 0.69 0.4 0.9
	Change from Baseline	n Mean SD Median Min. Max.	50 0.04 0.084 0.04 -0.2 0.3	50 0.08 0.099 0.08 -0.1 0.4

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 26 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Mental Health: 0-100 score

Analysis Time Point	100 Score		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score	n Mean SD Median Min. Max.	54 62.41 18.902 62.50 20.0 95.0	54 59.72 20.591 65.00 15.0 90.0
Week 4	Score	n Mean SD Median Min. Max.	54 62.13 19.753 65.00 25.0 95.0	54 65.00 21.191 70.00 10.0
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.28 11.672 0.00 -25.0 40.0	5.00

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 27 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Mental Health: 0-100 score

Analysis Time Point	100 Score		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score	n Mean SD Median Min. Max.	53 66.70 18.835 70.00 25.0	54 66.11 21.050 70.00 15.0 100.0
	Change from Baseline	n Mean SD Median Min. Max.	53 3.87 14.827 5.00 -25.0 65.0	54 6.39 16.323 5.00 -25.0 45.0
Week 12	Score	n Mean SD Median Min. Max.	53 63.30 20.638 65.00 5.0	53 62.08 20.391 65.00 20.0
	Change from Baseline	n Mean SD Median Min. Max.	53 0.47 15.910 0.00 -35.0 70.0	53 2.26 15.980 0.00 -30.0 50.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 28 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Mental Health: 0-100 score

Analysis Time Poi	nt		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score	n Mean SD Median Min. Max.	20.0	19.264 65.00 25.0
	Change from Baseline	n Mean SD Median Min. Max.	53 2.55 15.981 0.00 -30.0 50.0	53 5.00 16.984 5.00 -30.0 50.0
Week 20	Score	n Mean SD Median Min. Max.	52 63.94 20.468 67.50 20.0 100.0	20.687 65.00 15.0
	Change from Baseline	n Mean SD Median Min. Max.	52 1.15 17.110 0.00 -45.0 45.0	52 4.42 18.005 2.50 -35.0 45.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 29 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Mental Health: 0-100 score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	n Mean SD Median Min. Max.		20.859 70.00 15.0
	Change from Baseline	n Mean SD Median Min. Max.	52 2.31 18.108 0.00 -35.0 55.0	-40.0
Week 28	Score	n Mean SD Median Min. Max.	10.0	70.00 15.0
	Change from Baseline	n Mean SD Median Min. Max.	51 0.59 16.871 0.00 -35.0 40.0	51 5.00 20.857 5.00 -40.0 60.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 30 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Mental Health: 0-100 score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 64.80 22.268 67.50 15.0	50 68.20 19.840 72.50 25.0 100.0
	Change from Baseline	n Mean SD Median Min. Max.	50 2.90 16.416 2.50 -35.0 40.0	50 7.20 17.704 10.00 -30.0 50.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 31 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Mental Health: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score	n Mean SD Median Min. Max.	54 44.28 9.889 44.33 22.1 61.3	54 42.88 10.773 45.64 19.5 58.7
Week 4	Score	n Mean SD Median Min. Max.	54 44.13 10.335 45.64 24.7 61.3	
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.14 6.107 0.00 -13.1 20.9	54 2.76 7.896 2.61 -13.1 20.9

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 32 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Mental Health: norm-based score

Analysis Time Point	IM-Dased Score		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score	n Mean SD Median Min. Max.	53 46.52 9.855 48.25 24.7 64.0	54 46.22 11.013 48.25 19.5 64.0
	Change from Baseline	n Mean SD Median Min. Max.	53 2.02 7.758 2.61 -13.1 34.0	54 3.34 8.539 2.61 -13.1 23.5
Week 12	Score	n Mean SD Median Min. Max.	53 44.75 10.798 45.64 14.2 64.0	53 44.11 10.669 45.64 22.1 64.0
	Change from Baseline	n Mean SD Median Min. Max.	53 0.25 8.325 0.00 -18.3 36.6	53 1.18 8.361 0.00 -15.7 26.2

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 33 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Mental Health: norm-based score

Analysis Time Point	IM-Dased Score		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score	n Mean SD Median Min. Max.	53 45.83 9.880 45.64 22.1 64.0	53 45.54 10.079 45.64 24.7 64.0
	Change from Baseline	n Mean SD Median Min. Max.	53 1.33 8.361 0.00 -15.7 26.2	53 2.62 8.886 2.61 -15.7 26.2
Week 20	Score	n Mean SD Median Min. Max.	52 45.08 10.709 46.95 22.1 64.0	52 45.59 10.823 45.64 19.5 64.0
	Change from Baseline	n Mean SD Median Min. Max.	52 0.60 8.952 0.00 -23.5 23.5	52 2.31 9.420 1.30 -18.3 23.5

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 34 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Mental Health: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	Median	52 45.69 11.320 45.64 22.1 64.0	10.914 48.25 19.5
	Change from Baseline	Median Min.	52 1.21 9.475 0.00 -18.3 28.8	2.62 -20.9
Week 28	Score	n Mean SD Median Min. Max.	51 44.66 11.354 48.25 16.9 64.0	11.604 48.25
	Change from Baseline	SD Median Min.	51 0.31 8.828 0.00 -18.3 20.9	10.912 2.61 -20.9

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 35 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Mental Health: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 45.53 11.651 46.95 19.5 64.0	50 47.31 10.381 49.56 24.7 64.0
	Change from Baseline	n Mean SD Median Min. Max.	50 1.52 8.589 1.30 -18.3 20.9	50 3.77 9.263 5.23 -15.7 26.2

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 36 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Physical Functioning: 0-100 score

Analysis Time Point	ng. 0-100 score		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score		54 63.06 26.977 62.51 10.0	
Week 4	Score	n Mean SD Median Min. Max.	54 66.67 24.514 70.00 10.0	
	Change from Baseline	n Mean SD Median Min. Max.	54 3.61 15.029 2.49 -45.0 40.0	5.00

2019N406842<u>00</u> 200622

Protocol: 200622 Page 37 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Physical Functioning: 0-100 score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score			27.311 79.99 5.0
	Change from Baseline	n Mean SD Median Min. Max.	16.542 5.00	20.954 5.00 -50.0
Week 12	Score		23.944 70.00 10.0	79.99 5.0
	Change from Baseline	n Mean SD Median Min. Max.	53 6.89 13.202 5.00 -30.0 45.0	

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 38 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Physical Functioning: 0-100 score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score	n Mean SD Median Min. Max.	53 73.21 24.001 79.99 10.0	25.062 79.99 5.0
	Change from Baseline	SD	53 10.57 19.057 5.01 -55.0 60.0	20.976 10.00
Week 20	Score	Median	52 69.62 26.250 72.50 0.0 100.0	26.621 79.99 5.0
	Change from Baseline	n Mean SD Median Min. Max.	52 7.40 18.511 5.00 -45.0 65.0	

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 39 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Physical Functioning: 0-100 score

Analysis Time Point	ing. 0-100 Score		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	n Mean SD Median Min. Max.	52 71.64 26.359 79.99 5.0 100.0	51 73.92 25.794 79.99 10.0
	Change from Baseline	n Mean SD Median Min. Max.	52 9.42 21.274 10.00 -70.0 70.0	51 11.96 20.834 5.00 -15.0 65.0
Week 28	Score	n Mean SD Median Min. Max.	51 69.71 25.483 70.00 10.0	51 75.29 25.247 79.99 5.0 100.0
	Change from Baseline	n Mean SD Median Min. Max.	51 8.24 18.543 5.00 -65.0 60.0	51 12.55 19.605 5.00 -10.0 65.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 40 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Physical Functioning: 0-100 score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 70.80 25.642 77.50 15.0 100.0	50 78.00 23.776 85.00 5.0
	Change from Baseline	n Mean SD Median Min. Max.	50 8.20 20.070 5.00 -60.0 65.0	50 14.50 21.123 5.00 -30.0 70.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 41 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Physical Functioning: norm-based score

Analysis Time Point			Placebo (N=54)	11.189 46.06 19.3 57.5  54 47.16 9.598 46.06 21.2 57.5  54 3.97 7.452 1.92 -13.4
Baseline	Score	n Mean SD Median Min. Max.	54 43.40 10.326 43.19 23.1 57.5	43.19 11.189 46.06 19.3
Week 4	Score	n Mean SD Median Min. Max.	54 44.78 9.383 46.06 23.1 57.5	47.16 9.598 46.06 21.2
	Change from Baseline		54 1.38 5.752 0.95 -17.2 15.3	3.97 7.452 1.92

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 42 of 90

Population: Intent-to-Treat

Table 3.1
Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Physical Functioning: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score		21.2	10.454 49.88 21.2
	Change from Baseline	n Mean SD Median Min. Max.	53 2.92 6.332 1.91 -15.3 21.1	8.020 1.92
Week 12	Score		9.165 46.06	53 47.36 10.548 49.88 21.2 57.5
	Change from Baseline	n Mean SD Median Min. Max.	53 2.64 5.053 1.91 -11.5 17.2	

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 43 of 90

Population: Intent-to-Treat

Table 3.1
Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Physical Functioning: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score	SD Median	53 47.29 9.187 49.88 23.1 57.5	9.593 49.88
	Change from Baseline	Min.	53 4.04 7.295 1.92 -21.1 23.0	
Week 20	Score		52 45.91 10.047 47.02 19.3 57.5	10.190
	Change from Baseline	n Mean SD Median Min. Max.	52 2.83 7.086 1.91 -17.2 24.9	2.87 -5.7

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 44 of 90

Population: Intent-to-Treat

Table 3.1
Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Physical Functioning: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	Median	52 46.68 10.089 49.88 21.2 57.5	9.873 49.88 23.1
	Change from Baseline	Median Min.	52 3.61 8.143 3.83 -26.8 26.8	1.91 -5.7
Week 28	Score		51 45.95 9.754 46.06 23.1 57.5	9.663
	Change from Baseline	SD Median Min.		7.503 1.91 -3.8

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 45 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Physical Functioning: norm-based score

Analysis Time	Point		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 46.36 9.815 48.93 25.0 57.5	50 49.12 9.100 51.80 21.2 57.5
	Change from Baseline	n Mean SD Median Min. Max.	50 3.14 7.682 1.91 -23.0 24.9	50 5.55 8.085 1.92 -11.5 26.8

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 46 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Response Consistency Index

Analysis Time Po	-		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score	n Mean SD Median Min. Max.	54 0.15 0.563 0.00 0.0	54 0.04 0.191 0.00 0.0 1.0
Week 4	Score	n Mean SD Median Min. Max.	54 0.13 0.516 0.00 0.0	54 0.06 0.302 0.00 0.0 2.0
	Change from Baseline	n Mean SD Median Min. Max.	54 -0.02 0.629 0.00 -3.0 3.0	54 0.02 0.363 0.00 -1.0 2.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 47 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Response Consistency Index

Analysis Time Point	ency index		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score	n Mean SD Median Min. Max.	53 0.00 0.000 0.000 0.00	54 0.06 0.302 0.00 0.0
	Change from Baseline	n Mean SD Median Min. Max.	53 -0.15 0.568 0.00 -3.0 0.0	54 0.02 0.363 0.00 -1.0 2.0
Week 12	Score	n Mean SD Median Min. Max.	53 0.02 0.137 0.00 0.0	53 0.15 0.632 0.00 0.0 4.0
	Change from Baseline	n Mean SD Median Min. Max.	53 -0.13 0.590 0.00 -3.0 1.0	53 0.11 0.640 0.00 -1.0 4.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 48 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Response Consistency Index

Analysis Time Point	ncy index		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score	n Mean SD Median Min. Max.	53 0.13 0.621 0.00 0.0 4.0	53 0.11 0.577 0.00 0.0 4.0
	Change from Baseline	n Mean SD Median Min. Max.	53 -0.02 0.747 0.00 -3.0 4.0	53 0.08 0.583 0.00 -1.0 4.0
Week 20	Score	n Mean SD Median Min. Max.	52 0.02 0.139 0.00 0.0	52 0.06 0.235 0.00 0.0
	Change from Baseline	n Mean SD Median Min. Max.	52 -0.13 0.595 0.00 -3.0 1.0	52 0.02 0.242 0.00 -1.0 1.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 49 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Response Consistency Index

Analysis Time Point	-		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	n Mean SD Median Min. Max.	52 0.04 0.194 0.00 0.0	51 0.16 0.758 0.00 0.0 5.0
	Change from Baseline	n Mean SD Median Min. Max.	52 -0.12 0.548 0.00 -3.0 1.0	51 0.12 0.791 0.00 -1.0 5.0
Week 28	Score	n Mean SD Median Min. Max.	51 0.06 0.311 0.00 0.0 2.0	51 0.06 0.238 0.00 0.0
	Change from Baseline	n Mean SD Median Min. Max.	51 -0.10 0.539 0.00 -3.0 1.0	51 0.02 0.316 0.00 -1.0 1.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 50 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Response Consistency Index

Analysis Time Poin	t		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 0.06 0.314 0.00 0.0	50 0.16 0.738 0.00 0.0
	Change from Baseline	n Mean SD Median Min. Max.	50 -0.06 0.470 0.00 -3.0 1.0	50 0.12 0.773 0.00 -1.0 5.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 51 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score	n Mean SD Median Min. Max.	54 74.07 28.533 83.33 0.0 100.0	
Week 4	Score	n Mean SD Median Min. Max.	54 74.23 27.342 79.17 0.0 100.0	91.67
	Change from Baseline	n Mean SD Median Min. Max.	54 0.15 20.509 0.00 -66.7 41.7	54 9.72 22.358 0.00 -41.7 75.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 52 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Role Emotional: 0-100 score

Analysis Time Point	-100 Scole		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score	n Mean SD Median Min. Max.	53 77.99 26.000 83.33 16.7 100.0	54 76.39 24.960 83.33 25.0
	Change from Baseline	n Mean SD Median Min. Max.	53 3.46 24.593 0.00 -75.0 66.7	54 5.09 23.202 0.00 -58.3 66.7
Week 12	Score	n Mean SD Median Min. Max.	53 74.69 26.602 75.00 16.7 100.0	53 71.86 24.473 75.00 8.3 100.0
	Change from Baseline	n Mean SD Median Min. Max.	53 0.16 25.866 0.00 -83.3 75.0	53 0.47 22.846 0.00 -58.3 66.7

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 53 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Analysis Time Point	-100 Scole		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score	n Mean SD Median Min. Max.	53 77.20 27.403 83.33 8.3 100.0	53 78.46 23.595 83.33 8.3 100.0
	Change from Baseline	n Mean SD Median Min. Max.	53 2.67 26.443 0.00 -75.0 66.7	53 7.08 22.253 0.00 -33.3 66.7
Week 20	Score	n Mean SD Median Min. Max.	52 77.88 27.805 91.67 0.0 100.0	52 76.60 25.407 83.33 0.0 100.0
	Change from Baseline	n Mean SD Median Min. Max.	52 3.85 25.269 0.00 -75.0 66.7	52 4.65 20.104 0.00 -33.3 50.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 54 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Analysis Time Point	7-100 Score		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	n Mean SD Median Min. Max.	52 75.32 27.064 79.17 16.7 100.0	51 79.41 24.173 83.33 16.7 100.0
	Change from Baseline	n Mean SD Median Min. Max.	52 1.28 26.217 0.00 -75.0 66.7	51 8.01 24.264 0.00 -50.0 58.3
Week 28	Score	n Mean SD Median Min. Max.	51 74.51 28.646 83.33 0.0 100.0	51 76.80 23.882 83.33 25.0
	Change from Baseline	n Mean SD Median Min. Max.	51 0.98 24.981 0.00 -100.0 66.7	51 5.07 23.039 0.00 -33.3 58.3

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 55 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Analysis Time	Point		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 75.67 28.315 87.50 8.3 100.0	50 83.00 21.558 91.67 16.7 100.0
	Change from Baseline	n Mean SD Median Min. Max.	50 2.50 22.977 0.00 -58.3 66.7	50 10.17 22.543 8.33 -33.3 75.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 56 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score	n Mean SD Median Min. Max.	54 45.34 11.922 49.20 14.4 56.2	54 44.18 11.571 45.72 14.4 56.2
Week 4	Score	n Mean SD Median Min. Max.	54 45.40 11.424 47.46 14.4 56.2	54 48.24 9.185 52.69 21.4 56.2
	Change from Baseline	n Mean SD Median Min. Max.	54 0.06 8.569 0.00 -27.9 17.4	54 4.06 9.341 0.00 -17.4 31.3

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 57 of 90

Population: Intent-to-Treat

Table 3.1
Summary of SF-36 Health Survey Domain Scores

Analysis Time Point	Jim-pased Scole		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score	n Mean SD Median Min. Max.	53 46.97 10.864 49.20 21.4 56.2	54 46.30 10.429 49.20 24.8 56.2
	Change from Baseline	n Mean SD Median Min. Max.	53 1.45 10.276 0.00 -31.3 27.9	54 2.13 9.694 0.00 -24.4 27.9
Week 12	Score	n Mean SD Median Min. Max.	53 45.59 11.115 45.72 21.4 56.2	53 44.41 10.225 45.72 17.9 56.2
	Change from Baseline	n Mean SD Median Min. Max.	53 0.07 10.808 0.00 -34.8 31.3	53 0.20 9.545 0.00 -24.4 27.9

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 58 of 90

Population: Intent-to-Treat

Table 3.1
Summary of SF-36 Health Survey Domain Scores

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score	n Mean SD Median Min. Max.	53 46.64 11.450 49.20 17.9 56.2	53 47.17 9.859 49.20 17.9 56.2
	Change from Baseline	n Mean SD Median Min. Max.	53 1.12 11.048 0.00 -31.3 27.9	53 2.96 9.298 0.00 -13.9 27.9
Week 20	Score	n Mean SD Median Min. Max.	52 46.93 11.618 52.69 14.4 56.2	52 46.39 10.616 49.20 14.4 56.2
	Change from Baseline	n Mean SD Median Min. Max.	52 1.61 10.559 0.00 -31.3 27.9	52 1.94 8.400 0.00 -13.9 20.9

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 59 of 90

Population: Intent-to-Treat

Table 3.1
Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Role Emotional: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	n Mean SD Median Min. Max.	21.4	49.20 21.4
	Change from Baseline	n Mean SD Median Min. Max.	10.955	51 3.35 10.138 0.00 -20.9 24.4
Week 28	Score	n Mean SD Median Min. Max.	51 45.52 11.969 49.20 14.4 56.2	49.20
	Change from Baseline	n Mean SD Median Min. Max.	51 0.41 10.438 0.00 -41.8 27.9	51 2.12 9.626 0.00 -13.9 24.4

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 60 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 46.00 11.831 50.95 17.9 56.2	50 49.07 9.008 52.69 21.4 56.2
	Change from Baseline	n Mean SD Median Min. Max.	50 1.05 9.601 0.00 -24.4 27.9	50 4.25 9.420 3.48 -13.9 31.3

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 61 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Role Physical: 0-100 score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score	n Mean SD Median Min. Max.	54 51.74 29.326 50.00 0.0	28.291
Week 4	Score	n Mean SD Median Min. Max.	54 57.41 28.579 62.50 0.0 100.0	
	Change from Baseline	n Mean SD Median Min. Max.	54 5.67 17.563 6.25 -25.0 43.8	3.13

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 62 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Role Physical: 0-100 score

Analysis Time Point	100 SCOIE		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score	n Mean SD Median Min. Max.	53 58.25 29.335 62.50 0.0 100.0	54 63.19 27.570 65.63 6.3 100.0
	Change from Baseline	n Mean SD Median Min. Max.	53 6.49 19.839 6.25 -31.3 68.8	54 13.43 25.450 9.38 -37.5 93.8
Week 12	Score	n Mean SD Median Min. Max.	53 56.96 28.527 56.25 0.0 100.0	53 61.67 27.244 62.50 0.0 100.0
	Change from Baseline	n Mean SD Median Min. Max.	53 5.19 20.019 6.25 -43.8 56.3	53 11.56 25.162 6.25 -37.5 93.8

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 63 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Role Physical: 0-100 score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score	Median	29.503 62.50 0.0	26.620 68.75 0.0
	Change from Baseline	Median Min.	53 9.43 19.249 6.25 -31.3 62.5	6.25 -31.3
Week 20	Score	SD Median	52 57.45 29.211 50.00 0.0 100.0	27.842 75.00 0.0
	Change from Baseline	SD Median	52 6.13 19.744 6.25 -37.5 62.5	23.507 6.25 -25.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 64 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Role Physical: 0-100 score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score			30.261 75.00 0.0
	Change from Baseline	n Mean SD Median Min. Max.	52 8.77 19.697 6.25 -37.5 75.0	26.815 12.50 -31.3
Week 28	Score	Median	28.267 56.25 6.3	68.75 0.0
	Change from Baseline	n Mean SD Median Min. Max.	51 10.17 23.683 6.25 -37.5 81.3	

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 65 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Role Physical: 0-100 score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 59.63 29.645 59.38 0.0 100.0	50 66.38 27.108 71.88 0.0 100.0
	Change from Baseline	n Mean SD Median Min. Max.	50 8.25 21.630 6.25 -37.5 81.3	50 15.63 27.177 12.50 -25.0 93.8

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 66 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Role Physical: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score	n Mean SD Median Min. Max.	54 39.82 10.536 39.19 21.2 57.2	54 39.11 10.164 39.19 21.2 57.2
Week 4	Score	n Mean SD Median Min. Max.	54 41.85 10.268 43.68 21.2 57.2	54 43.02 9.973 43.68 23.5 57.2
	Change from Baseline	n Mean SD Median Min. Max.	54 2.04 6.310 2.24 -9.0 15.7	54 3.91 8.347 1.12 -9.0 29.2

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 67 of 90

Population: Intent-to-Treat

Table 3.1
Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Role Physical: norm-based score

Analysis Time Point	Im-Dased Scole		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score	n Mean SD Median Min. Max.	53 42.16 10.540 43.68 21.2 57.2	54 43.93 9.906 44.81 23.5 57.2
	Change from Baseline	n Mean SD Median Min. Max.	53 2.33 7.128 2.24 -11.2 24.7	54 4.82 9.144 3.37 -13.5 33.7
Week 12	Score	n Mean SD Median Min. Max.	53 41.69 10.250 41.44 21.2 57.2	53 43.39 9.788 43.68 21.2 57.2
	Change from Baseline	n Mean SD Median Min. Max.	53 1.86 7.193 2.25 -15.7 20.2	53 4.15 9.040 2.25 -13.5 33.7

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 68 of 90

Population: Intent-to-Treat

Table 3.1
Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Role Physical: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score	n Mean SD Median Min. Max.		
	Change from Baseline	Min.	53 3.39 6.916 2.24 -11.2 22.5	
Week 20	Score	n Mean SD Median Min. Max.	52 41.87 10.496 39.19 21.2 57.2	10.003
	Change from Baseline	n Mean SD Median Min. Max.	52 2.20 7.094 2.24 -13.5 22.5	2.25 -9.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 69 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Role Physical: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	n Mean SD Median Min. Max.	52 42.82 10.210 43.68 21.2 57.2	
	Change from Baseline	n Mean SD Median Min. Max.	7.077	
Week 28	Score	n Mean SD Median Min. Max.		51 43.37 10.212 45.93 21.2 57.2
	Change from Baseline	n Mean SD Median Min. Max.	51 3.65 8.509 2.25 -13.5 29.2	51 4.18 9.558 2.24 -18.0 33.7

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 70 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Role Physical: norm-based score

Analysis Time Pos	int		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 42.65 10.651 42.56 21.2 57.2	50 45.08 9.739 47.05 21.2 57.2
	Change from Baseline	n Mean SD Median Min. Max.	50 2.96 7.771 2.25 -13.5 29.2	50 5.61 9.764 4.49 -9.0 33.7

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 71 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Social Functioning: 0-100 score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score		54 62.73 29.087 75.00 0.0	62.50 0.0
Week 4	Score	n Mean SD Median Min. Max.	54 65.74 30.733 75.00 0.0 100.0	
	Change from Baseline	n Mean SD Median Min. Max.	0.00	54 7.64 20.520 0.00 -50.0 50.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 72 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Social Functioning: 0-100 score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score			75.00 25.0
	Change from Baseline	n Mean SD Median Min. Max.	53 8.49 23.612 0.00 -50.0 62.5	20.841 12.50
Week 12	Score		0.0	26.332 62.50 12.5
	Change from Baseline	n Mean SD Median Min. Max.	53 5.90 21.734 0.00 -37.5 75.0	53 7.55 22.779 0.00 -37.5 75.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 73 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Social Functioning: 0-100 score

Analysis Time Point	ig. 0-100 Score		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score	n Mean SD Median Min. Max.	53 71.70 27.859 75.00 0.0 100.0	53 70.05 24.921 75.00 12.5 100.0
	Change from Baseline	n Mean SD Median Min. Max.	53 8.96 22.784 0.00 -25.0 62.5	53 11.56 18.645 12.50 -50.0 50.0
Week 20	Score	n Mean SD Median Min. Max.	52 69.95 30.544 75.00 0.0 100.0	52 71.39 24.795 75.00 25.0 100.0
	Change from Baseline	n Mean SD Median Min. Max.	52 7.69 23.891 0.00 -50.0 75.0	52 12.26 21.364 12.50 -37.5 62.5

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 74 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Social Functioning: 0-100 score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	SD Median	52 70.43 28.335 75.00 0.0 100.0	27.395 75.00 12.5
	Change from Baseline	Median Min.	52 8.17 21.277 0.00 -37.5 62.5	12.50 -37.5
Week 28	Score		29.136 75.00 0.0	28.414 75.00 0.0
	Change from Baseline	SD Median	51 8.82 21.549 0.00 -37.5 62.5	26.501 12.50 -50.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 75 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Social Functioning: 0-100 score

Analysis Time Point			Placebo 3	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 71.00 29.390 75.00 0.0 100.0	50 72.00 26.069 75.00 12.5 100.0
	Change from Baseline	n Mean SD Median Min. Max.	50 9.00 23.151 12.50 -50.0 62.5	50 13.00 22.863 12.50 -50.0 50.0

#### 2019N406842<u>00</u> 200<del>6</del>22

#### CONFIDENTIAL

Protocol: 200622 Page 76 of 90

Population: Intent-to-Treat

Table 3.1
Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Social Functioning: norm-based score

Analysis Time Poin	t		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score	n Mean SD Median Min. Max.	54 42.39 11.666 47.31 17.2 57.3	54 40.91 10.731 42.30 17.2 57.3
Week 4	Score	n Mean SD Median Min. Max.	54 43.60 12.326 47.31 17.2 57.3	10.579
	Change from Baseline	n Mean SD Median Min. Max.		54 3.06 8.230 0.00 -20.1 20.1

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 77 of 90

Population: Intent-to-Treat

Table 3.1
Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Social Functioning: norm-based score

Analysis Time Point	g. Horm-based score		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score	n Mean SD Median Min. Max.	53 45.80 11.278 47.31 17.2 57.3	54 45.36 9.563 47.31 27.3 57.3
	Change from Baseline	n Mean SD Median Min. Max.	53 3.41 9.470 0.00 -20.1 25.1	54 4.46 8.359 5.01 -20.1 25.1
Week 12	Score	n Mean SD Median Min. Max.	53 44.76 11.280 47.31 17.2 57.3	53 43.72 10.561 42.30 22.3 57.3
	Change from Baseline	n Mean SD Median Min. Max.	53 2.36 8.717 0.00 -15.0 30.1	53 3.03 9.136 0.00 -15.0 30.1

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 78 of 90

Population: Intent-to-Treat

Table 3.1
Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Social Functioning: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score	Median	53 45.99 11.174 47.31 17.2 57.3	9.995 47.31 22.3
	Change from Baseline	Median Min.	53 3.59 9.138 0.00 -10.0 25.1	5.01 -20.1
Week 20	Score		52 45.29 12.251 47.31 17.2 57.3	9.945
	Change from Baseline		52 3.09 9.582 0.00 -20.1 30.1	8.569 5.01 -15.0

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 79 of 90

Population: Intent-to-Treat

Table 3.1
Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Social Functioning: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	Median	52 45.48 11.365 47.31 17.2 57.3	10.987 47.31 22.3
	Change from Baseline	Median Min.	52 3.28 8.534 0.00 -15.0 25.1	5.01 -15.0
Week 28	Score		51 45.54 11.685 47.31 17.2 57.3	11.397
	Change from Baseline	SD Median Min.	51 3.54 8.642 0.00 -15.0 25.1	10.630 5.01 -20.1

# CONFIDENTIAL 2019N406842\_00 200622

Protocol: 200622 Page 80 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Social Functioning: norm-based score

Analysis Time F	Point		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 45.71 11.787 47.31 17.2 57.3	50 46.11 10.455 47.31 22.3 57.3
	Change from Baseline	n Mean SD Median Min. Max.	50 3.61 9.286 5.01 -20.1 25.1	50 5.21 9.169 5.01 -20.1 20.1

# CONFIDENTIAL 2019N406842\_00 200622

Protocol: 200622 Page 81 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Vitality: 0-100 score

Analysis Time Poin			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score	n Mean SD Median Min. Max.	54 38.89 21.122 37.50 0.0 87.5	54 39.70 22.751 40.63 0.0 87.5
Week 4	Score	n Mean SD Median Min. Max.	54 43.98 21.272 43.75 0.0 100.0	54 45.49 22.857 43.75 6.3 87.5
	Change from Baseline	n Mean SD Median Min. Max.	54 5.09 12.266 6.25 -18.8 25.0	54 5.79 16.860 0.00 -37.5 43.8

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 82 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Vitality: 0-100 score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score			20.914 43.75 6.3
	Change from Baseline	n Mean SD Median Min. Max.		-43.8
Week 12	Score	n Mean SD Median Min. Max.		
	Change from Baseline	n Mean SD Median Min. Max.	53 6.25 15.649 6.25 -18.8 68.8	53 5.90 20.960 0.00 -43.8 56.3

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 83 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Vitality: 0-100 score

Analysis Time Point	sole		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score	n Mean SD Median Min. Max.	53 46.46 22.585 50.00 6.3 93.8	53 45.28 20.762 43.75 6.3 81.3
	Change from Baseline	n Mean SD Median Min. Max.	53 7.43 16.764 6.25 -25.0 50.0	53 5.31 20.304 6.25 -37.5 56.3
Week 20	Score	n Mean SD Median Min. Max.	52 47.96 22.234 46.88 0.0 93.8	52 47.00 20.580 43.75 0.0 81.3
	Change from Baseline	n Mean SD Median Min. Max.	52 8.65 16.932 6.25 -25.0 68.8	52 6.85 20.609 6.25 -43.8 43.8

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 84 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Vitality: 0-100 score

Analysis Time Point	Sole		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	n Mean SD Median Min. Max.	52 48.68 22.799 50.00 0.0	51 49.63 21.773 50.00 0.0 81.3
	Change from Baseline	n Mean SD Median Min. Max.	52 9.38 18.913 6.25 -37.5 75.0	51 8.82 20.432 6.25 -25.0 62.5
Week 28	Score	n Mean SD Median Min. Max.	51 48.28 23.455 50.00 0.0 93.8	51 47.18 24.119 50.00 0.0 93.8
	Change from Baseline	n Mean SD Median Min. Max.	51 8.95 19.655 6.25 -37.5 62.5	51 7.23 20.516 6.25 -31.3 68.8

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 85 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Vitality: 0-100 score

Analysis Time			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 46.38 24.617 46.88 0.0 93.8	50 51.25 21.724 50.00 0.0 93.8
	Change from Baseline	n Mean SD Median Min. Max.	50 7.63 19.856 6.25 -37.5 68.8	50 10.75 19.358 6.25 -25.0 56.3

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 86 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Vitality: norm-based score

Analysis Time Point	sed scole		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Baseline	Score	n Mean SD Median Min. Max.	54 41.38 10.041 40.72 22.9 64.5	54 41.76 10.816 42.21 22.9 64.5
Week 4	Score	n Mean SD Median Min. Max.	54 43.80 10.112 43.69 22.9 70.4	54 44.51 10.865 43.69 25.9 64.5
	Change from Baseline	n Mean SD Median Min. Max.	54 2.42 5.832 2.97 -8.9 11.9	0.00

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 87 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Vitality: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 8	Score	n Mean SD Median Min. Max.		9.942 43.69 25.9
	Change from Baseline	n Mean SD Median Min. Max.	53 3.98 7.707 2.97 -5.9 26.7	9.779 2.97 -20.8
Week 12	Score		53 44.42 10.174 46.66 22.9 64.5	53 44.69 9.341 43.69 22.9 64.5
	Change from Baseline	n Mean SD Median Min. Max.	53 2.97 7.439 2.97 -8.9 32.7	-20.8

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 88 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Vitality: norm-based score

Analysis Time Point	sed Score		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 16	Score	n Mean SD Median Min. Max.	53 44.98 10.736 46.66 25.9 67.5	53 44.41 9.870 43.69 25.9 61.5
	Change from Baseline	n Mean SD Median Min. Max.	53 3.53 7.969 2.97 -11.9 23.8	53 2.52 9.653 2.97 -17.8 26.7
Week 20	Score	n Mean SD Median Min. Max.	52 45.69 10.569 45.18 22.9 67.5	52 45.23 9.783 43.69 22.9 61.5
	Change from Baseline	n Mean SD Median Min. Max.	52 4.11 8.049 2.97 -11.9 32.7	52 3.26 9.798 2.97 -20.8 20.8

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 89 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Vitality: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 24	Score	n Mean SD Median Min. Max.	52 46.03 10.838 46.66 22.9 70.4	51 46.48 10.350 46.66 22.9 61.5
	Change from Baseline	n Mean SD Median Min. Max.	52 4.46 8.990 2.97 -17.8 35.7	51 4.19 9.713 2.97 -11.9 29.7
Week 28	Score	n Mean SD Median Min. Max.	51 45.84 11.149 46.66 22.9 67.5	51 45.32 11.465 46.66 22.9 67.5
	Change from Baseline	n Mean SD Median Min. Max.	51 4.25 9.343 2.97 -17.8 29.7	51 3.44 9.753 2.97 -14.9 32.7

2019N406842<u>00</u> 200<del>6</del>22

Protocol: 200622 Page 90 of 90

Population: Intent-to-Treat

Table 3.1

Summary of SF-36 Health Survey Domain Scores

Domain: SF363-Vitality: norm-based score

Analysis Time Point			Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Week 32	Score	n Mean SD Median Min. Max.	50 44.93 11.702 45.18 22.9 67.5	50 47.25 10.327 46.66 22.9 67.5
	Change from Baseline	n Mean SD Median Min. Max.	50 3.62 9.439 2.97 -17.8 32.7	50 5.11 9.203 2.97 -11.9 26.7

Protocol: 200622 Page 1 of 8

Population: Intent-to-Treat

Table 90.118 Analysis of Change from Baseline in SF-36 Domain Score: Physical Functioning (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 54 66.02 (2.089) 3.47 (2.089)	54 54 73.22 (2.091) 10.68 (2.091)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		7.21 (1.32, 13.10) 0.017
Corrected Hedges g [3] 95% CI		0.47 (0.08, 0.85)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 548 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 8

Population: Intent-to-Treat

Table 90.118 Analysis of Change from Baseline in SF-36 Domain Score: Physical Functioning (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 69.61 (2.341) 7.06 (2.341)	54 54 73.13 (2.330) 10.58 (2.330)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		3.52 (-3.06, 10.10) 0.291
Corrected Hedges g [3] 95% CI		0.20 (-0.18, 0.58)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 549 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 8

Population: Intent-to-Treat

Table 90.118 Analysis of Change from Baseline in SF-36 Domain Score: Physical Functioning (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 12

· <del></del>	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 68.90 (2.137) 6.35 (2.137)	54 53 72.92 (2.134) 10.37 (2.134)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		4.02 (-2.00, 10.04) 0.188
Corrected Hedges g [3] 95% CI		0.26 (-0.13, 0.64)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 550 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 4 of 8

Population: Intent-to-Treat

Table 90.118 Analysis of Change from Baseline in SF-36 Domain Score: Physical Functioning (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 72.53 (2.372) 9.99 (2.372)	54 53 74.95 (2.369) 12.40 (2.369)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		2.41 (-4.26, 9.09) 0.475
Corrected Hedges g [3] 95% CI		0.14 (-0.24, 0.52)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 551 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 5 of 8 Population: Intent-to-Treat

Table 90.118 Analysis of Change from Baseline in SF-36 Domain Score:

> Physical Functioning (0-100 score) (Mixed Model Repeated Measures)

> > Mana a 1 d ------ a la

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 69.25 (2.484) 6.70 (2.484)	54 52 75.77 (2.480) 13.22 (2.480)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		6.52 (-0.48, 13.52) 0.067	
Corrected Hedges g [3] 95% CI		0.36 (-0.03, 0.75)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 552 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 6 of 8

Population: Intent-to-Treat

Table 90.118 Analysis of Change from Baseline in SF-36 Domain Score: Physical Functioning (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 71.26 (2.606) 8.71 (2.606)	54 51 73.46 (2.609) 10.91 (2.609)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		2.20 (-5.14, 9.54) 0.553
Corrected Hedges g [3] 95% CI		0.12 (-0.27, 0.50)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 553 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 7 of 8

Population: Intent-to-Treat

Table 90.118 Analysis of Change from Baseline in SF-36 Domain Score: Physical Functioning (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 69.83 (2.369) 7.29 (2.369)	54 51 74.38 (2.367) 11.84 (2.367)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		4.55 (-2.12, 11.22) 0.179	
Corrected Hedges g [3] 95% CI		0.27 (-0.12, 0.66)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 554 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 8 of 8

Population: Intent-to-Treat

Table 90.118 Analysis of Change from Baseline in SF-36 Domain Score: Physical Functioning (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 50 70.16 (2.480) 7.61 (2.480)	54 50 76.22 (2.477) 13.67 (2.477)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		6.06 (-0.92, 13.04) 0.088	
Corrected Hedges g [3] 95% CI		0.34 (-0.05, 0.74)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 555 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 1 of 8 Table 90.119

Population: Intent-to-Treat

Analysis of Change from Baseline in SF-36 Domain Score:

Role Physical (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 54 56.40 (2.609) 5.58 (2.609)	54 54 61.72 (2.611) 10.89 (2.611)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		5.31 (-2.04, 12.67) 0.155
Corrected Hedges g [3] 95% CI		0.28 (-0.10, 0.65)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 556 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 8 Table 90.119

Population: Intent-to-Treat

Analysis of Change from Baseline in SF-36 Domain Score:

Role Physical (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 56.96 (2.844) 6.14 (2.844)	54 54 64.21 (2.824) 13.39 (2.824)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		7.25 (-0.74, 15.23) 0.075
Corrected Hedges g [3] 95% CI		0.35 (-0.03, 0.73)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 557 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 8 Population: Intent-to-Treat

Table 90.119

Analysis of Change from Baseline in SF-36 Domain Score:

Role Physical (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 55.66 (2.838) 4.83 (2.838)	54 53 61.99 (2.829) 11.17 (2.829)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		6.34 (-1.64, 14.32) 0.118
Corrected Hedges g [3] 95% CI		0.31 (-0.08, 0.69)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 558 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 4 of 8 Table 90.119

Population: Intent-to-Treat

Analysis of Change from Baseline in SF-36 Domain Score:

Role Physical (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 59.89 (2.728) 9.07 (2.728)	54 53 62.18 (2.721) 11.35 (2.721)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		2.29 (-5.39, 9.96) 0.556	
Corrected Hedges g [3] 95% CI		0.11 (-0.27, 0.50)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 559 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 5 of 8 Population: Intent-to-Treat

Table 90.119 Analysis of Change from Baseline in SF-36 Domain Score:

> Role Physical (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 56.43 (2.797) 5.61 (2.797)	54 52 63.68 (2.790) 12.85 (2.790)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		7.24 (-0.63, 15.11) 0.071	
Corrected Hedges g [3] 95% CI		0.36 (-0.03, 0.74)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 560 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622

Population: Intent-to-Treat

Page 6 of 8

Table 90.119
Analysis of Change from Baseline in SF-36 Domain Score:

Role Physical (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 59.06 (3.021) 8.24 (3.021)	54 51 65.81 (3.026) 14.99 (3.026)	_
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		6.75 (-1.76, 15.26) 0.119	
Corrected Hedges g [3] 95% CI		0.31 (-0.08, 0.70)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 561 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 7 of 8 Population: Intent-to-Treat

Table 90.119 Analysis of Change from Baseline in SF-36 Domain Score:

> Role Physical (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 60.61 (3.099) 9.79 (3.099)	54 51 61.61 (3.094) 10.79 (3.094)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		1.00 (-7.71, 9.72) 0.820	
Corrected Hedges g [3] 95% CI		0.04 (-0.34, 0.43)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 562 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 8 of 8 Population: Intent-to-Treat

Table 90.119

Analysis of Change from Baseline in SF-36 Domain Score:

Role Physical (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 50 59.36 (3.051) 8.54 (3.051)	54 50 65.67 (3.045) 14.85 (3.045)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		6.31 (-2.27, 14.89) 0.148
Corrected Hedges g [3] 95% CI		0.29 (-0.10, 0.68)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 563 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 1 of 8

Population: Intent-to-Treat

Table 90.120 Analysis of Change from Baseline in SF-36 Domain Score:

> Bodily Pain (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 54 58.14 (2.407) 7.34 (2.407)	54 54 60.77 (2.407) 9.96 (2.407)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		2.63 (-4.15, 9.40) 0.443
Corrected Hedges g [3] 95% CI		0.15 (-0.23, 0.53)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 564 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 8

Population: Intent-to-Treat

Table 90.120 Analysis of Change from Baseline in SF-36 Domain Score: Bodily Pain (0-100 score)

(Mixed Model Repeated Measures)

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 58.78 (3.275) 7.97 (3.275)	54 54 67.67 (3.249) 16.87 (3.249)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		8.90 (-0.27, 18.07) 0.057
Corrected Hedges g [3] 95% CI		0.37 (-0.01, 0.75)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 565 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 8

Population: Intent-to-Treat

Table 90.120 Analysis of Change from Baseline in SF-36 Domain Score:

Bodily Pain (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 57.45 (2.948) 6.65 (2.948)	54 53 60.12 (2.941) 9.32 (2.941)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		2.67 (-5.62, 10.95) 0.524
Corrected Hedges g [3] 95% CI		0.12 (-0.26, 0.50)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 566 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 4 of 8

Population: Intent-to-Treat

Table 90.120 Analysis of Change from Baseline in SF-36 Domain Score:

Bodily Pain (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 62.68 (2.813) 11.88 (2.813)	54 53 58.91 (2.807) 8.11 (2.807)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-3.77 (-11.68, 4.13) 0.346
Corrected Hedges g [3] 95% CI		-0.18 (-0.56, 0.20)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 567 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 5 of 8 Population: Intent-to-Treat

Table 90.120

Analysis of Change from Baseline in SF-36 Domain Score:

Bodily Pain (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 61.83 (2.763) 11.03 (2.763)	54 52 62.48 (2.759) 11.67 (2.759)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.65 (-7.13, 8.42) 0.869
Corrected Hedges g [3] 95% CI		0.03 (-0.35, 0.42)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 568 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 6 of 8 Population: Intent-to-Treat

Table 90.120

Analysis of Change from Baseline in SF-36 Domain Score:

Bodily Pain (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 60.78 (3.026) 9.98 (3.026)	54 51 66.04 (3.037) 15.23 (3.037)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		5.26 (-3.27, 13.78) 0.224
Corrected Hedges g [3] 95% CI		0.24 (-0.15, 0.63)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 569 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622
Population: Intent-to-Treat

Table 90.120

Analysis of Change from Baseline in SF-36 Domain Score:

Bodily Pain (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 61.91 (2.976) 11.11 (2.976)	54 51 63.35 (2.970) 12.55 (2.970)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		1.44 (-6.92, 9.81) 0.733
Corrected Hedges g [3] 95% CI		0.07 (-0.32, 0.46)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 570 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 8 of 8 Population: Intent-to-Treat

Table 90.120

Analysis of Change from Baseline in SF-36 Domain Score:

Bodily Pain (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 50 61.43 (3.131) 10.63 (3.131)	54 50 67.65 (3.128) 16.85 (3.128)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		6.22 (-2.58, 15.03) 0.164
Corrected Hedges g [3] 95% CI		0.28 (-0.11, 0.67)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 571 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 1 of 8

Population: Intent-to-Treat

Table 90.121 Analysis of Change from Baseline in SF-36 Domain Score: General Health (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 43.46 (1.823) 4.39 (1.823)	54 54 45.62 (1.826) 6.55 (1.826)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		2.16 (-3.00, 7.32) 0.408
Corrected Hedges g [3] 95% CI		0.16 (-0.22, 0.54)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 572 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 8

Population: Intent-to-Treat

Table 90.121 Analysis of Change from Baseline in SF-36 Domain Score: General Health (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 46.11 (2.027) 7.04 (2.027)	54 54 46.83 (2.020) 7.76 (2.020)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.72 (-5.00, 6.44) 0.804
Corrected Hedges g [3] 95% CI		0.05 (-0.33, 0.43)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 573 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 8

Population: Intent-to-Treat

Table 90.121 Analysis of Change from Baseline in SF-36 Domain Score: General Health (0-100 score) (Mixed Model Repeated Measures)

Mana all i muma la

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 44.19 (2.142) 5.12 (2.142)	54 53 48.65 (2.139) 9.59 (2.139)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		4.46 (-1.58, 10.51) 0.146	
Corrected Hedges g [3] 95% CI		0.28 (-0.10, 0.67)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 574 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 4 of 8

Population: Intent-to-Treat

Table 90.121 Analysis of Change from Baseline in SF-36 Domain Score: General Health (0-100 score)

(Mixed Model Repeated Measures)

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 42.99 (2.340) 3.92 (2.340)	54 53 49.02 (2.337) 9.95 (2.337)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		6.03 (-0.58, 12.63) 0.073	
Corrected Hedges g [3] 95% CI		0.35 (-0.03, 0.74)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 575 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 5 of 8

Population: Intent-to-Treat

Table 90.121 Analysis of Change from Baseline in SF-36 Domain Score: General Health (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 43.13 (2.331) 4.06 (2.331)	54 52 47.63 (2.328) 8.56 (2.328)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		4.50 (-2.07, 11.08) 0.177	
Corrected Hedges g [3] 95% CI		0.27 (-0.12, 0.65)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 576 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 6 of 8 Population: Intent-to-Treat

Table 90.121 Analysis of Change from Baseline in SF-36 Domain Score:

> General Health (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 42.50 (2.440) 3.43 (2.440)	54 51 48.83 (2.442) 9.77 (2.442)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		6.34 (-0.55, 13.23) 0.071
Corrected Hedges g [3] 95% CI		0.36 (-0.03, 0.75)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 577 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 7 of 8

Population: Intent-to-Treat

Table 90.121 Analysis of Change from Baseline in SF-36 Domain Score: General Health (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 42.19 (2.609) 3.13 (2.609)	54 51 46.52 (2.607) 7.45 (2.607)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		4.33 (-3.03, 11.68) 0.246	
Corrected Hedges g [3] 95% CI		0.23 (-0.16, 0.62)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 578 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 8 of 8

Population: Intent-to-Treat

Table 90.121 Analysis of Change from Baseline in SF-36 Domain Score: General Health (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 50 43.23 (2.438) 4.16 (2.438)	54 50 48.65 (2.434) 9.58 (2.434)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		5.42 (-1.46, 12.29) 0.121	
Corrected Hedges g [3] 95% CI		0.31 (-0.08, 0.71)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 579 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 1 of 8

Population: Intent-to-Treat

Table 90.122 Analysis of Change from Baseline in SF-36 Domain Score: Vitality (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 44.52 (1.919) 4.93 (1.919)	54 54 45.30 (1.920) 5.72 (1.920)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.78 (-4.63, 6.19) 0.774
Corrected Hedges g [3] 95% CI		0.06 (-0.32, 0.43)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 580 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 8

Population: Intent-to-Treat Table 90.122

Analysis of Change from Baseline in SF-36 Domain Score:

Vitality (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 47.68 (2.345) 8.10 (2.345)	54 54 46.59 (2.328) 7.00 (2.328)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-1.09 (-7.68, 5.49) 0.742
Corrected Hedges g [3] 95% CI		-0.06 (-0.44, 0.32)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 581 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 8

Population: Intent-to-Treat

Table 90.122 Analysis of Change from Baseline in SF-36 Domain Score: Vitality (0-100 score)

(Mixed Model Repeated Measures)

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 45.53 (2.247) 5.94 (2.247)	54 53 45.14 (2.240) 5.55 (2.240)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.39 (-6.71, 5.93) 0.903	
Corrected Hedges g [3] 95% CI		-0.02 (-0.40, 0.36)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 582 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 4 of 8

Population: Intent-to-Treat

Table 90.122 Analysis of Change from Baseline in SF-36 Domain Score: Vitality (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 46.72 (2.340) 7.13 (2.340)	54 53 44.56 (2.337) 4.98 (2.337)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-2.15 (-8.74, 4.43) 0.518
Corrected Hedges g [3] 95% CI		-0.13 (-0.51, 0.26)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 583 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 5 of 8 Population: Intent-to-Treat

Table 90.122

Analysis of Change from Baseline in SF-36 Domain Score:

Vitality (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 47.82 (2.302) 8.23 (2.302)	54 52 45.99 (2.299) 6.41 (2.299)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-1.82 (-8.30, 4.66) 0.578	
Corrected Hedges g [3] 95% CI		-0.11 (-0.49, 0.28)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 584 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 6 of 8 Population: Intent-to-Treat

Table 90.122

Analysis of Change from Baseline in SF-36 Domain Score:

Vitality (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 48.58 (2.503) 8.99 (2.503)	54 51 47.75 (2.510) 8.17 (2.510)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.83 (-7.88, 6.23) 0.816
Corrected Hedges g [3] 95% CI		-0.05 (-0.43, 0.34)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 585 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 7 of 8

Population: Intent-to-Treat

Table 90.122 Analysis of Change from Baseline in SF-36 Domain Score: Vitality (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 48.05 (2.571) 8.46 (2.571)	54 51 46.00 (2.567) 6.41 (2.567)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-2.05 (-9.28, 5.18) 0.575
Corrected Hedges g [3] 95% CI		-0.11 (-0.50, 0.28)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 586 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 8 of 8 Population: Intent-to-Treat

Table 90.122 Analysis of Change from Baseline in SF-36 Domain Score:

> Vitality (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 50 47.01 (2.532) 7.43 (2.532)	54 50 50.43 (2.528) 10.85 (2.528)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		3.42 (-3.70, 10.54) 0.343
Corrected Hedges g [3] 95% CI		0.19 (-0.20, 0.58)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 587 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 1 of 8 Population: Intent-to-Treat

Table 90.123

Analysis of Change from Baseline in SF-36 Domain Score:

Social Functioning (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 64.01 (2.652) 3.32 (2.652)	54 54 68.07 (2.652) 7.38 (2.652)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		4.06 (-3.41, 11.53) 0.283
Corrected Hedges g [3] 95% CI		0.21 (-0.17, 0.58)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 588 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 8 Population: Intent-to-Treat

Table 90.123 Analysis of Change from Baseline in SF-36 Domain Score:

> Social Functioning (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 69.47 (2.665) 8.78 (2.665)	54 54 71.29 (2.644) 10.60 (2.644)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		1.81 (-5.66, 9.29) 0.631
Corrected Hedges g [3] 95% CI		0.09 (-0.29, 0.47)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 589 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 8

Population: Intent-to-Treat

Table 90.123 Analysis of Change from Baseline in SF-36 Domain Score:

Social Functioning (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 66.89 (2.776) 6.20 (2.776)	54 53 67.25 (2.769) 6.55 (2.769)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.36 (-7.45, 8.16) 0.928	
Corrected Hedges g [3] 95% CI		0.02 (-0.36, 0.40)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 590 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 4 of 8 Table 90.123

Population: Intent-to-Treat

Analysis of Change from Baseline in SF-36 Domain Score:

Social Functioning (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 70.04 (2.540) 9.35 (2.540)	54 53 71.44 (2.534) 10.75 (2.534)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		1.40 (-5.75, 8.55) 0.699
Corrected Hedges g [3] 95% CI		0.08 (-0.31, 0.46)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 591 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 5 of 8 Population: Intent-to-Treat

Table 90.123 Analysis of Change from Baseline in SF-36 Domain Score:

> Social Functioning (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 68.30 (2.898) 7.61 (2.898)	54 52 71.84 (2.895) 11.15 (2.895)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		3.54 (-4.61, 11.70) 0.391	
Corrected Hedges g [3] 95% CI		0.17 (-0.22, 0.55)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 592 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 6 of 8 Population: Intent-to-Treat

Table 90.123 Analysis of Change from Baseline in SF-36 Domain Score:

Social Functioning (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 68.81 (2.772) 8.12 (2.772)	54 51 71.33 (2.777) 10.64 (2.777)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		2.52 (-5.29, 10.34) 0.523
Corrected Hedges g [3] 95% CI		0.13 (-0.26, 0.51)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 593 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 7 of 8 Population: Intent-to-Treat

Table 90.123

Analysis of Change from Baseline in SF-36 Domain Score:

Social Functioning (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 68.91 (3.103) 8.22 (3.103)	54 51 70.62 (3.099) 9.93 (3.099)	•
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		1.71 (-7.02, 10.43) 0.698	
Corrected Hedges g [3] 95% CI		0.08 (-0.31, 0.46)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 594 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 8 of 8 Population: Intent-to-Treat

Table 90.123 Analysis of Change from Baseline in SF-36 Domain Score:

> Social Functioning (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 50 70.13 (2.896) 9.44 (2.896)	54 50 72.95 (2.894) 12.26 (2.894)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		2.82 (-5.32, 10.97) 0.493	
Corrected Hedges g [3] 95% CI		0.14 (-0.26, 0.53)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 595 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 1 of 8

Population: Intent-to-Treat

Table 90.124 Analysis of Change from Baseline in SF-36 Domain Score:

Role Emotional (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 54 73.60 (2.530) 0.74 (2.530)	54 54 81.80 (2.532) 8.95 (2.532)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		8.21 (1.08, 15.33) 0.024
Corrected Hedges g [3] 95% CI		0.44 (0.06, 0.82)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 596 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 8

Population: Intent-to-Treat

Table 90.124 Analysis of Change from Baseline in SF-36 Domain Score: Role Emotional (0-100 score)

(Mixed Model Repeated Measures)

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 76.72 (2.842) 3.86 (2.842)	54 54 77.11 (2.825) 4.25 (2.825)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.39 (-7.59, 8.37) 0.923
Corrected Hedges g [3] 95% CI		0.02 (-0.36, 0.40)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 597 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 8

Population: Intent-to-Treat

Table 90.124 Analysis of Change from Baseline in SF-36 Domain Score:

> Role Emotional (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 73.52 (2.875) 0.66 (2.875)	54 53 72.14 (2.868) -0.72 (2.868)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-1.38 (-9.46, 6.70) 0.735
Corrected Hedges g [3] 95% CI		-0.07 (-0.45, 0.32)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 598 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 4 of 8 Population: Intent-to-Treat

Table 90.124 Analysis of Change from Baseline in SF-36 Domain Score:

> Role Emotional (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 76.05 (2.883) 3.19 (2.883)	54 53 78.78 (2.877) 5.93 (2.877)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		2.74 (-5.37, 10.84) 0.505	
Corrected Hedges g [3] 95% CI		0.13 (-0.25, 0.51)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 599 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 5 of 8

Population: Intent-to-Treat

Table 90.124 Analysis of Change from Baseline in SF-36 Domain Score: Role Emotional (0-100 score)

(Mixed Model Repeated Measures)

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 76.90 (2.810) 4.04 (2.810)	54 52 76.33 (2.804) 3.47 (2.804)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.57 (-8.47, 7.33) 0.886
Corrected Hedges g [3] 95% CI		-0.03 (-0.41, 0.36)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 600 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 6 of 8 Population: Intent-to-Treat

Table 90.124 Analysis of Change from Baseline in SF-36 Domain Score:

> Role Emotional (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 74.40 (2.980) 1.54 (2.980)	54 51 79.16 (2.988) 6.31 (2.988)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		4.77 (-3.63, 13.17) 0.263	
Corrected Hedges g [3] 95% CI		0.22 (-0.17, 0.61)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 601 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 7 of 8

Population: Intent-to-Treat

Table 90.124 Analysis of Change from Baseline in SF-36 Domain Score:

> Role Emotional (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 73.60 (2.900) 0.74 (2.900)	54 51 76.83 (2.897) 3.97 (2.897)	_
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		3.23 (-4.93, 11.38) 0.434	
Corrected Hedges g [3] 95% CI		0.15 (-0.23, 0.54)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 602 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 8 of 8

Population: Intent-to-Treat

Table 90.124 Analysis of Change from Baseline in SF-36 Domain Score:

> Role Emotional (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 50 75.00 (2.769) 2.15 (2.769)	54 50 81.85 (2.766) 8.99 (2.766)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		6.84 (-0.95, 14.64) 0.085	
Corrected Hedges g [3] 95% CI		0.35 (-0.05, 0.74)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 603 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 1 of 8

Population: Intent-to-Treat

Table 90.125 Analysis of Change from Baseline in SF-36 Domain Score: Mental Health (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 54 61.41 (1.769) 0.05 (1.769)	54 54 66.13 (1.772) 4.77 (1.772)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		4.72 (-0.27, 9.71) 0.064
Corrected Hedges g [3] 95% CI		0.36 (-0.02, 0.74)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 604 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 8

Population: Intent-to-Treat

Table 90.125 Analysis of Change from Baseline in SF-36 Domain Score:

Mental Health (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 65.54 (2.030) 4.18 (2.030)	54 54 67.08 (2.019) 5.72 (2.019)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		1.54 (-4.17, 7.24) 0.594
Corrected Hedges g [3] 95% CI		0.10 (-0.28, 0.48)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 605 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 8

Population: Intent-to-Treat

Table 90.125 Analysis of Change from Baseline in SF-36 Domain Score: Mental Health (0-100 score)

(Mixed Model Repeated Measures)

Visit: Week 12

· <del></del>	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 62.18 (2.090) 0.82 (2.090)	54 53 62.64 (2.084) 1.28 (2.084)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.46 (-5.42, 6.34) 0.877
Corrected Hedges g [3] 95% CI		0.03 (-0.35, 0.41)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 606 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 4 of 8

Population: Intent-to-Treat

Table 90.125 Analysis of Change from Baseline in SF-36 Domain Score: Mental Health (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 53 64.41 (2.047) 3.04 (2.047)	54 53 65.29 (2.043) 3.92 (2.043)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.88 (-4.88, 6.64) 0.762	
Corrected Hedges g [3] 95% CI		0.06 (-0.32, 0.44)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 607 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 5 of 8

Population: Intent-to-Treat

Table 90.125 Analysis of Change from Baseline in SF-36 Domain Score:

Mental Health (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 62.85 (2.237) 1.48 (2.237)	54 52 64.92 (2.233) 3.56 (2.233)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		2.07 (-4.22, 8.37) 0.515
Corrected Hedges g [3] 95% CI		0.13 (-0.26, 0.51)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 608 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 6 of 8

Population: Intent-to-Treat

Table 90.125 Analysis of Change from Baseline in SF-36 Domain Score: Mental Health (0-100 score) (Mixed Model Repeated Measures)

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 52 63.96 (2.347) 2.60 (2.347)	54 51 66.91 (2.353) 5.54 (2.353)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		2.95 (-3.67, 9.56) 0.379
Corrected Hedges g [3] 95% CI		0.17 (-0.21, 0.56)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 609 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 7 of 8

Population: Intent-to-Treat

Table 90.125 Analysis of Change from Baseline in SF-36 Domain Score: Mental Health (0-100 score)

(Mixed Model Repeated Measures)

Mana all i muma la

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 51 61.96 (2.449) 0.60 (2.449)	54 51 65.50 (2.446) 4.14 (2.446)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		3.54 (-3.34, 10.43) 0.310	
Corrected Hedges g [3] 95% CI		0.20 (-0.19, 0.59)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 610 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 8 of 8

Population: Intent-to-Treat

Table 90.125 Analysis of Change from Baseline in SF-36 Domain Score: Mental Health (0-100 score)

(Mixed Model Repeated Measures)

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	54 50 64.15 (2.212) 2.79 (2.212)	54 50 67.79 (2.211) 6.43 (2.211)	-
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		3.64 (-2.58, 9.87) 0.249	
Corrected Hedges g [3] 95% CI		0.23 (-0.16, 0.62)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 611 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

## CONFIDENTIAL

Protocol: 200622 Page 1 of 17

Population: Intent-to-Treat

Table 3.4 Summary of Work Productivity and Activity Impairment

Visit: Week 0

		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Work time missed due to health (%)	n Mean SD Median Min. Max.	31 20.8 32.92 0.0 0	30 20.8 34.04 0.0 0
Impairment while working due to health (%)	n Mean SD Median Min. Max.	29 30.7 27.51 30.0 0	27 42.2 25.32 40.0 0
Overall work impairment due to health (%)	n Mean SD Median Min. Max.	31 40.9 35.34 30.0 0	30 53.1 31.46 55.0 0
Activity impairment due to health (%)	n Mean SD Median Min. Max.	54 40.4 28.61 40.0 0	54 46.3 30.49 50.0 0

PPD

# CONFIDENTIAL

Protocol: 200622 Page 2 of 17

Population: Intent-to-Treat

Table 3.4 Summary of Work Productivity and Activity Impairment

Visit: Week 4

		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Work time missed due to health (%)	n Mean SD Median Min. Max.	27 21.2 34.11 0.0 0	26 18.0 33.06 0.0 0
Work time missed due to health change from baseline (%)	n Mean SD Median Min. Max.	-100	1.2 36.58 0.0 -100 88
Impairment while working due to health (%)	n Mean SD Median Min. Max.	25 31.2 29.20 30.0 0	24 24.6 23.95 20.0 0
<pre>Impairment while working due to health change from baseline (%)</pre>	n Mean SD Median Min. Max.	22 -1.8 13.32 0.0 -30 20	19 -18.4 23.16 -10.0 -70 20

# CONFIDENTIAL

Protocol: 200622 Page 3 of 17

Population: Intent-to-Treat

Table 3.4 Summary of Work Productivity and Activity Impairment

Visit: Week 4

		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Overall work impairment due to health (%)	n Mean SD Median Min. Max.	27 41.7 37.21 31.4 0	26 34.6 34.35 20.0 0
Overall work impairment due to health change from baseline (%)	n Mean SD Median Min. Max.	26 -2.1 24.68 0.0 -50 70	23 -15.6 34.37 -10.0 -100 62
Activity impairment due to health (%)	n Mean SD Median Min. Max.	51 36.3 28.84 30.0 0	51 31.6 28.03 20.0 0
Activity impairment due to health change from baseline (%)	n Mean SD Median Min. Max.	51 -3.7 17.66 0.0 -40 40	51 -13.7 25.77 -10.0 -80 30

# CONFIDENTIAL

Protocol: 200622 Page 4 of 17

Population: Intent-to-Treat

# Table 3.4 Summary of Work Productivity and Activity Impairment

Visit: Week 8

		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Work time missed due to health (%)	n Mean SD Median Min. Max.	27 15.8 23.45 0.0 0	26 16.5 29.45 0.0 0
Work time missed due to health change from baseline (%)	n Mean SD Median Min. Max.		23 -3.9 34.20 0.0 -100 88
Impairment while working due to health (%)	n Mean SD Median Min. Max.	27 25.9 27.49 30.0 0	25 32.8 30.21 30.0 0
<pre>Impairment while working due to health change from baseline (%)</pre>	n Mean SD Median Min. Max.	23 -3.5 16.13 0.0 -30 20	20 -13.5 26.21 -10.0 -70 30

Protocol: 200622 Page 5 of 17

Population: Intent-to-Treat

Table 3.4 Summary of Work Productivity and Activity Impairment

Visit: Week 8

		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Overall work impairment due to health (%)	n Mean SD Median Min. Max.	27 33.2 33.30 30.0 0	26 39.2 34.69 30.0 0
Overall work impairment due to health change from baseline (%)	n Mean SD Median Min. Max.	25 -5.3 25.97 -0.7 -80 50	23 -13.9 37.03 -10.0 -100 62
Activity impairment due to health (%)	n Mean SD Median Min. Max.	49 31.8 27.13 30.0 0	47 32.6 28.70 30.0 0
Activity impairment due to health change from baseline (%)	n Mean SD Median Min. Max.	49 -8.6 21.21 -10.0 -70 40	47 -12.8 31.19 -10.0 -80 100

Protocol: 200622 Page 6 of 17

Population: Intent-to-Treat

Table 3.4 Summary of Work Productivity and Activity Impairment

Visit: Week 12

		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Work time missed due to health (%)	n Mean SD Median Min. Max.	26 19.5 35.42 0.0 0	23 24.6 36.70 0.0 0
Work time missed due to health change from baseline (%)	n	23	21
	Mean SD Median Min. Max.	-1.7 37.77 0.0 -71 100	3.5 34.63 0.0 -70 77
Impairment while working due to health (%)	n Mean SD Median Min. Max.	23 29.6 29.00 20.0 0	20 29.5 26.85 20.0 0
<pre>Impairment while working due to health change from baseline (%)</pre>	n	19	18
change from baseffine (o)	Mean SD Median Min. Max.	-5.8 24.11 0.0 -70 30	-11.7 22.29 -5.0 -60 20

# CONFIDENTIAL

Protocol: 200622 Page 7 of 17

Population: Intent-to-Treat

Table 3.4 Summary of Work Productivity and Activity Impairment

Visit: Week 12

		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Overall work impairment due to health (%)	n Mean SD Median Min. Max.	26 40.2 37.36 30.0 0	23 44.5 37.23 50.0 0
Overall work impairment due to health change from baseline (%)	n Mean SD Median Min. Max.	23 -4.6 33.20 0.0 -91 80	21 -8.2 30.19 -5.6 -69 50
Activity impairment due to health (%)	n Mean SD Median Min. Max.	46 36.3 28.00 40.0 0	45 35.1 29.74 30.0 0
Activity impairment due to health change from baseline (%)	n Mean SD Median Min. Max.	46 -3.7 21.54 0.0 -50 50	45 -9.3 27.75 -10.0 -80 100

Protocol: 200622
Population: Intent-to-Treat

Table 3.4

Summary of Work Productivity and Activity Impairment

Visit: Week 16

		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Work time missed due to health (%)	n Mean SD Median Min. Max.	23 13.9 29.08 0.0 0	19 10.8 20.35 0.0 0
Work time missed due to health change from baseline (%)	n Mean SD Median Min. Max.	21 -5.7 39.30 0.0 -100 100	19 -9.3 39.38 0.0 -100 54
Impairment while working due to health (%)	n Mean SD Median Min. Max.	21 31.9 29.60 30.0 0	19 23.2 22.37 20.0 0
Impairment while working due to health change from baseline (%)	n Mean SD Median Min. Max.	2.8 28.03 0.0 -40 80	17 -14.7 -25.52 -10.0 -70 -20

Protocol: 200622 Page 9 of 17

Population: Intent-to-Treat

Table 3.4 Summary of Work Productivity and Activity Impairment

Visit: Week 16

		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Overall work impairment due to health (%)	n Mean SD Median Min. Max.	23 40.2 34.66 48.0 0	19 29.6 28.24 20.0 0
Overall work impairment due to health change from baseline (%)	n Mean SD Median Min. Max.	1.8 36.37 0.0 -41 90	19 -21.9 43.00 -10.0 -100 63
Activity impairment due to health (%)	n Mean SD Median Min. Max.	45 33.6 27.81 40.0 0	44 30.0 26.33 30.0 0
Activity impairment due to health change from baseline (%)	n Mean SD Median Min. Max.	45 -7.3 19.70 0.0 -60 40	44 -14.1 28.64 -10.0 -80 50

Protocol: 200622 Page 10 of 17

Population: Intent-to-Treat

Table 3.4 Summary of Work Productivity and Activity Impairment

Visit: Week 20

		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Work time missed due to health (%)	n Mean SD Median Min. Max.	21 20.3 35.87 0.0 0	20 15.3 27.49 0.0 0
Work time missed due to health change from baseline (%)	n Mean SD Median Min. Max.	-70	19 -2.8 30.61 0.0 -100 50
Impairment while working due to health (%)	n Mean SD Median Min. Max.	19 32.6 33.47 30.0 0	19 23.2 19.74 20.0 0
<pre>Impairment while working due to health change from baseline (%)</pre>	n Mean SD Median Min. Max.	16 1.3 32.22 0.0 -40 100	16 -16.9 23.87 -10.0 -70 20

# 2019N406842<u>00</u> 200<del>6</del>22

# CONFIDENTIAL

Protocol: 200622 Page 11 of 17

Population: Intent-to-Treat

Table 3.4 Summary of Work Productivity and Activity Impairment

Visit: Week 20

		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Overall work impairment due to health (%)	n Mean SD Median Min. Max.	21 40.7 38.44 32.3 0	20 34.7 28.05 33.1 0
Overall work impairment due to health change from baseline (%)	n Mean SD Median Min. Max.	3.9 39.33 0.0 -61 100	19 -16.2 34.76 -10.0 -100 50
Activity impairment due to health (%)	n Mean SD Median Min. Max.	46 37.8 29.73 35.0 0	42 32.4 29.78 20.0 0
Activity impairment due to health change from baseline (%)	n Mean SD Median Min. Max.	46 -1.7 24.97 0.0 -50 70	42 -11.9 29.40 -10.0 -80 100

Protocol: 200622 Page 12 of 17

Population: Intent-to-Treat

Table 3.4 Summary of Work Productivity and Activity Impairment

Visit: Week 24

		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Work time missed due to health (%)	n Mean SD Median Min. Max.	20 11.1 24.44 0.0 0	20 14.7 32.08 0.0 0
Work time missed due to health change from baseline (%)	n Mean SD Median Min. Max.	18 -5.9 26.68 0.0 -65 68	19 -3.0 49.60 0.0 -100 100
Impairment while working due to health (%)	n Mean SD Median Min. Max.	20 35.0 33.32 30.0 0	19 18.4 23.40 10.0 0
<pre>Impairment while working due to health change from baseline (%)</pre>	n Mean SD Median Min. Max.	4.7 26.95 0.0 -40 60	16 -17.5 29.78 -10.0 -60 40

Protocol: 200622 Page 13 of 17

Population: Intent-to-Treat

Table 3.4 Summary of Work Productivity and Activity Impairment

Visit: Week 24

		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Overall work impairment due to health (%)	n Mean SD Median Min. Max.	20 37.7 36.04 30.0 0	20 26.2 33.62 10.0 0
Overall work impairment due to health change from baseline (%)	n Mean SD Median Min. Max.	18 0.5 31.40 0.0 -57 71	19 -23.3 39.44 -10.0 -100 51
Activity impairment due to health (%)	n Mean SD Median Min. Max.	43 35.8 30.26 30.0 0	42 25.7 28.21 15.0 0
Activity impairment due to health change from baseline (%)	n Mean SD Median Min. Max.	43 -4.7 22.50 0.0 -70 30	42 -17.9 29.26 -10.0 -80 40

Protocol: 200622 Page 14 of 17

Population: Intent-to-Treat

Table 3.4 Summary of Work Productivity and Activity Impairment

Visit: Week 28

		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Work time missed due to health (%)	n Mean SD Median Min. Max.	22 11.2 22.74 0.0 0	23 12.8 25.69 0.0 0
Work time missed due to health change from baseline (%)	n Mean SD Median Min. Max.	20 -4.4 22.89 0.0 -70 50	21 -5.8 39.60 0.0 -100 93
Impairment while working due to health (%)	n Mean SD Median Min. Max.	22 29.1 31.61 25.0 0	22 20.0 19.02 15.0 0
<pre>Impairment while working due to health change from baseline (%)</pre>	n Mean SD Median Min. Max.	19 -1.6 19.79 0.0 -40 40	18 -19.4 23.13 -10.0 -70

Protocol: 200622 Page 15 of 17

Population: Intent-to-Treat

Table 3.4 Summary of Work Productivity and Activity Impairment

Visit: Week 28

		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Overall work impairment due to health (%)	n Mean SD Median Min. Max.	22 32.4 35.13 25.0 0	23 30.3 27.39 20.0 0
Overall work impairment due to health change from baseline (%)	n Mean SD Median Min. Max.	20 -4.2 23.02 0.0 -61 40	21 -20.6 38.93 -10.0 -100 65
Activity impairment due to health (%)	n Mean SD Median Min. Max.	43 35.1 28.32 30.0 0	43 26.0 24.89 20.0 0
Activity impairment due to health change from baseline (%)	n Mean SD Median Min. Max.	43 -5.3 20.86 0.0 -70 40	43 -17.2 29.87 -10.0 -80 50

Protocol: 200622 Page 16 of 17

Population: Intent-to-Treat

Table 3.4 Summary of Work Productivity and Activity Impairment

Visit: Week 32

		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Work time missed due to health (%)	n Mean SD Median Min. Max.	21 6.6 19.66 0.0 0	20 15.2 32.46 0.0 0
Work time missed due to health change from baseline (%)	n Mean SD Median Min. Max.	18 -7.5 19.75 0.0 -70 12	2.4 37.93 0.0 -100 93
Impairment while working due to health (%)	n Mean SD Median Min. Max.	21 29.0 27.55 30.0 0	18 18.3 19.48 10.0 0
<pre>Impairment while working due to health change from baseline (%)</pre>	n Mean SD Median Min. Max.	17 -2.4 21.66 0.0 -50 40	16 -20.6 22.94 -10.0 -70 0

# 2019N406842<u>00</u> 200<del>6</del>22

# CONFIDENTIAL

Protocol: 200622 Page 17 of 17

Population: Intent-to-Treat

Table 3.4 Summary of Work Productivity and Activity Impairment

Visit: Week 32

		Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Overall work impairment due to health (%)	n Mean SD Median Min. Max.	21 30.8 29.30 30.0 0	20 30.9 32.00 20.0 0
Overall work impairment due to health change from baseline (%)	n Mean SD Median Min. Max.	18 -5.4 25.46 0.0 -71 40	19 -17.0 39.63 -10.0 -100 65
Activity impairment due to health (%)	n Mean SD Median Min. Max.	41 36.1 29.49 30.0 0	42 22.9 25.88 10.0 0
Activity impairment due to health change from baseline (%)	n Mean SD Median Min. Max.	41 -3.7 24.98 0.0 -70 40	42 -19.0 27.66 -10.0 -80 40

Protocol: 200622 Page 1 of 8

Population: Intent-to-Treat

Table 90.126

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI):

Work Time Missed Due to Health (%) (Mixed Model Repeated Measures)

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	29 26 18.53 (6.007) 0.55 (6.007)	28 23 18.50 (6.261) 0.52 (6.261)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.03 (-17.47, 17.41) 0.997
Corrected Hedges g [3] 95% CI		0.00 (-0.56, 0.56)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 629 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 8

Population: Intent-to-Treat

Table 90.126

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI):

Work Time Missed Due to Health (%) (Mixed Model Repeated Measures)

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	29 25 17.60 (5.056) -0.38 (5.056)	28 23 11.72 (5.194) -6.26 (5.194)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-5.88 (-20.50, 8.74) 0.421
Corrected Hedges g [3] 95% CI		-0.23 (-0.80, 0.34)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 630 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 8

Population: Intent-to-Treat

Table 90.126

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI):

Work Time Missed Due to Health (%) (Mixed Model Repeated Measures)

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	29 23 18.68 (7.168) 0.70 (7.168)	28 21 15.19 (7.353) -2.79 (7.353)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-3.49 (-24.27, 17.29) 0.736
Corrected Hedges g [3] 95% CI		-0.10 (-0.69, 0.49)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 631 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 4 of 8

Population: Intent-to-Treat

Table 90.126

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI):

Work Time Missed Due to Health (%) (Mixed Model Repeated Measures)

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	29 21 16.55 (6.319) -1.43 (6.319)	28 19 15.58 (6.538) -2.40 (6.538)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.97 (-19.55, 17.61) 0.916
Corrected Hedges g [3] 95% CI		-0.03 (-0.65, 0.59)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 632 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 5 of 8

Population: Intent-to-Treat

Table 90.126

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI):

Work Time Missed Due to Health (%) (Mixed Model Repeated Measures)

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	29 19 24.77 (7.379) 6.79 (7.379)	28 19 18.60 (7.357) 0.62 (7.357)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-6.17 (-27.48, 15.13) 0.558
Corrected Hedges g [3] 95% CI		-0.19 (-0.83, 0.45)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 633 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 6 of 8

Population: Intent-to-Treat

Table 90.126

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI):

Work Time Missed Due to Health (%) (Mixed Model Repeated Measures)

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	29 18 13.14 (7.715) -4.84 (7.715)	28 19 20.53 (7.443) 2.56 (7.443)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		7.40 (-14.90, 29.70) 0.498
Corrected Hedges g [3] 95% CI		0.22 (-0.42, 0.87)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 634 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 7 of 8

Population: Intent-to-Treat

Table 90.126

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI):

Work Time Missed Due to Health (%) (Mixed Model Repeated Measures)

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	29 20 15.10 (5.552) -2.88 (5.552)	28 21 13.68 (5.429) -4.30 (5.429)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-1.42 (-17.30, 14.45) 0.856
Corrected Hedges g [3] 95% CI		-0.06 (-0.67, 0.56)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 635 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 8 of 8

Population: Intent-to-Treat

Table 90.126

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI):

Work Time Missed Due to Health (%) (Mixed Model Repeated Measures)

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	29 18 12.65 (6.395) -5.33 (6.395)	28 19 20.32 (6.293) 2.34 (6.293)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		7.67 (-10.71, 26.05) 0.399
Corrected Hedges g [3] 95% CI		0.28 (-0.37, 0.92)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 636 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 1 of 8

Population: Intent-to-Treat

Table 90.133

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Impairment While Working Due to Health (%) (Mixed Model Repeated Measures)

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	25 22 30.62 (3.329) -3.34 (3.329)	25 19 18.31 (3.528) -15.64 (3.528)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-12.31 (-22.27, -2.34) 0.017
Corrected Hedges g [3] 95% CI		-0.78 (-1.41, -0.14)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 637 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 8

Population: Intent-to-Treat

Table 90.133

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Impairment While Working Due to Health (%)

(Mixed Model Repeated Measures)

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	25 23 26.89 (4.056) -7.06 (4.056)	25 20 24.19 (4.251) -9.76 (4.251)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-2.70 (-14.81, 9.42) 0.655	
Corrected Hedges g [3] 95% CI		-0.14 (-0.74, 0.46)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 638 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 8

Population: Intent-to-Treat

Table 90.133

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Impairment While Working Due to Health (%) (Mixed Model Repeated Measures)

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	25 19 31.87 (5.251) -2.09 (5.251)	25 18 27.28 (5.431) -6.67 (5.431)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-4.58 (-20.16, 10.99) 0.553
Corrected Hedges g [3] 95% CI		-0.20 (-0.84, 0.45)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 639 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 4 of 8

Population: Intent-to-Treat

Table 90.133

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Impairment While Working Due to Health (%) (Mixed Model Repeated Measures)

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	25 18 29.64 (5.713) -4.31 (5.713)	25 17 21.10 (5.812) -12.86 (5.812)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-8.55 (-25.37, 8.27) 0.309
Corrected Hedges g [3] 95% CI		-0.35 (-1.01, 0.32)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 640 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 5 of 8

Population: Intent-to-Treat

Table 90.133

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Impairment While Working Due to Health (%) (Mixed Model Repeated Measures)

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	25 16 31.45 (5.917) -2.50 (5.917)	25 16 24.50 (5.903) -9.45 (5.903)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-6.95 (-24.34, 10.44) 0.420
Corrected Hedges g [3] 95% CI		-0.29 (-0.98, 0.41)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 641 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 6 of 8

Population: Intent-to-Treat

Table 90.133

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Impairment While Working Due to Health (%)

(Mixed Model Repeated Measures)

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	25 17 35.49 (6.220) 1.54 (6.220)	25 16 23.23 (6.452) -10.72 (6.452)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-12.26 (-30.79, 6.28) 0.187
Corrected Hedges g [3] 95% CI		-0.46 (-1.16, 0.23)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 642 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 7 of 8

Population: Intent-to-Treat

Table 90.133

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Impairment While Working Due to Health (%) (Mixed Model Repeated Measures)

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	25 19 30.57 (4.449) -3.39 (4.449)	25 18 19.51 (4.606) -14.44 (4.606)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-11.05 (-24.26, 2.15) 0.098
Corrected Hedges g [3] 95% CI		-0.56 (-1.21, 0.10)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 643 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 8 of 8

Population: Intent-to-Treat

Table 90.133

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Impairment While Working Due to Health (%)

(Mixed Model Repeated Measures)

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	25 17 28.19 (4.616) -5.76 (4.616)	25 16 20.34 (4.698) -13.61 (4.698)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-7.86 (-21.56, 5.85) 0.251
Corrected Hedges g [3] 95% CI		-0.41 (-1.09, 0.28)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 644 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 1 of 8

Population: Intent-to-Treat

Table 90.140

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Overall Work Impairment Due to Health (%)

(Mixed Model Repeated Measures)

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	29 26 40.50 (5.316) -4.03 (5.316)	28 23 31.10 (5.577) -13.44 (5.577)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-9.41 (-24.95, 6.14) 0.230	
Corrected Hedges g [3] 95% CI		-0.34 (-0.91, 0.22)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 645 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 8

Population: Intent-to-Treat

Table 90.140

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Overall Work Impairment Due to Health (%)

(Mixed Model Repeated Measures)

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	29 25 37.24 (5.607) -7.29 (5.607)	28 23 31.99 (5.776) -12.54 (5.776)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-5.24 (-21.60, 11.12) 0.522
Corrected Hedges g [3] 95% CI		-0.18 (-0.75, 0.38)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 646 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 8

Population: Intent-to-Treat

Table 90.140

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Overall Work Impairment Due to Health (%) (Mixed Model Repeated Measures)

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	29 23 41.83 (6.722) -2.70 (6.722)	28 21 41.37 (7.022) -3.17 (7.022)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.47 (-20.24, 19.30) 0.962
Corrected Hedges g [3] 95% CI		-0.01 (-0.61, 0.58)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 647 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 4 of 8

Population: Intent-to-Treat

Table 90.140

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Overall Work Impairment Due to Health (%)

(Mixed Model Repeated Measures)

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	29 21 43.83 (6.945) -0.70 (6.945)	28 19 27.63 (7.218) -16.90 (7.218)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-16.20 (-36.60, 4.19) 0.116
Corrected Hedges g [3] 95% CI		-0.50 (-1.13, 0.13)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 648 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.140

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Overall Work Impairment Due to Health (%)

(Mixed Model Repeated Measures)

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	29 19 47.80 (7.500) 3.27 (7.500)	28 19 36.10 (7.543) -8.43 (7.543)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-11.70 (-33.53, 10.13) 0.284
Corrected Hedges g [3] 95% CI		-0.35 (-0.99, 0.29)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 649 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.140

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Overall Work Impairment Due to Health (%)

(Mixed Model Repeated Measures)

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	29 18 43.49 (7.518) -1.04 (7.518)	28 19 31.89 (7.461) -12.64 (7.461)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-11.60 (-33.26, 10.06) 0.285
Corrected Hedges g [3] 95% CI		-0.35 (-1.00, 0.30)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 650 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.140

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Overall Work Impairment Due to Health (%)

(Mixed Model Repeated Measures)

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	29 20 39.78 (6.190) -4.75 (6.190)	28 21 30.13 (6.204) -14.40 (6.204)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-9.64 (-27.49, 8.20) 0.282
Corrected Hedges g [3] 95% CI		-0.34 (-0.95, 0.28)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 651 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.140

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Overall Work Impairment Due to Health (%)

(Mixed Model Repeated Measures)

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	29 18 38.66 (6.743) -5.87 (6.743)	28 19 31.15 (6.659) -13.38 (6.659)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-7.51 (-26.90, 11.89) 0.438
Corrected Hedges g [3] 95% CI		-0.25 (-0.90, 0.39)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 652 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.147

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Activity Impairment Due to Health (%)

(Mixed Model Repeated Measures)

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 51 37.87 (2.814) -4.24 (2.814)	51 51 29.40 (2.822) -12.71 (2.822)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-8.47 (-16.42, -0.53) 0.037	
Corrected Hedges g [3] 95% CI		-0.42 (-0.81, -0.03)	

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 653 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.147

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Activity Impairment Due to Health (%)

(Mixed Model Repeated Measures)

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 49 33.37 (3.232) -8.74 (3.232)	51 47 30.20 (3.299) -11.91 (3.299)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-3.17 (-12.38, 6.04) 0.496
Corrected Hedges g [3] 95% CI		-0.14 (-0.54, 0.26)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 654 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.147

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Activity Impairment Due to Health (%)

(Mixed Model Repeated Measures)

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 46 37.83 (3.169) -4.29 (3.169)	51 45 33.14 (3.225) -8.97 (3.225)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-4.68 (-13.71, 4.35) 0.306
Corrected Hedges g [3] 95% CI		-0.22 (-0.63, 0.20)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 655 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.147

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Activity Impairment Due to Health (%)

(Mixed Model Repeated Measures)

Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 45 35.03 (2.953) -7.08 (2.953)	51 44 27.91 (2.997) -14.20 (2.997)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-7.12 (-15.52, 1.28) 0.095
Corrected Hedges g [3] 95% CI		-0.36 (-0.77, 0.06)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 656 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.147

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Activity Impairment Due to Health (%)

(Mixed Model Repeated Measures)

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 46 40.02 (3.464) -2.09 (3.464)	51 42 30.45 (3.591) -11.66 (3.591)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-9.57 (-19.52, 0.38) 0.059
Corrected Hedges g [3] 95% CI		-0.41 (-0.83, 0.02)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 657 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.147

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Activity Impairment Due to Health (%)

(Mixed Model Repeated Measures)

Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 43 37.82 (3.411) -4.29 (3.411)	51 42 25.17 (3.447) -16.94 (3.447)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-12.65 (-22.32, -2.97) 0.011
Corrected Hedges g [3] 95% CI		-0.56 (-0.99, -0.13)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 658 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.147

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Activity Impairment Due to Health (%)

(Mixed Model Repeated Measures)

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 43 37.04 (3.175) -5.07 (3.175)	51 43 24.96 (3.204) -17.15 (3.204)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-12.08 (-21.09, -3.07) 0.009
Corrected Hedges g [3] 95% CI		-0.57 (-1.00, -0.14)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 659 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.147

Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI): Activity Impairment Due to Health (%)

(Mixed Model Repeated Measures)

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	52 41 38.50 (3.461) -3.61 (3.461)	51 42 21.91 (3.473) -20.20 (3.473)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-16.59 (-26.39, -6.80) 0.001
Corrected Hedges g [3] 95% CI		-0.74 (-1.18, -0.29)

Note: Analysis performed using mixed model repeated measures with covariates of baseline, baseline OCS dose region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 660 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.3

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During the 32-Week Treatment Period by Age (Treatment Policy Estimand)

Menolizumah

Age: 12-<18 Years

	Placebo (N=54)	300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from stu Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study	2 (67%)	1 0 0 0
Subjects with no HES flare who complete study	1 (33%)	1 (100%)
Comparison Mepolizumab 300mg vs Placebo [1] CMH p-value [2] Logistic regression [3]		Non-estimable
Odds ratio (95% CI) p-value Unadjusted odds ratio (95% CI) [4]		Non-estimable Non-estimable 1.00 (<0.01,19.00)
Relative risk (95% CI) [5] Risk difference (95% CI) [5] Fisher's Exact p-value (2-sided)		0.00 (0.00,4.24) -0.67 (-0.99,0.59) 1.000

Mepolizumab (Nucala) - HES Seite 661 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS ( $0-<=20 \,\mathrm{mg/day}$  and  $>20 \,\mathrm{mg/day}$  prednisone or equivalent) and region.

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose and region.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.
PPD PPD

Population: Intent-to-Treat

Table 90.3

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During the 32-Week Treatment Period by Age (Treatment Policy Estimand)

Manalizumah

Age: 18-64 Years

	Placebo 300mg SC (N=54) (N=54)	
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study	41 49 23 (56%) 13 (27%) 21 (51%) 12 (24%) 2 (5%) 1 (2%) 18 (44%) 36 (73%)	
Comparison Mepolizumab 300mg vs Placebo [1]  CMH p-value [2]  Logistic regression [3]  Odds ratio (95% CI)  p-value  Unadjusted odds ratio (95% CI) [4]  Relative risk (95% CI) [5]  Risk difference (95% CI) [5]  Fisher's Exact p-value (2-sided)	0.002 0.26 (0.11,0.65) 0.004 0.29 (0.11,0.75) 0.47 (0.25,0.85) -0.30 (-0.48,-0.07) 0.005	

Mepolizumab (Nucala) - HES Seite 662 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS ( $0-<=20 \,\mathrm{mg/day}$  and  $>20 \,\mathrm{mg/day}$  prednisone or equivalent) and region.

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose and region.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.
PPD PPD

Population: Intent-to-Treat

Table 90.3

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During the 32-Week Treatment Period by Age (Treatment Policy Estimand)

Menolizumah

Age: >=65 Years

	Placebo (N=54)	300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study	10 5 (50%) 5 (50%) 0 5 (50%)	` ,
Comparison Mepolizumab 300mg vs Placebo [1] CMH p-value [2] Logistic regression [3] Odds ratio (95% CI) p-value Unadjusted odds ratio (95% CI) [4] Relative risk (95% CI) [5] Risk difference (95% CI) [5] Fisher's Exact p-value (2-sided)		0.679  3.05 (0.05,205.71) 0.603 1.00 (0.05,19.26) 1.00 (0.17,3.18) 0.00 (-0.55,0.55) 1.000

Mepolizumab (Nucala) - HES Seite 663 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose and region.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.
PPD PPD

Population: Intent-to-Treat

Table 90.4

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During the 32-Week Treatment Period by Gender (Treatment Policy Estimand)

Manalizumah

Gender: Female

	Placebo (N=54)	300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study	27 17 (63%) 16 (59%) 1 (4%) 10 (37%)	6 (20%)
Comparison Mepolizumab 300mg vs Placebo [1] CMH p-value [2] Logistic regression [3] Odds ratio (95% CI) p-value Unadjusted odds ratio (95% CI) [4] Relative risk (95% CI) [5] Risk difference (95% CI) [5] Fisher's Exact p-value (2-sided)		<0.001 0.10 (0.02,0.41) 0.001 0.15 (0.04,0.55) 0.32 (0.09,0.69) -0.43 (-0.65,-0.16) 0.001

Mepolizumab (Nucala) - HES Seite 664 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS ( $0-<=20 \,\mathrm{mg/day}$  and  $>20 \,\mathrm{mg/day}$  prednisone or equivalent) and region.

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose and region.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score. statistic.

Population: Intent-to-Treat

## Table 90.4

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During the 32-Week Treatment Period by Gender (Treatment Policy Estimand)

Menolizumah

Gender: Male

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study	1 (4%)	
Comparison Mepolizumab 300mg vs Placebo [1] CMH p-value [2] Logistic regression [3] Odds ratio (95% CI) p-value Unadjusted odds ratio (95% CI) [4] Relative risk (95% CI) [5] Risk difference (95% CI) [5] Fisher's Exact p-value (2-sided)		0.484 0.64 (0.20,2.09) 0.461 0.65 (0.18,2.27) 0.78 (0.36,1.52) -0.11 (-0.38,0.17) 0.573

Mepolizumab (Nucala) - HES Seite 665 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose and region.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score. statistic.

Population: Intent-to-Treat

Table 90.5

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During the 32-Week Treatment Period by Region (Treatment Policy Estimand)

Menolizumah

Region: Europe

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study	33 18 (55%) 16 (48%) 2 (6%) 15 (45%)	10 (32%) 0
Comparison Mepolizumab 300mg vs Placebo [1]  CMH p-value [2]  Logistic regression [3]  Odds ratio (95% CI)  p-value  Unadjusted odds ratio (95% CI) [4]  Relative risk (95% CI) [5]  Risk difference (95% CI) [5]  Fisher's Exact p-value (2-sided)		0.116 0.40 (0.14,1.12) 0.080 0.40 (0.13,1.23) 0.59 (0.30,1.06) -0.22 (-0.46,0.03) 0.084

Mepolizumab (Nucala) - HES Seite 666 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS ( $0-<=20 \,\mathrm{mg/day}$  and  $>20 \,\mathrm{mg/day}$  prednisone or equivalent).

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.
PPD PPD

Population: Intent-to-Treat

Table 90.5

Manalizumah

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During the 32-Week Treatment Period by Region (Treatment Policy Estimand)

Region: Rest of World

	Placebo (N=54)	300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study		23 5 (22%) 4 (17%) 1 (4%) 18 (78%)
Comparison Mepolizumab 300mg vs Placebo [1] CMH p-value [2] Logistic regression [3] Odds ratio (95% CI) p-value Unadjusted odds ratio (95% CI) [4] Relative risk (95% CI) [5] Risk difference (95% CI) [5] Fisher's Exact p-value (2-sided)		0.007 0.10 (0.02,0.51) 0.006 0.22 (0.04,0.91) 0.38 (0.10,0.89) -0.35 (-0.61,-0.05) 0.029

Mepolizumab (Nucala) - HES Seite 667 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS ( $0-<=20 \,\mathrm{mg/day}$  and  $>20 \,\mathrm{mg/day}$  prednisone or equivalent).

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.
PPD PPD

Population: Intent-to-Treat

Table 90.6

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During the 32-Week Treatment Period by Duration of Disease (Treatment Policy Estimand)

Mepolizumah

Duration of disease: <2.76 Years

	Placebo (N=54)	300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study	32 16 (50%) 15 (47%) 1 (3%) 16 (50%)	7 (32%) 1 (5%)
Comparison Mepolizumab 300mg vs Placebo [1] CMH p-value [2] Logistic regression [3] Odds ratio (95% CI) p-value Unadjusted odds ratio (95% CI) [4] Relative risk (95% CI) [5] Risk difference (95% CI) [5] Fisher's Exact p-value (2-sided)		0.172 0.44 (0.13,1.46) 0.182 0.58 (0.16,1.98) 0.73 (0.34,1.37) -0.14 (-0.39,0.14) 0.407

Mepolizumab (Nucala) - HES Seite 668 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS  $(0-<=20 \, \text{mg/day} \text{ and } >20 \, \text{mg/day} \text{ prednisone or equivalent)}$  and region.

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose and region.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.
PPD PPD

Population: Intent-to-Treat

Table 90.6

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During the 32-Week Treatment Period by Duration of Disease (Treatment Policy Estimand)

Menolizumah

Duration of disease: >=2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study	, ,	7 (22%) 7 (22%) 0
Comparison Mepolizumab 300mg vs Placebo [1]  CMH p-value [2]  Logistic regression [3]  Odds ratio (95% CI)  p-value  Unadjusted odds ratio (95% CI) [4]  Relative risk (95% CI) [5]  Risk difference (95% CI) [5]  Fisher's Exact p-value (2-sided)		0.004 0.15 (0.04,0.52) 0.003 0.17 (0.04,0.62) 0.34 (0.14,0.74) -0.42 (-0.64,-0.10) 0.004

Mepolizumab (Nucala) - HES Seite 669 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS ( $0-<=20 \,\mathrm{mg/day}$  and  $>20 \,\mathrm{mg/day}$  prednisone or equivalent) and region.

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose and region.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.
PPD PPD

Population: Intent-to-Treat

Table 90.7

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During the 32-Week Treatment Period by Baseline Blood Eosinophils (Treatment Policy Estimand)

Manalizumah

Baseline blood eosinophils: <1.5 10^9/L

	Placebo (N=54)	300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study	30 16 (53%) 16 (53%) 0 14 (47%)	10 (38%) 9 (35%) 1 (4%)
Comparison Mepolizumab 300mg vs Placebo [1]  CMH p-value [2]  Logistic regression [3]  Odds ratio (95% CI)  p-value  Unadjusted odds ratio (95% CI) [4]  Relative risk (95% CI) [5]  Risk difference (95% CI) [5]  Fisher's Exact p-value (2-sided)		0.192 0.37 (0.11,1.24) 0.107 0.55 (0.16,1.80) 0.72 (0.36,1.30) -0.15 (-0.40,0.12) 0.295

Mepolizumab (Nucala) - HES Seite 670 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose and region.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.7

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During the 32-Week Treatment Period by Baseline Blood Eosinophils (Treatment Policy Estimand)

Manalizumah

Baseline blood eosinophils: >=1.5 10^9/L

	Placebo (N=54)	300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study	24 14 (58%) 12 (50%) 2 (8%) 10 (42%)	5 (18%) 5 (18%)
Comparison Mepolizumab 300mg vs Placebo [1] CMH p-value [2] Logistic regression [3] Odds ratio (95% CI) p-value Unadjusted odds ratio (95% CI) [4] Relative risk (95% CI) [5] Risk difference (95% CI) [5] Fisher's Exact p-value (2-sided)		0.007 0.14 (0.03,0.53) 0.004 0.16 (0.04,0.63) 0.31 (0.06,0.76) -0.40 (-0.63,-0.12) 0.004

Mepolizumab (Nucala) - HES Seite 671 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS ( $0-<=20 \,\mathrm{mg/day}$  and  $>20 \,\mathrm{mg/day}$  prednisone or equivalent) and region.

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose and region.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.19
Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare

During Week 20 Through Week 32 by Age (Treatment Policy Estimand)

Menolizumah

Age: 12-<18 Years

	Placebo (N=54)	300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study	3 2 (67%) 2 (67%) 0 1 (33%)	1 0 0 0 1 (100%)
Comparison Mepolizumab 300mg vs Placebo [1]  CMH p-value [2]  Logistic regression [3]  Odds ratio (95% CI)  p-value  Unadjusted odds ratio (95% CI) [4]  Relative risk (95% CI) [5]		Non-estimable Non-estimable Non-estimable 1.00 (<0.01,19.00) 0.00 (0.00,4.24)
Risk difference (95% CI) [5] Fisher's Exact p-value (2-sided)		-0.67 (-0.99,0.59) 1.000

Mepolizumab (Nucala) - HES Seite 672 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS ( $0-<=20 \,\mathrm{mg/day}$  and  $>20 \,\mathrm{mg/day}$  prednisone or equivalent) and region.

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose and region.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.
PPD PPD

Population: Intent-to-Treat

Table 90.19

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During Week 20 Through Week 32 by Age (Treatment Policy Estimand)

Menolizumah

Age: 18-64 Years

	Placebo (N=54)	300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study	41 15 (37%) 13 (32%) 2 (5%) 26 (63%)	6 (12%) 1 (2%)
Comparison Mepolizumab 300mg vs Placebo [1] CMH p-value [2] Logistic regression [3] Odds ratio (95% CI) p-value Unadjusted odds ratio (95% CI) [4] Relative risk (95% CI) [5] Risk difference (95% CI) [5] Fisher's Exact p-value (2-sided)		0.013 0.28 (0.10,0.79) 0.016 0.29 (0.09,0.89) 0.39 (0.14,0.90) -0.22 (-0.40,-0.03) 0.025

Mepolizumab (Nucala) - HES Seite 673 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS ( $0-<=20 \,\mathrm{mg/day}$  and  $>20 \,\mathrm{mg/day}$  prednisone or equivalent) and region.

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose and region.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.
PPD PPD

Population: Intent-to-Treat

Table 90.19

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During Week 20 Through Week 32 by Age (Treatment Policy Estimand)

Menolizumah

Age: >=65 Years

	Placebo 300mg SC (N=54) (N=54)
n Subjects with >=1 HES flare or who withdraw from Subjects with >=1 HES flare Subjects with no HES flare who withdraw from s Subjects with no HES flare who complete study	2 (20%) 1 (25%)
Comparison Mepolizumab 300mg vs Placebo [1] CMH p-value [2] Logistic regression [3]	0.258
Odds ratio (95% CI) p-value Unadjusted odds ratio (95% CI) [4]	292.21 (0.02,>999.99) 0.244 3.56 (0.16,85.59)
Relative risk (95% CI) [5] Risk difference (95% CI) [5] Fisher's Exact p-value (2-sided)	2.50 (0.18,25.54) 0.30 (-0.25,0.81) 0.520

Mepolizumab (Nucala) - HES Seite 674 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS ( $0-<=20 \,\mathrm{mg/day}$  and  $>20 \,\mathrm{mg/day}$  prednisone or equivalent) and region.

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose and region.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.
PPD PPD

Population: Intent-to-Treat

Table 90.20

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During Week 20 Through Week 32 by Gender (Treatment Policy Estimand)

Manalizumah

Gender: Female

	Placebo (N=54)	300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study		
Comparison Mepolizumab 300mg vs Placebo [1] CMH p-value [2] Logistic regression [3] Odds ratio (95% CI) p-value Unadjusted odds ratio (95% CI) [4] Relative risk (95% CI) [5] Risk difference (95% CI) [5] Fisher's Exact p-value (2-sided)		0.096 0.27 (0.06,1.15) 0.077 0.31 (0.06,1.34) 0.40 (0.06,1.12) -0.20 (-0.42,0.02) 0.114

Mepolizumab (Nucala) - HES Seite 675 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS ( $0-<=20 \,\mathrm{mg/day}$  and  $>20 \,\mathrm{mg/day}$  prednisone or equivalent) and region.

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose and region.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.
PPD PPD

Population: Intent-to-Treat

Table 90.20

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During Week 20 Through Week 32 by Gender (Treatment Policy Estimand)

Mana 1 - - - - - la

Gender: Male

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study	9 (33%)	24 5 (21%) 3 (13%) 2 (8%) 19 (79%)
Comparison Mepolizumab 300mg vs Placebo [1] CMH p-value [2] Logistic regression [3] Odds ratio (95% CI) p-value Unadjusted odds ratio (95% CI) [4] Relative risk (95% CI) [5] Risk difference (95% CI) [5] Fisher's Exact p-value (2-sided)		0.362 0.51 (0.13,1.95) 0.328 0.45 (0.10,1.82) 0.56 (0.17,1.44) -0.16 (-0.41,0.10) 0.235

Mepolizumab (Nucala) - HES Seite 676 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose and region.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.  $\begin{array}{c} \\ \\ \\ \\ \end{array}$ 

Population: Intent-to-Treat

Table 90.21

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During Week 20 Through Week 32 by Region (Treatment Policy Estimand)

Menolizumah

Region: Europe

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study	33 12 (36%) 10 (30%) 2 (6%) 21 (64%)	5 (16%) 0
Comparison Mepolizumab 300mg vs Placebo [1]  CMH p-value [2]  Logistic regression [3]  Odds ratio (95% CI)  p-value  Unadjusted odds ratio (95% CI) [4]  Relative risk (95% CI) [5]  Risk difference (95% CI) [5]  Fisher's Exact p-value (2-sided)		0.095 0.34 (0.10,1.12) 0.075 0.34 (0.08,1.25) 0.44 (0.10,1.09) -0.20 (-0.41,0.02) 0.091

Mepolizumab (Nucala) - HES Seite 677 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS ( $0-<=20 \,\mathrm{mg/day}$  and  $>20 \,\mathrm{mg/day}$  prednisone or equivalent).

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.
PPD PPD

Population: Intent-to-Treat

Table 90.21

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During Week 20 Through Week 32 by Region (Treatment Policy Estimand)

Manalizumah

Region: Rest of World

	Placebo (N=54)	300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study	7 (33%)	23 4 (17%) 2 (9%) 2 (9%) 19 (83%)
Comparison Mepolizumab 300mg vs Placebo [1]  CMH p-value [2]  Logistic regression [3]  Odds ratio (95% CI)  p-value  Unadjusted odds ratio (95% CI) [4]  Relative risk (95% CI) [5]  Risk difference (95% CI) [5]  Fisher's Exact p-value (2-sided)		0.161 0.31 (0.07,1.45) 0.137 0.43 (0.08,2.09) 0.52 (0.12,1.56) -0.16 (-0.42,0.11) 0.303

Mepolizumab (Nucala) - HES Seite 678 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS ( $0-<=20 \,\mathrm{mg/day}$  and  $>20 \,\mathrm{mg/day}$  prednisone or equivalent).

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.
PPD PPD

Population: Intent-to-Treat

Table 90.22

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During Week 20 Through Week 32 by Duration of Disease (Treatment Policy Estimand)

Manalizumah

Duration of disease: <2.76 Years

	Placebo (N=54)	300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study	9 (28%) 8 (25%)	22 4 (18%) 2 (9%) 2 (9%) 18 (82%)
Comparison Mepolizumab 300mg vs Placebo [1] CMH p-value [2] Logistic regression [3] Odds ratio (95% CI) p-value Unadjusted odds ratio (95% CI) [4] Relative risk (95% CI) [5] Risk difference (95% CI) [5] Fisher's Exact p-value (2-sided)		0.273 0.40 (0.09,1.83) 0.240 0.57 (0.11,2.49) 0.65 (0.10,1.78) -0.10 (-0.32,0.16) 0.523

Mepolizumab (Nucala) - HES Seite 679 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS ( $0-<=20 \,\mathrm{mg/day}$  and  $>20 \,\mathrm{mg/day}$  prednisone or equivalent) and region.

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose and region.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.
PPD PPD

Population: Intent-to-Treat

Table 90.22

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During Week 20 Through Week 32 by Duration of Disease (Treatment Policy Estimand)

Mepolizumab

Duration of disease: >=2.76 Years

	Placebo (N=54)	300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study		
Comparison Mepolizumab 300mg vs Placebo [1]  CMH p-value [2]  Logistic regression [3]  Odds ratio (95% CI)  p-value  Unadjusted odds ratio (95% CI) [4]  Relative risk (95% CI) [5]  Risk difference (95% CI) [5]  Fisher's Exact p-value (2-sided)		0.023 0.21 (0.06,0.77) 0.019 0.23 (0.05,0.93) 0.34 (0.10,0.88) -0.30 (-0.54,-0.03) 0.029

Mepolizumab (Nucala) - HES Seite 680 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose and region.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.
PPD PPD

Population: Intent-to-Treat

## Table 90.23

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During Week 20 Through Week 32 by Baseline Blood Eosinophils (Treatment Policy Estimand)

Manalizumah

Baseline blood eosinophils: <1.5 10^9/L

	Placebo (N=54)	300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study	30 12 (40%) 12 (40%) 0 18 (60%)	,
Comparison Mepolizumab 300mg vs Placebo [1]  CMH p-value [2]  Logistic regression [3]  Odds ratio (95% CI)  p-value  Unadjusted odds ratio (95% CI) [4]  Relative risk (95% CI) [5]  Risk difference (95% CI) [5]  Fisher's Exact p-value (2-sided)		0.201 0.33 (0.09,1.20) 0.092 0.46 (0.11,1.65) 0.58 (0.20,1.30) -0.17 (-0.41,0.08) 0.253

Mepolizumab (Nucala) - HES Seite 681 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS ( $0-<=20 \,\mathrm{mg/day}$  and  $>20 \,\mathrm{mg/day}$  prednisone or equivalent) and region.

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose and region.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.23

Subgroup Analysis of Proportion of Subjects Who Experience a HES Flare During Week 20 Through Week 32 by Baseline Blood Eosinophils (Treatment Policy Estimand)

Manalizumah

Baseline blood eosinophils: >=1.5 10^9/L

	Placebo (N=54)	300mg SC (N=54)
n Subjects with >=1 HES flare or who withdraw from study Subjects with >=1 HES flare Subjects with no HES flare who withdraw from study Subjects with no HES flare who complete study	, ,	3 (11%) 3 (11%) 0
Comparison Mepolizumab 300mg vs Placebo [1]  CMH p-value [2]  Logistic regression [3]  Odds ratio (95% CI)  p-value  Unadjusted odds ratio (95% CI) [4]  Relative risk (95% CI) [5]  Risk difference (95% CI) [5]  Fisher's Exact p-value (2-sided)		0.098 0.22 (0.04,1.13) 0.070 0.30 (0.04,1.54) 0.37 (0.06,1.26) -0.18 (-0.42,0.04) 0.157

Mepolizumab (Nucala) - HES Seite 682 von 1069

<sup>[1]</sup> Analysis compares the number of subjects who experience >=1 HES flare and/or withdraw from the study prematurely.

<sup>[2]</sup> Cochran-Mantel-Haenszel (CMH) test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[3]</sup> Logistic regression analysis adjusted for baseline OCS dose and region.

Note: Odds ratio and relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

<sup>[4]</sup> Exact method.

<sup>[5]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.11

Subgroup Analysis of Time to First HES Flare by Age

Age: 12-<18 Years

Cals	Placebo (N=54)	
Number of subjects in subgroup	3	1
Flare by week 4 Probability of a flare [1] 95% CI	0.0% (0.0, 0.0)	0.0% (0.0, 0.0)
Flare by week 8 Probability of a flare [1] 95% CI	33.3% (5.5, 94.6)	
Flare by week 12 Probability of a flare [1] 95% CI	66.7% (22.6, 99.1)	
Flare by week 16 Probability of a flare [1] 95% CI	66.7% (22.6, 99.1)	0.0% (0.0, 0.0)
Flare by week 20 Probability of a flare [1] 95% CI	66.7% (22.6, 99.1)	

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 683 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose and region. Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo. PPD

Protocol: 200622
Population: Intent-to-Treat

Table 90.11

Subgroup Analysis of Time to First HES Flare by Age

Age: 12-<18 Years

	Placebo (N=54)	
Flare by week 24 Probability of a flare [1] 95% CI	66.7% (22.6, 99.1)	0.0% (0.0, 0.0)
Flare by week 28 Probability of a flare [1] 95% CI	66.7% (22.6, 99.1)	0.0% (0.0, 0.0)
Flare by week 32 Probability of a flare [1] 95% CI	66.7% (22.6, 99.1)	0.0% (0.0, 0.0)
n HES flare Withdrawn - censored Completed - censored	3 2 (67%) 0 1 (33%)	1 0 0 1 (100%)
Comparison Mepolizumab 300mg vs Placebo Stratified Log-Rank p-value [1] Cox regression [2] Hazard ratio 95% CI for hazard ratio Wald Chi-Square p-value		Non-estimable Non-estimable Non-estimable Non-estimable

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 684 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose and region. Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo. PPD

Protocol: 200622
Population: Intent-to-Treat
Page 3 of 6

Table 90.11

Subgroup Analysis of Time to First HES Flare by Age

Age: 18-64 Years

als	Placebo (N=54)	2
Number of subjects in subgroup	41	49
Flare by week 4 Probability of a flare [1] 95% CI	4.9% (1.2, 18.1)	
Flare by week 8 Probability of a flare [1] 95% CI	12.3% (5.3, 27.0)	6.1% (2.0, 17.8)
Flare by week 12 Probability of a flare [1] 95% CI	19.8% (10.4, 35.7)	
Flare by week 16 Probability of a flare [1] 95% CI	29.8% (18.2, 46.5)	
Flare by week 20 Probability of a flare [1] 95% CI	37.3% (24.4, 54.1)	

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 685 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20 mg/day and >20 mg/day prednisone or equivalent) and region.

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose and region. Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo.

Protocol: 200622 Page 4 of 6

Population: Intent-to-Treat

Table 90.11 Subgroup Analysis of Time to First HES Flare by Age

Age: 18-64 Years

Sals	Placebo (N=54)	
Flare by week 24 Probability of a flare [1] 95% CI	47.4% (33.4, 63.7)	14.3% (7.1, 27.6)
Flare by week 28 Probability of a flare [1] 95% CI	49.9% (35.7, 66.0)	
Flare by week 32 Probability of a flare [1] 95% CI	52.4% (38.0, 68.3)	24.9% (14.9, 39.6)
n HES flare Withdrawn - censored Completed - censored	41 21 (51%) 2 (5%) 18 (44%)	1 (2%)
Comparison Mepolizumab 300mg vs Placebo Stratified Log-Rank p-value [1] Cox regression [2] Hazard ratio 95% CI for hazard ratio Wald Chi-Square p-value		0.002 0.32 (0.15, 0.66) 0.002

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 686 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20 mg/day and >20 mg/day prednisone or equivalent) and region.

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose and region. Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo. PPD

Protocol: 200622

Population: Intent-to-Treat

Page 5 of 6

Table 90.11
Subgroup Analysis of Time to First HES Flare by Age

Age: >=65 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	10	4
Flare by week 4 Probability of a flare [1] 95% CI	20.0% (5.4, 59.1)	
Flare by week 8 Probability of a flare [1] 95% CI	20.0% (5.4, 59.1)	
Flare by week 12 Probability of a flare [1] 95% CI	40.0% (17.3, 74.7)	
Flare by week 16 Probability of a flare [1] 95% CI	40.0% (17.3, 74.7)	
Flare by week 20 Probability of a flare [1] 95% CI	50.0% (24.7, 81.6)	

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 687 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose and region. Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo.

Protocol: 200622 Page 6 of 6

Population: Intent-to-Treat

Table 90.11 Subgroup Analysis of Time to First HES Flare by Age

Age: >=65 Years

15	Placebo (N=54)	
Flare by week 24 Probability of a flare [1] 95% CI	50.0% (24.7, 81.6)	
Flare by week 28 Probability of a flare [1] 95% CI	50.0% (24.7, 81.6)	
Flare by week 32 Probability of a flare [1] 95% CI	50.0% (24.7, 81.6)	
n HES flare Withdrawn - censored Completed - censored	10 5 (50%) 0 5 (50%)	4 2 (50%) 0 2 (50%)
Comparison Mepolizumab 300mg vs Placebo Stratified Log-Rank p-value [1] Cox regression [2] Hazard ratio 95% CI for hazard ratio Wald Chi-Square p-value		0.929 1.74 (0.10, 29.97) 0.703

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 688 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20 mg/day and >20 mg/day prednisone or equivalent) and region.

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose and region. Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 1 of 4

Population: Intent-to-Treat

Table 90.12

Subgroup Analysis of Time to First HES Flare by Gender

Gender: Female

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	27	30
Flare by week 4 Probability of a flare [1] 95% CI	11.1% (3.7, 30.6)	3.3% (0.5, 21.4)
Flare by week 8 Probability of a flare [1] 95% CI	22.4% (10.7, 43.2)	3.3% (0.5, 21.4)
Flare by week 12 Probability of a flare [1] 95% CI	37.9% (22.5, 59.1)	3.3% (0.5, 21.4)
Flare by week 16 Probability of a flare [1] 95% CI	49.6% (32.5, 69.7)	
Flare by week 20 Probability of a flare [1] 95% CI	57.3% (39.6, 76.2)	6.7% (1.7, 24.1)

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 689 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose and region. Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo.

Protocol: 200622 Page 2 of 4

Population: Intent-to-Treat

Table 90.12 Subgroup Analysis of Time to First HES Flare by Gender

Gender: Female

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Flare by week 24 Probability of a flare [1] 95% CI	61.2% (43.3, 79.3)	10.0% (3.3, 27.9)
Flare by week 28 Probability of a flare [1] 95% CI	61.2% (43.3, 79.3)	
Flare by week 32 Probability of a flare [1] 95% CI	61.2% (43.3, 79.3)	20.3% (9.7, 39.7)
n HES flare Withdrawn - censored Completed - censored	27 16 (59%) 1 (4%) 10 (37%)	30 6 (20%) 0 24 (80%)
Comparison Mepolizumab 300mg vs Placebo Stratified Log-Rank p-value [1] Cox regression [2] Hazard ratio 95% CI for hazard ratio Wald Chi-Square p-value		<0.001 0.13 (0.04, 0.40) <0.001

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 690 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose and region. Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 3 of 4

Population: Intent-to-Treat

Table 90.12 Subgroup Analysis of Time to First HES Flare by Gender

Gender: Male

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	27	24
Flare by week 4 Probability of a flare [1] 95% CI	3.7% (0.5, 23.5)	
Flare by week 8 Probability of a flare [1] 95% CI	7.4% (1.9, 26.5)	
Flare by week 12 Probability of a flare [1] 95% CI	14.8% (5.8, 34.8)	
Flare by week 16 Probability of a flare [1] 95% CI	18.5% (8.2, 38.9)	
Flare by week 20 Probability of a flare [1] 95% CI	25.9% (13.3, 46.8)	

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 691 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose and region. Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 4 of 4

Population: Intent-to-Treat

Table 90.12 Subgroup Analysis of Time to First HES Flare by Gender

Gender: Male

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Flare by week 24 Probability of a flare [1] 95% CI	37.0% (21.9, 57.9)	
Flare by week 28 Probability of a flare [1] 95% CI	40.7% (25.0, 61.4)	
Flare by week 32 Probability of a flare [1] 95% CI	44.4% (28.2, 64.8)	34.0% (18.7, 56.7)
n HES flare Withdrawn - censored Completed - censored		24 8 (33%) 1 (4%) 15 (63%)
Comparison Mepolizumab 300mg vs Placebo Stratified Log-Rank p-value [1] Cox regression [2] Hazard ratio 95% CI for hazard ratio Wald Chi-Square p-value		0.488 0.74 (0.29, 1.87) 0.522

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 692 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose and region. Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 1 of 4 Population: Intent-to-Treat

Table 90.13 Subgroup Analysis of Time to First HES Flare by Region

Region: Europe

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	33	31
Flare by week 4 Probability of a flare [1] 95% CI	6.1% (1.6, 22.1)	6.5% (1.7, 23.4)
Flare by week 8 Probability of a flare [1] 95% CI	12.1% (4.7, 29.1)	6.5% (1.7, 23.4)
Flare by week 12 Probability of a flare [1] 95% CI	21.5% (10.9, 40.0)	
Flare by week 16 Probability of a flare [1] 95% CI	31.0% (18.0, 49.9)	
Flare by week 20 Probability of a flare [1] 95% CI	40.4% (25.8, 59.2)	
Flare by week 24 Probability of a flare [1] 95% CI	43.5% (28.5, 62.2)	19.4% (9.2, 38.1)

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 693 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent).

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose.

Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo.

Protocol: 200622 Page 2 of 4

Population: Intent-to-Treat

Table 90.13

Subgroup Analysis of Time to First HES Flare by Region

Region: Europe

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Flare by week 28 Probability of a flare [1] 95% CI	46.6% (31.3, 65.1)	
Flare by week 32 Probability of a flare [1] 95% CI	49.8% (34.1, 67.9)	
n HES flare Withdrawn - censored Completed - censored	33 16 (48%) 2 (6%) 15 (45%)	0
Comparison Mepolizumab 300mg vs Placebo Stratified Log-Rank p-value [1] Cox regression [2] Hazard ratio 95% CI for hazard ratio Wald Chi-Square p-value		0.169 0.54 (0.24, 1.21) 0.134

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 694 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent).

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose.

Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo.

Protocol: 200622 Page 3 of 4 Population: Intent-to-Treat

Table 90.13

Subgroup Analysis of Time to First HES Flare by Region

Region: Rest of World

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	21	23
Flare by week 4 Probability of a flare [1] 95% CI	9.5% (2.5, 33.0)	4.3% (0.6, 27.1)
Flare by week 8 Probability of a flare [1] 95% CI	19.0% (7.6, 43.1)	
Flare by week 12 Probability of a flare [1] 95% CI	33.3% (17.5, 57.5)	
Flare by week 16 Probability of a flare [1] 95% CI	38.1% (21.2, 61.9)	
Flare by week 20 Probability of a flare [1] 95% CI	42.9% (25.1, 66.2)	
Flare by week 24 Probability of a flare [1] 95% CI	57.1% (37.7, 78.1)	

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 695 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent).

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose.

Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo.

Protocol: 200622 Page 4 of 4 Population: Intent-to-Treat

Table 90.13 Subgroup Analysis of Time to First HES Flare by Region

Region: Rest of World

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Flare by week 28 Probability of a flare [1] 95% CI	57.1% (37.7, 78.1)	
Flare by week 32 Probability of a flare [1] 95% CI	57.1% (37.7, 78.1)	
n HES flare Withdrawn - censored Completed - censored		23 4 (17%) 1 (4%) 18 (78%)
Comparison Mepolizumab 300mg vs Placebo Stratified Log-Rank p-value [1] Cox regression [2] Hazard ratio 95% CI for hazard ratio Wald Chi-Square p-value		0.002 0.13 (0.04, 0.50) 0.003

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 696 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent).

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose.

Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo.

Protocol: 200622 Page 1 of 4

Population: Intent-to-Treat

Table 90.14

Subgroup Analysis of Time to First HES Flare by Duration of Disease

Duration of Disease: <2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	32	22
Flare by week 4 Probability of a flare [1] 95% CI	3.1% (0.4, 20.2)	13.6% (4.6, 36.6)
Flare by week 8 Probability of a flare [1] 95% CI	12.6% (4.9, 30.2)	18.2% (7.2, 41.5)
Flare by week 12 Probability of a flare [1] 95% CI	25.6% (13.7, 44.7)	22.7% (10.2, 46.3)
Flare by week 16 Probability of a flare [1] 95% CI	32.0% (18.7, 51.4)	22.7% (10.2, 46.3)
Flare by week 20 Probability of a flare [1] 95% CI	35.3% (21.3, 54.6)	22.7% (10.2, 46.3)

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 697 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose and region. Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 2 of 4

Population: Intent-to-Treat

Table 90.14

Subgroup Analysis of Time to First HES Flare by Duration of Disease

Duration of Disease: <2.76 Years

	Placebo (N=54)	
Flare by week 24 Probability of a flare [1] 95% CI	45.0% (29.6, 63.8)	
Flare by week 28 Probability of a flare [1] 95% CI	45.0% (29.6, 63.8)	
Flare by week 32 Probability of a flare [1] 95% CI	48.2% (32.5, 66.8)	
n HES flare Withdrawn - censored Completed - censored	32 15 (47%) 1 (3%) 16 (50%)	1 (5%)
Comparison Mepolizumab 300mg vs Placebo Stratified Log-Rank p-value [1] Cox regression [2] Hazard ratio 95% CI for hazard ratio Wald Chi-Square p-value		0.130 0.50 (0.19, 1.30) 0.156

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 698 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose and region. Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 3 of 4

Population: Intent-to-Treat

Table 90.14 Subgroup Analysis of Time to First HES Flare by Duration of Disease

Duration of Disease: >=2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	22	32
Flare by week 4 Probability of a flare [1] 95% CI	13.6% (4.6, 36.6)	0.0% (0.0, 0.0)
Flare by week 8 Probability of a flare [1] 95% CI	18.2% (7.2, 41.5)	0.0% (0.0, 0.0)
Flare by week 12 Probability of a flare [1] 95% CI	27.3% (13.3, 50.9)	0.0% (0.0, 0.0)
Flare by week 16 Probability of a flare [1] 95% CI	36.4% (20.1, 59.7)	
Flare by week 20 Probability of a flare [1] 95% CI	50.0% (31.6, 71.8)	6.3% (1.6, 22.7)

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 699 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose and region. Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 4 of 4

Population: Intent-to-Treat

Table 90.14

Subgroup Analysis of Time to First HES Flare by Duration of Disease

Duration of Disease: >=2.76 Years

3e. 7-2.70 lears	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Flare by week 24 Probability of a flare [1] 95% CI	54.5% (35.7, 75.6)	9.4% (3.1, 26.3)
Flare by week 28 Probability of a flare [1] 95% CI	59.1% (39.9, 79.1)	
Flare by week 32 Probability of a flare [1] 95% CI	59.1% (39.9, 79.1)	
n HES flare Withdrawn - censored Completed - censored	22 13 (59%) 1 (5%) 8 (36%)	32 7 (22%) 0 25 (78%)
Comparison Mepolizumab 300mg vs Placebo Stratified Log-Rank p-value [1] Cox regression [2] Hazard ratio 95% CI for hazard ratio Wald Chi-Square p-value		0.003 0.23 (0.09, 0.60) 0.002

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 700 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose and region. Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo.

Protocol: 200622 Page 1 of 4

Population: Intent-to-Treat

Table 90.15
Subgroup Analysis of Time to First HES Flare by Baseline Blood Eosinophils

Baseline Blood Eosinophils: <1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	30	26
Flare by week 4 Probability of a flare [1] 95% CI	6.7% (1.7, 24.1)	3.8% (0.6, 24.3)
Flare by week 8 Probability of a flare [1] 95% CI	13.3% (5.2, 31.7)	7.7% (2.0, 27.4)
Flare by week 12 Probability of a flare [1] 95% CI	23.3% (11.9, 42.8)	11.5% (3.9, 31.6)
Flare by week 16 Probability of a flare [1] 95% CI	33.3% (19.5, 53.1)	
Flare by week 20 Probability of a flare [1] 95% CI	36.7% (22.2, 56.4)	

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 701 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose and region. Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 2 of 4

Population: Intent-to-Treat

Table 90.15
Subgroup Analysis of Time to First HES Flare by Baseline Blood Eosinophils

Baseline Blood Eosinophils: <1.5 10^9/L

	Placebo (N=54)	
Flare by week 24 Probability of a flare [1] 95% CI	46.7% (30.9, 65.7)	
Flare by week 28 Probability of a flare [1] 95% CI	50.0% (33.9, 68.7)	
Flare by week 32 Probability of a flare [1] 95% CI	53.3% (37.0, 71.6)	
n HES flare Withdrawn - censored Completed - censored	30 16 (53%) 0 14 (47%)	26 9 (35%) 1 (4%) 16 (62%)
Comparison Mepolizumab 300mg vs Placebo Stratified Log-Rank p-value [1] Cox regression [2] Hazard ratio 95% CI for hazard ratio Wald Chi-Square p-value		0.058 0.37 (0.16, 0.90) 0.028

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 702 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose and region. Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 3 of 4

Population: Intent-to-Treat

Baseline Blood Eosinophils: >=1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	24	28
Flare by week 4 Probability of a flare [1] 95% CI	8.3% (2.2, 29.4)	7.1% (1.8, 25.7)
Flare by week 8 Probability of a flare [1] 95% CI	16.9% (6.7, 39.0)	7.1% (1.8, 25.7)
Flare by week 12 Probability of a flare [1] 95% CI	30.0% (15.6, 52.9)	7.1% (1.8, 25.7)
Flare by week 16 Probability of a flare [1] 95% CI	34.4% (18.9, 57.2)	
Flare by week 20 Probability of a flare [1] 95% CI	47.5% (29.7, 69.2)	7.1% (1.8, 25.7)

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 703 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose and region. Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 4 of 4

Population: Intent-to-Treat

Table 90.15
Subgroup Analysis of Time to First HES Flare by Baseline Blood Eosinophils

Baseline Blood Eosinophils: >=1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Flare by week 24 Probability of a flare [1] 95% CI	51.9% (33.6, 72.9)	10.7% (3.6, 29.6)
Flare by week 28 Probability of a flare [1] 95% CI	51.9% (33.6, 72.9)	
Flare by week 32 Probability of a flare [1] 95% CI	51.9% (33.6, 72.9)	
n HES flare Withdrawn - censored Completed - censored	24 12 (50%) 2 (8%) 10 (42%)	28 5 (18%) 0 23 (82%)
Comparison Mepolizumab 300mg vs Placebo Stratified Log-Rank p-value [1] Cox regression [2] Hazard ratio 95% CI for hazard ratio Wald Chi-Square p-value		0.020 0.27 (0.09, 0.77) 0.015

Note: Subjects withdrawing from the study prematurely prior to reporting a HES flare are censored at the date of study withdrawal.

Mepolizumab (Nucala) - HES Seite 704 von 1069

<sup>[1]</sup> Log-Rank test stratified by baseline OCS (0-<=20mg/day and >20mg/day prednisone or equivalent) and region.

<sup>[2]</sup> Cox proportional hazards regression analysis adjusted for baseline OCS dose and region. Hazard ratio <1 indicates a lower risk of HES flare with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 1 of 3 Population: Intent-to-Treat

Table 90.26 Subgroup Analysis of Rate of HES Flares by Age

Age (years): 12-<18 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
All HES flare		
n	3	1
0	1 (33%)	1 (100%)
1	0	0
2	1 (33%)	0
3	1 (33%)	0
4	0	0
Adjusted mean rate/year [1] Comparison Mepolizumab 300mg vs Placebo	Non-estimable	Non-estimable
Wilcoxon Rank Sum Test p-value [2] Negative binomial model [1]		Non-estimable
Rate ratio		Non-estimable
95% CI for rate ratio		Non-estimable
p-value		Non-estimable

Note: For subjects withdrawing prematurely from the study during the 32-week treatment period, all data up to the time of study withdrawal is used to calculate the rate of HES flares.

Mepolizumab (Nucala) - HES Seite 705 von 1069

<sup>[1]</sup> Negative binomial generalised linear model including baseline OCS dose, region, treatment and observed time (offset variable). Rate ratio <1 indicates a lower flare rate with Mepolizumab compared with Placebo. [2] Wilcoxon test stratified by baseline OCS (0-<=20mg/day, >20mg/day prednisone or equivalent) and region.

Protocol: 200622 Page 2 of 3 Population: Intent-to-Treat

Table 90.26 Subgroup Analysis of Rate of HES Flares by Age

Age (years): 18-64 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
All HES flare		
n	41	49
0	20 (49%)	37 (76%)
1	12 (29%)	10 (20%)
2	5 (12%)	2 (4%)
3	3 (7%)	0
4	1 (2%)	0
Adjusted mean rate/year [1] Comparison Mepolizumab 300mg vs Placebo	1.38	0.45
Wilcoxon Rank Sum Test p-value [2] Negative binomial model [1]		0.003
Rate ratio		0.32
95% CI for rate ratio		(0.17,0.63)
p-value		<0.001

Note: For subjects withdrawing prematurely from the study during the 32-week treatment period, all data up to the time of study withdrawal is used to calculate the rate of HES flares.

Mepolizumab (Nucala) - HES Seite 706 von 1069

<sup>[1]</sup> Negative binomial generalised linear model including baseline OCS dose, region, treatment and observed time (offset variable). Rate ratio <1 indicates a lower flare rate with Mepolizumab compared with Placebo.

<sup>[2]</sup> Wilcoxon test stratified by baseline OCS (0-<=20mg/day, >20mg/day prednisone or equivalent) and region.

Protocol: 200622 Page 3 of 3 Population: Intent-to-Treat

Table 90.26 Subgroup Analysis of Rate of HES Flares by Age

Age (years): >=65 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
All HES flare			
n	10	4	
0	5 (50%)	2 (50%)	
1	3 (30%)	1 (25%)	
2	1 (10%)	1 (25%)	
3	1 (10%)	0	
4	0	0	
Adjusted mean rate/year [1] Comparison Mepolizumab 300mg vs Placebo	0.93	2.02	
Wilcoxon Rank Sum Test p-value [2] Negative binomial model [1]		0.879	
Rate ratio		2.17	
95% CI for rate ratio		(0.18,26.55)	
p-value		0.545	

Note: For subjects withdrawing prematurely from the study during the 32-week treatment period, all data up to the time of study withdrawal is used to calculate the rate of HES flares.

Mepolizumab (Nucala) - HES Seite 707 von 1069

<sup>[1]</sup> Negative binomial generalised linear model including baseline OCS dose, region, treatment and observed time (offset variable). Rate ratio <1 indicates a lower flare rate with Mepolizumab compared with Placebo. [2] Wilcoxon test stratified by baseline OCS (0-<=20mg/day, >20mg/day prednisone or equivalent) and region.

Protocol: 200622 Page 1 of 2

Population: Intent-to-Treat Table 90.27 Subgroup Analysis of Rate of HES Flares by Gender

Gender: Female

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
All HES flare		
n	27	30
0	11 (41%)	24 (80%)
1	7 (26%)	4 (13%)
2 3	5 (19%)	2 (7%)
3	3 (11%)	0
4	1 (4%)	0
Adjusted mean rate/year [1] Comparison Mepolizumab 300mg vs Placebo	1.63	0.37
Wilcoxon Rank Sum Test p-value [2] Negative binomial model [1]		0.002
Rate ratio		0.23
95% CI for rate ratio		(0.10,0.53)
p-value		<0.001

Note: For subjects withdrawing prematurely from the study during the 32-week treatment period, all data up to the time of study withdrawal is used to calculate the rate of HES flares.

Mepolizumab (Nucala) - HES Seite 708 von 1069

<sup>[1]</sup> Negative binomial generalised linear model including baseline OCS dose, region, treatment and observed time (offset variable). Rate ratio <1 indicates a lower flare rate with Mepolizumab compared with Placebo.

<sup>[2]</sup> Wilcoxon test stratified by baseline OCS (0-<=20mg/day, >20mg/day prednisone or equivalent) and region.

Protocol: 200622 Page 2 of 2 Population: Intent-to-Treat

Table 90.27 Subgroup Analysis of Rate of HES Flares by Gender

Gender: Male

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
All HES flare		
n	27	24
0	15 (56%)	16 (67%)
1	8 (30%)	7 (29%)
2 3	2 (7%)	1 (4%)
3	2 (7%)	0
4	0	0
Adjusted mean rate/year [1] Comparison Mepolizumab 300mg vs Placebo	0.85	0.66
Wilcoxon Rank Sum Test p-value [2] Negative binomial model [1]		0.385
Rate ratio		0.77
95% CI for rate ratio		(0.33,1.81)
p-value		0.549

Note: For subjects withdrawing prematurely from the study during the 32-week treatment period, all data up to the time of study withdrawal is used to calculate the rate of HES flares.

Mepolizumab (Nucala) - HES Seite 709 von 1069

<sup>[1]</sup> Negative binomial generalised linear model including baseline OCS dose, region, treatment and observed time (offset variable). Rate ratio <1 indicates a lower flare rate with Mepolizumab compared with Placebo.

<sup>[2]</sup> Wilcoxon test stratified by baseline OCS (0-<=20mg/day, >20mg/day prednisone or equivalent) and region.

Protocol: 200622 Page 1 of 2 Population: Intent-to-Treat

Table 90.28 Subgroup Analysis of Rate of HES Flares by Region

Region: Europe

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
All HES flare		
n	33	31
0	17 (52%)	21 (68%)
1	8 (24%)	8 (26%)
2	4 (12%)	2 (6%)
3	3 (9%)	0
4	1 (3%)	0
Adjusted mean rate/year [1] Comparison Mepolizumab 300mg vs Placebo	1.44	0.62
Wilcoxon Rank Sum Test p-value [2] Negative binomial model [1]		0.131
Rate ratio		0.43
95% CI for rate ratio		(0.20,0.92)
p-value		0.029

Note: For subjects withdrawing prematurely from the study during the 32-week treatment period, all data up to the time of study withdrawal is used to calculate the rate of HES flares.

Mepolizumab (Nucala) - HES Seite 710 von 1069

<sup>[1]</sup> Negative binomial generalised linear model including baseline OCS dose, treatment and observed time (offset variable). Rate ratio <1 indicates a lower flare rate with Mepolizumab compared with Placebo.

<sup>[2]</sup> Wilcoxon test stratified by baseline OCS (0-<=20mg/day, >20mg/day prednisone or equivalent)

Protocol: 200622 Page 2 of 2 Population: Intent-to-Treat

Table 90.28 Subgroup Analysis of Rate of HES Flares by Region

Region: Rest of World

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
All HES flare		
n	21	23
0	9 (43%)	19 (83%)
1	7 (33%)	3 (13%)
2	3 (14%)	1 (4%)
3	2 (10%)	0
4	0	0
Adjusted mean rate/year [1] Comparison Mepolizumab 300mg vs Placebo	1.53	0.30
Wilcoxon Rank Sum Test p-value [2] Negative binomial model [1]		0.003
Rate ratio		0.19
95% CI for rate ratio		(0.06,0.59)
p-value		0.004

Note: For subjects withdrawing prematurely from the study during the 32-week treatment period, all data up to the time of study withdrawal is used to calculate the rate of HES flares.

Mepolizumab (Nucala) - HES Seite 711 von 1069

<sup>[1]</sup> Negative binomial generalised linear model including baseline OCS dose, treatment and observed time (offset variable). Rate ratio <1 indicates a lower flare rate with Mepolizumab compared with Placebo.

<sup>[2]</sup> Wilcoxon test stratified by baseline OCS (0-<=20mg/day, >20mg/day prednisone or equivalent)

Protocol: 200622 Page 1 of 2

Population: Intent-to-Treat Table 90.29 Subgroup Analysis of Rate of HES Flares by Duration of Disease

Duration of disease: <2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
All HES flare		
n	32	22
0	17 (53%)	15 (68%)
1	10 (31%)	6 (27%)
2	4 (13%)	1 (5%)
3	1 (3%)	0
4	0	0
Adjusted mean rate/year [1] Comparison Mepolizumab 300mg vs Placebo	1.11	0.55
Wilcoxon Rank Sum Test p-value [2] Negative binomial model [1]		0.092
Rate ratio		0.50
95% CI for rate ratio		(0.21,1.18)
p-value		0.112

Note: For subjects withdrawing prematurely from the study during the 32-week treatment period, all data up to the time of study withdrawal is used to calculate the rate of HES flares.

Mepolizumab (Nucala) - HES Seite 712 von 1069

<sup>[1]</sup> Negative binomial generalised linear model including baseline OCS dose, region, treatment and observed time (offset variable). Rate ratio <1 indicates a lower flare rate with Mepolizumab compared with Placebo.

<sup>[2]</sup> Wilcoxon test stratified by baseline OCS (0-<=20mg/day, >20mg/day prednisone or equivalent) and region.

Protocol: 200622 Page 2 of 2

Population: Intent-to-Treat Table 90.29 Subgroup Analysis of Rate of HES Flares by Duration of Disease

Duration of disease: >=2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
All HES flare			
n	22	32	
0	9 (41%)	25 (78%)	
1	5 (23%)	5 (16%)	
2 3	3 (14%)	2 (6%)	
3	4 (18%)	0	
4	1 (5%)	0	
Adjusted mean rate/year [1] Comparison Mepolizumab 300mg vs Placebo	1.95	0.45	
Wilcoxon Rank Sum Test p-value [2] Negative binomial model [1]		0.008	
Rate ratio		0.23	
95% CI for rate ratio		(0.10,0.54)	
p-value		<0.001	

Note: For subjects withdrawing prematurely from the study during the 32-week treatment period, all data up to the time of study withdrawal is used to calculate the rate of HES flares.

[2] Wilcoxon test stratified by baseline OCS (0-<=20mg/day, >20mg/day prednisone or equivalent) and region.

Mepolizumab (Nucala) - HES Seite 713 von 1069

<sup>[1]</sup> Negative binomial generalised linear model including baseline OCS dose, region, treatment and observed time (offset variable). Rate ratio <1 indicates a lower flare rate with Mepolizumab compared with Placebo.

Protocol: 200622 Page 1 of 2 Population: Intent-to-Treat

Table 90.30

Subgroup Analysis of Rate of HES Flares by Baseline Blood Eosinophils

Baseline blood eosinophils: <1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
All HES flare			
n	30	26	
0	14 (47%)	17 (65%)	
1	8 (27%)	7 (27%)	
2 3	5 (17%)	2 (8%)	
3	3 (10%)	0	
4	0	0	
Adjusted mean rate/year [1] Comparison Mepolizumab 300mg vs Placebo	1.48	0.61	
Wilcoxon Rank Sum Test p-value [2] Negative binomial model [1]		0.049	
Rate ratio		0.42	
95% CI for rate ratio		(0.19, 0.89)	
p-value		0.023	

Note: For subjects withdrawing prematurely from the study during the 32-week treatment period, all data up to the time of study withdrawal is used to calculate the rate of HES flares.

Mepolizumab (Nucala) - HES Seite 714 von 1069

<sup>[1]</sup> Negative binomial generalised linear model including baseline OCS dose, region, treatment and observed time (offset variable). Rate ratio <1 indicates a lower flare rate with Mepolizumab compared with Placebo.

<sup>[2]</sup> Wilcoxon test stratified by baseline OCS (0-<=20mg/day, >20mg/day prednisone or equivalent) and region.

Protocol: 200622 Page 2 of 2 Population: Intent-to-Treat

Table 90.30 Subgroup Analysis of Rate of HES Flares by Baseline Blood Eosinophils

Baseline blood eosinophils: >=1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
All HES flare			
n	24	28	
0	12 (50%)	23 (82%)	
1	7 (29%)	4 (14%)	
2	2 (8응)	1 (4%)	
3	2 (8%)	0	
4	1 (4%)	0	
Adjusted mean rate/year [1] Comparison Mepolizumab 300mg vs Placebo	1.40	0.32	
Wilcoxon Rank Sum Test p-value [2] Negative binomial model [1]		0.029	
Rate ratio		0.23	
95% CI for rate ratio		(0.08,0.65)	
p-value		0.005	

Note: For subjects withdrawing prematurely from the study during the 32-week treatment period, all data up to the time of study withdrawal is used to calculate the rate of HES flares.

Mepolizumab (Nucala) - HES Seite 715 von 1069

<sup>[1]</sup> Negative binomial generalised linear model including baseline OCS dose, region, treatment and observed time (offset variable). Rate ratio <1 indicates a lower flare rate with Mepolizumab compared with Placebo.

<sup>[2]</sup> Wilcoxon test stratified by baseline OCS (0-<=20mg/day, >20mg/day prednisone or equivalent) and region.

Protocol: 200622 Page 1 of 3

Population: Intent-to-Treat

Table 90.50 Subgroup Analysis of Change from Baseline in Total BFI Score at Week 32 by Age (Mixed Model Repeated Measures)

Age (years): 12-<18 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	3	1
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	2 2 Non-estimable Non-estimable	1 1 Non-estimable Non-estimable

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatique/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

Mepolizumab (Nucala) - HES Seite 716 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 3

Population: Intent-to-Treat

Table 90.50 Subgroup Analysis of Change from Baseline in Total BFI Score at Week 32 by Age (Mixed Model Repeated Measures)

Mana all i muna ala

Age (years): 18-64 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	41	49	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	37 28 3.45 (0.323) -0.33 (0.323)	45 33 2.56 (0.294) -1.22 (0.294)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.89 (-1.76, -0.02) 0.045	
Corrected Hedges g [3] 95% CI		-0.52 (-1.03, 0.00)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatique/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

Mepolizumab (Nucala) - HES Seite 717 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 3 of 3

Population: Intent-to-Treat

Table 90.50

Subgroup Analysis of Change from Baseline in Total BFI Score at Week 32 by Age (Mixed Model Repeated Measures)

Age (years): >=65 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	10	4
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	10 6 Non-estimable Non-estimable	4 2 Non-estimable Non-estimable

Scale 0 = No fatigue/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

Mepolizumab (Nucala) - HES Seite 718 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Protocol: 200622 Page 1 of 2

Population: Intent-to-Treat

Table 90.51
Subgroup Analysis of Change from Baseline in Total BFI Score at Week 32 by Gender (Mixed Model Repeated Measures)

Gender: Female

are	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	27	30
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	27 22 3.48 (0.421) -0.79 (0.421)	27 19 3.22 (0.432) -1.05 (0.432)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.26 (-1.48, 0.96) 0.667
Corrected Hedges g [3] 95% CI		-0.13 (-0.75, 0.48)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatique/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

FFD

Mepolizumab (Nucala) - HES Seite 719 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 2 of 2

Population: Intent-to-Treat

Table 90.51
Subgroup Analysis of Change from Baseline in Total BFI Score at Week 32 by Gender (Mixed Model Repeated Measures)

Gender: Male

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	27	24
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	22 14 3.12 (0.369) -0.43 (0.369)	23 17 2.04 (0.347) -1.51 (0.347)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-1.08 (-2.14, -0.02) 0.047
Corrected Hedges g [3] 95% CI		-0.74 (-1.47, -0.01)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatique/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

Mepolizumab (Nucala) - HES Seite 720 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.52

Subgroup Analysis of Change from Baseline in Total BFI Score at Week 32 by Region (Mixed Model Repeated Measures)

Region: Europe

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	33	31
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	31 23 3.01 (0.456) -0.85 (0.363)	30 25 2.66 (0.456) -1.58 (0.360)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.74 (-1.76, 0.29) 0.155
Corrected Hedges g [3] 95% CI		-0.41 (-0.98, 0.16)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of treatment and visit, plus interaction terms for visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

Mepolizumab (Nucala) - HES Seite 721 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.52
Subgroup Analysis of Change from Baseline in Total BFI Score at Week 32 by Region (Mixed Model Repeated Measures)

Region: Rest of World

ot of world	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	21	23
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	18 13 3.44 (0.710) -0.58 (0.533)	20 11 3.85 (0.693) -0.61 (0.528)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.04 (-1.57, 1.50) 0.960
Corrected Hedges g [3] 95% CI		-0.02 (-0.82, 0.78)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of treatment and visit, plus interaction terms for visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

Mepolizumab (Nucala) - HES Seite 722 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.53

Subgroup Analysis of Change from Baseline in Total BFI Score at Week 32 by Duration of Disease (Mixed Model Repeated Measures)

Duration of disease: <2.76 Years

- 4100400.	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	32	22
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	31 22 3.11 (0.394) -0.79 (0.394)	22 15 3.13 (0.484) -0.77 (0.484)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.02 (-1.24, 1.28) 0.975
Corrected Hedges g [3] 95% CI		0.01 (-0.65, 0.67)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

Mepolizumab (Nucala) - HES Seite 723 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.53

Subgroup Analysis of Change from Baseline in Total BFI Score at Week 32 by Duration of Disease (Mixed Model Repeated Measures)

Menolizumah

Duration of disease: >=2.76 Years

	Placebo (N=54)	300mg SC (N=54)	
Number of subjects in subgroup	22	32	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	18 14 3.90 (0.450) -0.09 (0.450)	28 21 2.48 (0.364) -1.51 (0.364)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-1.42 (-2.60, -0.23) 0.020	
Corrected Hedges g [3] 95% CI		-0.83 (-1.53, -0.12)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

Mepolizumab (Nucala) - HES Seite 724 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.54
Subgroup Analysis of Change from Baseline in Total BFI Score at Week 32
by Baseline Blood Eosinophils

(Mixed Model Repeated Measures)

Baseline blood eosinophils: <1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	30	26	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	28 25 3.09 (0.493) -0.73 (0.404)	26 19 3.51 (0.527) -0.88 (0.439)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.15 (-1.35, 1.05) 0.805	
Corrected Hedges g [3] 95% CI		-0.07 (-0.67, 0.52)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of treatment and visit, plus an interaction term for visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

Mepolizumab (Nucala) - HES Seite 725 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.54
Subgroup Analysis of Change from Baseline in Total BFI Score at Week 32
by Baseline Blood Eosinophils

(Mixed Model Repeated Measures)

Baseline blood eosinophils: >=1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	24	28
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	21 11 Non-estimable Non-estimable	24 17 Non-estimable Non-estimable

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of treatment and visit, plus an interaction term for visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue/Does not interfere to 10 = As bad as you can imagine/Completely interferes.

Mepolizumab (Nucala) - HES Seite 726 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.33

Subgroup Analysis of Change from Baseline in Mean Daily Fatigue Severity -Worst Level of Fatigue in Past 24 Hours (BFI Item 3) at Week 32 by Age (Mixed Model Repeated Measures)

Age (years): 12-<18 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	3	1
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	3 3 Non-estimable Non-estimable	1 1 Non-estimable Non-estimable

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 727 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.33

Subgroup Analysis of Change from Baseline in Mean Daily Fatigue Severity -Worst Level of Fatigue in Past 24 Hours (BFI Item 3) at Week 32 by Age (Mixed Model Repeated Measures)

Age (years): 18-64 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	41	49	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	41 35 4.16 (0.337) -0.16 (0.337)	49 46 3.29 (0.297) -1.03 (0.297)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.87 (-1.76, 0.02) 0.057	
Corrected Hedges g [3] 95% CI		-0.43 (-0.87, 0.02)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 728 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.33

Subgroup Analysis of Change from Baseline in Mean Daily Fatigue Severity -Worst Level of Fatigue in Past 24 Hours (BFI Item 3) at Week 32 by Age (Mixed Model Repeated Measures)

Age (years): >=65 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	10	4	•
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	10 9 5.19 (0.780) -0.04 (0.780)	4 3 4.63 (1.465) -0.60 (1.465)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.56 (-4.45, 3.32) 0.752	
Corrected Hedges g [3] 95% CI		-0.22 (-1.53, 1.09)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 729 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.34

Subgroup Analysis of Change from Baseline in Mean Daily Fatigue Severity -Worst Level of Fatique in Past 24 Hours (BFI Item 3) at Week 32 by Gender (Mixed Model Repeated Measures)

Gender: Female

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	27	30	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	27 25 4.46 (0.429) -0.19 (0.429)	30 28 3.72 (0.402) -0.93 (0.402)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.74 (-1.94, 0.46) 0.219	
Corrected Hedges g [3] 95% CI		-0.34 (-0.88, 0.20)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 730 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.34

Subgroup Analysis of Change from Baseline in Mean Daily Fatigue Severity -Worst Level of Fatique in Past 24 Hours (BFI Item 3) at Week 32 by Gender (Mixed Model Repeated Measures)

Mana a 1 d ------ a la

Gender: Male

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	27	24
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	27 22 3.78 (0.404) -0.56 (0.404)	24 22 3.31 (0.413) -1.03 (0.413)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.47 (-1.66, 0.72) 0.432
Corrected Hedges g [3] 95% CI		-0.24 (-0.83, 0.35)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 731 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.35

Subgroup Analysis of Change from Baseline in Mean Daily Fatigue Severity -Worst Level of Fatique in Past 24 Hours (BFI Item 3) at Week 32 by Region (Mixed Model Repeated Measures)

Region: Europe

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	33	31	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	33 29 4.17 (0.379) -0.39 (0.379)	31 29 3.52 (0.378) -1.05 (0.378)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.65 (-1.73, 0.42) 0.231	
Corrected Hedges g [3] 95% CI		-0.32 (-0.83, 0.20)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 732 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.35

Subgroup Analysis of Change from Baseline in Mean Daily Fatigue Severity -Worst Level of Fatique in Past 24 Hours (BFI Item 3) at Week 32 by Region (Mixed Model Repeated Measures)

Mana a 1 d ------ a la

Region: Rest of World

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	21	23	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	21 18 4.28 (0.471) -0.13 (0.471)	23 21 3.32 (0.451) -1.08 (0.451)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.95 (-2.28, 0.38) 0.155	
Corrected Hedges g [3] 95% CI		-0.46 (-1.10, 0.18)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 733 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.36

Subgroup Analysis of Change from Baseline in Mean Daily Fatigue Severity -Worst Level of Fatique in Past 24 Hours (BFI Item 3) at Week 32 by Duration of Disease (Mixed Model Repeated Measures)

Mana a 1 d ------ a la

Duration of disease: <2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	32	22	-
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	32 29 3.79 (0.360) -0.55 (0.360)	22 20 3.41 (0.440) -0.93 (0.440)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.38 (-1.53, 0.77) 0.509	
Corrected Hedges g [3] 95% CI		-0.19 (-0.76, 0.38)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 734 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.36

Subgroup Analysis of Change from Baseline in Mean Daily Fatigue Severity -Worst Level of Fatique in Past 24 Hours (BFI Item 3) at Week 32 by Duration of Disease (Mixed Model Repeated Measures)

Duration of disease: >=2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	22	32	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	22 18 4.77 (0.472) 0.10 (0.472)	32 30 3.55 (0.371) -1.11 (0.371)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-1.22 (-2.43, -0.01) 0.048	
Corrected Hedges g [3] 95% CI		-0.59 (-1.19, 0.00)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 735 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.37

Subgroup Analysis of Change from Baseline in Mean Daily Fatigue Severity -Worst Level of Fatique in Past 24 Hours (BFI Item 3) at Week 32 by Baseline Blood Eosinophils (Mixed Model Repeated Measures)

Baseline blood eosinophils: <1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	30	26
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	30 29 4.14 (0.384) -0.49 (0.384)	26 24 3.71 (0.421) -0.91 (0.421)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.42 (-1.58, 0.73) 0.463
Corrected Hedges g [3] 95% CI		-0.20 (-0.74, 0.34)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 736 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.37

Subgroup Analysis of Change from Baseline in Mean Daily Fatigue Severity -Worst Level of Fatique in Past 24 Hours (BFI Item 3) at Week 32 by Baseline Blood Eosinophils (Mixed Model Repeated Measures)

Baseline blood eosinophils: >=1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	24	28	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	24 18 4.44 (0.437) 0.07 (0.437)	28 26 3.19 (0.386) -1.17 (0.386)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-1.24 (-2.42, -0.06) 0.039	
Corrected Hedges g [3] 95% CI		-0.64 (-1.25, -0.02)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = No fatigue to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 737 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.41

Subgroup Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) at

Week 32 by Age

(Mixed Model Repeated Measures)

Age (years): 12-<18 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	3	1
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	3 3 Non-estimable Non-estimable	1 1 Non-estimable Non-estimable

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Seite 738 von 1069 Mepolizumab (Nucala) - HES

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.41

Subgroup Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) at Week 32 by Age

(Mixed Model Repeated Measures)

Age (years): 18-64 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	41	49
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	41 35 3.33 (0.307) -0.99 (0.307)	49 46 2.61 (0.272) -1.71 (0.272)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.72 (-1.53, 0.10) 0.084
Corrected Hedges g [3] 95% CI		-0.39 (-0.83, 0.06)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 739 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.41

Subgroup Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) at Week 32 by Age

(Mixed Model Repeated Measures)

Age (years): >=65 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	10	4
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	10 9 3.92 (0.588) -0.52 (0.589)	4 3 2.16 (1.071) -2.28 (1.071)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-1.76 (-4.59, 1.07) 0.197
Corrected Hedges g [3] 95% CI		-0.91 (-2.27, 0.45)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 740 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.42

Subgroup Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) at

Mana a 1 d ------ a la

Week 32 by Gender

(Mixed Model Repeated Measures)

Gender: Female

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	27	30	-
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	27 25 3.83 (0.399) -0.64 (0.399)	30 28 2.86 (0.375) -1.61 (0.375)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.97 (-2.08, 0.14) 0.086	
Corrected Hedges g [3] 95% CI		-0.48 (-1.03, 0.07)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 741 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.42

Subgroup Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) at Week 32 by Gender

(Mixed Model Repeated Measures)

Mana a 1 d ------ a la

Gender: Male

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	27	24	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	27 22 2.78 (0.334) -1.48 (0.334)	24 22 2.53 (0.341) -1.73 (0.341)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.25 (-1.23, 0.73) 0.608	
Corrected Hedges g [3] 95% CI		-0.15 (-0.75, 0.44)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 742 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.43

Subgroup Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) at

Week 32 by Region

(Mixed Model Repeated Measures)

Region: Europe

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	33	31	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	33 29 3.20 (0.336) -1.14 (0.336)	31 29 2.62 (0.337) -1.72 (0.337)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.58 (-1.53, 0.38) 0.231	
Corrected Hedges g [3] 95% CI		-0.31 (-0.83, 0.20)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 743 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.43

Subgroup Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) at

Week 32 by Region (Mixed Model Repeated Measures)

Region: Rest of World

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	21	23	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	21 18 3.72 (0.423) -0.70 (0.423)	23 21 2.74 (0.407) -1.68 (0.407)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.98 (-2.18, 0.22) 0.108	
Corrected Hedges g [3] 95% CI		-0.52 (-1.16, 0.12)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 744 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.44

Subgroup Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) at Week 32 by Duration of Disease (Mixed Model Repeated Measures)

Duration of disease: <2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	32	22	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	32 29 3.09 (0.340) -1.08 (0.340)	22 20 3.03 (0.414) -1.14 (0.414)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.06 (-1.15, 1.03) 0.914	
Corrected Hedges g [3] 95% CI		-0.03 (-0.60, 0.54)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 745 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.44

Subgroup Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) at Week 32 by Duration of Disease (Mixed Model Repeated Measures)

Duration of disease: >=2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	22	32	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	22 18 3.82 (0.402) -0.76 (0.402)	32 30 2.50 (0.314) -2.08 (0.314)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-1.32 (-2.35, -0.29) 0.013	
Corrected Hedges g [3] 95% CI		-0.76 (-1.36, -0.15)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 746 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.45

Subgroup Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) at Week 32 by Baseline Blood Eosinophils (Mixed Model Repeated Measures)

Baseline blood eosinophils: <1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	30	26	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	30 29 3.24 (0.302) -1.21 (0.302)	26 24 3.08 (0.331) -1.37 (0.331)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.16 (-1.07, 0.74) 0.722	
Corrected Hedges g [3] 95% CI		-0.10 (-0.64, 0.44)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 747 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.45

Subgroup Analysis of Change from Baseline in Most Bothersome HES Symptom Severity Score (HES-DS) at Week 32 by Baseline Blood Eosinophils (Mixed Model Repeated Measures)

Baseline blood eosinophils: >=1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	24	28	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	24 18 3.62 (0.431) -0.67 (0.431)	28 26 2.25 (0.381) -2.04 (0.381)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-1.37 (-2.54, -0.21) 0.022	
Corrected Hedges g [3] 95% CI		-0.71 (-1.33, -0.09)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = None to 10 = As bad as you can imagine.

Mepolizumab (Nucala) - HES Seite 748 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-To-Treat

Table 90.57

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: 12-<18 Years Visit: Week 4

SIC. WEEK 4	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	3	1
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 1 (33%) 0 2 (67%) 0 0	0 0 0 0 0 0 0 1 (100%)
Median response	4.0	7.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		Non-estimable
Inverse odds ratio 95% CI for inverse odds ratio p-value		Non-estimable Non-estimable Non-estimable

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 749 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Population: Intent-To-Treat

Table 90.57

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: 12-<18 Years Visit: Week 8

ste. Heek c	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	3	1
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (33%) 1 (33%) 0 1 (33%) 0 0	0 0 0 0 0 0 0 1 (100%)
Median response	2.0	7.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		Non-estimable
Inverse odds ratio 95% CI for inverse odds ratio p-value		Non-estimable Non-estimable Non-estimable

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 750 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Population: Intent-To-Treat

Table 90.57

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: 12-<18 Years Visit: Week 12

SIL. WEEK 12	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	3	1
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 2 (67%) 0 0 0 0 1 (33%)	0 0 0 0 0 0 1 (100%)
Median response	2.0	7.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		Non-estimable
Inverse odds ratio 95% CI for inverse odds ratio p-value		Non-estimable Non-estimable Non-estimable

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 751 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Population: Intent-To-Treat

Table 90.57

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: 12-<18 Years Visit: Week 16

sic. week 10	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	3	1
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 0 1 (33%) 0 1 (33%) 0 1 (33%)	0 0 0 0 0 0 1 (100%)
Median response	5.0	7.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		Non-estimable
Inverse odds ratio 95% CI for inverse odds ratio p-value		Non-estimable Non-estimable Non-estimable

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 752 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Population: Intent-To-Treat

Table 90.57

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: 12-<18 Years Visit: Week 20

SIL. WEEK 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	3	1
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 0 2 (67%) 0 0 0 1 (33%)	0 0 0 0 0 0 1 (100%)
Median response	3.0	7.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		Non-estimable
Inverse odds ratio 95% CI for inverse odds ratio p-value		Non-estimable Non-estimable Non-estimable

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 753 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Population: Intent-To-Treat

Table 90.57

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: 12-<18 Years Visit: Week 24

SIL. WEEK 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	3	1
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 0 1 (33%) 1 (33%) 0 0 1 (33%)	0 0 0 0 0 0 1 (100%)
Median response	4.0	7.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		Non-estimable
Inverse odds ratio 95% CI for inverse odds ratio p-value		Non-estimable Non-estimable Non-estimable

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 754 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Population: Intent-To-Treat

Table 90.57

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Mass a 1 - - - - - la

Age: 12-<18 Years Visit: Week 28

Placebo (N=54)	Mepolizumab 300mg SC (N=54)
3	1
0 0 1 (33%) 0 1 (33%) 0 1 (33%)	0 0 0 0 0 0 0 1 (100%)
5.0	7.0
	Non-estimable Non-estimable Non-estimable Non-estimable
	(N=54)  3  0 0 1 (33%) 0 1 (33%) 0 1 (33%)

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 755 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Population: Intent-To-Treat

Table 90.57

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: 12-<18 Years Visit: Week 32

SIL. WEEK 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	3	1
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 0 1 (33%) 1 (33%) 0 0 1 (33%)	0 0 0 0 0 0 1 (100%)
Median response	4.0	7.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		Non-estimable
Inverse odds ratio 95% CI for inverse odds ratio p-value		Non-estimable Non-estimable Non-estimable

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 756 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 9 of 24

Population: Intent-To-Treat

Table 90.57

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: 18-64 Years Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	41	49
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (5%) 6 (15%) 7 (17%) 19 (46%) 3 (7%) 1 (2%) 3 (7%)	9 (18%) 8 (16%) 10 (20%) 17 (35%) 1 (2%) 2 (4%) 2 (4%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.032 0.43 (0.20,0.94) 0.034

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 757 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 10 of 24

Population: Intent-To-Treat

Table 90.57

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: 18-64 Years Visit: Week 8

SIC. Week o	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	41	49
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	4 (10%) 5 (12%) 9 (22%) 15 (37%) 2 (5%) 2 (5%) 4 (10%)	12 (24%) 4 (8%) 6 (12%) 17 (35%) 3 (6%) 0 7 (14%)
Median response	4.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.574 0.80 (0.38,1.69) 0.561

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 758 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 11 of 24

Population: Intent-To-Treat

Table 90.57
Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: 18-64 Years Visit: Week 12

sit: week 12	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	41	49
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (12%) 7 (17%) 5 (12%) 12 (29%) 4 (10%) 2 (5%) 6 (15%)	11 (22%) 6 (12%) 10 (20%) 11 (22%) 4 (8%) 0 7 (14%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.210 0.67 (0.32,1.40) 0.282

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 759 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 12 of 24

Population: Intent-To-Treat

Table 90.57
Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: 18-64 Years Visit: Week 16

SIC. WEEK IO	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	41	49
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (12%) 3 (7%) 7 (17%) 13 (32%) 3 (7%) 3 (7%) 7 (17%)	14 (29%) 6 (12%) 10 (20%) 7 (14%) 3 (6%) 0 9 (18%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.031 0.45 (0.21,0.95) 0.037

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 760 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 13 of 24

Population: Intent-To-Treat

Table 90.57

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: 18-64 Years Visit: Week 20

sit: week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	41	49
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (12%) 3 (7%) 5 (12%) 13 (32%) 5 (12%) 1 (2%) 9 (22%)	11 (22%) 9 (18%) 8 (16%) 9 (18%) 2 (4%) 0 10 (20%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.049 0.48 (0.23,1.03) 0.059

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 761 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 14 of 24

Population: Intent-To-Treat

Table 90.57

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: 18-64 Years Visit: Week 24

sit: week 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	41	49
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (7%) 7 (17%) 5 (12%) 11 (27%) 4 (10%) 2 (5%) 9 (22%)	11 (22%) 7 (14%) 8 (16%) 9 (18%) 3 (6%) 0 11 (22%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.099 0.60 (0.29,1.26) 0.178

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 762 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 15 of 24

Population: Intent-To-Treat

Table 90.57
Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: 18-64 Years Visit: Week 28

sit: week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	41	49
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	6 (15%) 3 (7%) 5 (12%) 14 (34%) 3 (7%) 1 (2%) 9 (22%)	14 (29%) 8 (16%) 4 (8%) 8 (16%) 3 (6%) 3 (6%) 9 (18%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.134 0.58 (0.27,1.22) 0.152

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 763 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 16 of 24

Population: Intent-To-Treat

Table 90.57
Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: 18-64 Years Visit: Week 32

sic. week 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	41	49
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (7%) 6 (15%) 9 (22%) 9 (22%) 4 (10%) 0 10 (24%)	16 (33%) 3 (6%) 7 (14%) 6 (12%) 3 (6%) 3 (6%) 11 (22%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.163
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.61 (0.29,1.28) 0.187

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 764 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 17 of 24

Population: Intent-To-Treat

Table 90.57

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: >=65 Years Visit: Week 4

sit: week 4	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	10	4
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 1 (10%) 1 (10%) 5 (50%) 2 (20%) 1 (10%)	1 (25%) 1 (25%) 0 1 (25%) 0 0 0 1 (25%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.709 2.43 (0.06,100.02) 0.640

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 765 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 18 of 24

Population: Intent-To-Treat

Table 90.57

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: >=65 Years Visit: Week 8

SIC. WEEK O	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	10	4
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (10%) 0 1 (10%) 4 (40%) 2 (20%) 1 (10%)	0 2 (50%) 1 (25%) 0 0 1 (25%)
Median response	4.0	2.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.334 0.16 (<0.01,6.51) 0.331

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 766 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 19 of 24

Population: Intent-To-Treat

Table 90.57

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: >=65 Years Visit: Week 12

Tel meen 12	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	10	4
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 0 1 (10%) 5 (50%) 3 (30%) 0 1 (10%)	2 (50%) 0 1 (25%) 0 0 0 1 (25%)
Median response	4.0	2.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.327 0.08 (<0.01,4.18) 0.212

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 767 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 20 of 24

Population: Intent-To-Treat

Table 90.57

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: >=65 Years Visit: Week 16

sit: week io	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	10	4
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 1 (10%) 3 (30%) 2 (20%) 1 (10%) 1 (10%) 2 (20%)	1 (25%) 1 (25%) 1 (25%) 0 0 0 1 (25%)
Median response	4.0	2.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.349 0.45 (0.01,21.31) 0.683

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 768 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 21 of 24

Mara a 1 d mara a la

Population: Intent-To-Treat

Table 90.57
Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: >=65 Years Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	10	4
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 2 (20%) 1 (10%) 3 (30%) 0 1 (10%) 3 (30%)	1 (25%) 1 (25%) 0 0 1 (25%) 0 1 (25%)
Median response	4.0	3.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.681 4.31 (0.09,201.88) 0.456

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 769 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 22 of 24

Population: Intent-To-Treat

Table 90.57
Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: >=65 Years Visit: Week 24

SIC. WEEK 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	10	4
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 4 (40%) 0 2 (20%) 2 (20%) 0 2 (20%)	2 (50%) 0 0 0 1 (25%) 0 1 (25%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.827 1.70 (0.04,66.72) 0.776

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 770 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 23 of 24

Population: Intent-To-Treat

Table 90.57

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: >=65 Years Visit: Week 28

SIC. Week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	10	4
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (20%) 1 (10%) 2 (20%) 3 (30%) 0 0 2 (20%)	2 (50%) 0 1 (25%) 0 0 0 1 (25%)
Median response	3.5	2.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.613 0.48 (0.01,18.79) 0.696

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 771 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 24 of 24

Population: Intent-To-Treat

Table 90.57

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Age

Age: >=65 Years Visit: Week 32

sit: week 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	10	4
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 2 (20%) 1 (10%) 2 (20%) 2 (20%) 0 3 (30%)	2 (50%) 0 0 1 (25%) 0 0 1 (25%)
Median response	4.5	2.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.386 0.70 (0.02,27.31) 0.847

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 772 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 1 of 16

Population: Intent-To-Treat

Table 90.58

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Gender

Gender: Female
Visit: Week 4

sit: week 4	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	30
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 5 (19%) 2 (7%) 12 (44%) 5 (19%) 1 (4%) 0	7 (23%) 5 (17%) 5 (17%) 8 (27%) 0 2 (7%) 3 (10%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio		0.039 0.39 (0.15,1.05)
p-value		0.062

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 773 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 2 of 16

Mana 1 - - - - - la

Population: Intent-To-Treat

Table 90.58
Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Gender

Subgroup Analysis of Clinician-Rated Overall Response to inerapy by Gende

Gender: Female
Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	 27	30
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	4 (15%) 1 (4%) 2 (7%) 11 (41%) 4 (15%) 3 (11%) 2 (7%)	8 (27%) 2 (7%) 2 (7%) 10 (33%) 2 (7%) 0 6 (20%)
Median response	4.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.189 0.52 (0.19,1.40) 0.196

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 774 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 3 of 16

Population: Intent-To-Treat

Table 90.58

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Gender

Gender: Female
Visit: Week 12

sit: week 12	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	30
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 5 (19%) 3 (11%) 11 (41%) 3 (11%) 0 3 (11%)	8 (27%) 3 (10%) 5 (17%) 5 (17%) 2 (7%) 0 7 (23%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.122 0.55 (0.21,1.45) 0.228

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 775 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 4 of 16

Population: Intent-To-Treat

Table 90.58

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Gender

Gender: Female
Visit: Week 16

sit: week 16	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	30
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 1 (4%) 6 (22%) 8 (30%) 4 (15%) 2 (7%) 4 (15%)	7 (23%) 5 (17%) 6 (20%) 2 (7%) 3 (10%) 0 7 (23%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.029 0.35 (0.13,0.94) 0.036

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 776 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 5 of 16

Population: Intent-To-Treat

Table 90.58

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Gender

Gender: Female
Visit: Week 20

SIC. WEEK 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	30
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 1 (4%) 5 (19%) 9 (33%) 4 (15%) 2 (7%) 4 (15%)	5 (17%) 4 (13%) 7 (23%) 5 (17%) 1 (3%) 0 8 (27%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.073 0.44 (0.17,1.16) 0.097

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 777 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 6 of 16

Population: Intent-To-Treat

Table 90.58

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Gender

Gender: Female
Visit: Week 24

SIC. WEEK 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	30
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 5 (19%) 1 (4%) 10 (37%) 4 (15%) 1 (4%) 4 (15%)	6 (20%) 4 (13%) 5 (17%) 4 (13%) 3 (10%) 0 8 (27%)
Median response	4.0	3.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.229 0.67 (0.26,1.73) 0.404

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 778 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 7 of 16

Population: Intent-To-Treat

Table 90.58

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Gender

Gender: Female
Visit: Week 28

SIC: Week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	30
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (19%) 0 3 (11%) 11 (41%) 2 (7%) 1 (4%) 5 (19%)	6 (20%) 6 (20%) 2 (7%) 5 (17%) 2 (7%) 2 (7%) 7 (23%)
Median response	4.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.208 0.53 (0.20,1.43) 0.210

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 779 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 8 of 16

Population: Intent-To-Treat

Table 90.58

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Gender

Gender: Female
Visit: Week 32

Placebo (N=54)	Mepolizumab 300mg SC (N=54)
27	30
2 (7%) 3 (11%) 5 (19%) 7 (26%) 4 (15%) 0 6 (22%)	8 (27%) 2 (7%) 5 (17%) 4 (13%) 2 (7%) 2 (7%) 7 (23%)
4.0	3.5
	0.118 0.44 (0.16,1.16) 0.097
	(N=54)  27  2 (7%) 3 (11%) 5 (19%) 7 (26%) 4 (15%) 0 6 (22%)

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 780 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 9 of 16

Population: Intent-To-Treat

Table 90.58

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Gender

Gender: Male
Visit: Week 4

SIC. WEEK T	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	24
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 3 (11%) 6 (22%) 14 (52%) 0 1 (4%) 3 (11%)	3 (13%) 4 (17%) 5 (21%) 10 (42%) 1 (4%) 0
Median response	4.0	3.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.282 0.49 (0.17,1.43) 0.192

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 781 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 10 of 16

Population: Intent-To-Treat

Table 90.58

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Gender

Gender: Male
Visit: Week 8

sic. week o	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	24
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 5 (19%) 8 (30%) 9 (33%) 0 0 3 (11%)	4 (17%) 4 (17%) 5 (21%) 7 (29%) 1 (4%) 1 (4%) 2 (8%)
Median response	3.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.757 1.08 (0.39,2.96) 0.885

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 782 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 11 of 16

Population: Intent-To-Treat

Table 90.58

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Gender

Gender: Male
Visit: Week 12

SIC. WEEK 12	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	24
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (11%) 4 (15%) 3 (11%) 6 (22%) 4 (15%) 2 (7%) 5 (19%)	5 (21%) 3 (13%) 6 (25%) 6 (25%) 2 (8%) 0
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.368
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.53 (0.19,1.47) 0.224

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 783 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 12 of 16

Population: Intent-To-Treat

Table 90.58

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Gender

Gender: Male
Visit: Week 16

SIC. WEEK IO	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	24
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (11%) 3 (11%) 5 (19%) 7 (26%) 1 (4%) 2 (7%) 6 (22%)	8 (33%) 2 (8%) 5 (21%) 5 (21%) 0 0 4 (17%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio		0.210 0.44 (0.16,1.21)
p-value		0.110

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 784 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 13 of 16

Population: Intent-To-Treat

Table 90.58

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Gender

Gender: Male
Visit: Week 20

SIC. WEEK 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	24
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (11%) 4 (15%) 3 (11%) 7 (26%) 1 (4%) 0 9 (33%)	7 (29%) 6 (25%) 1 (4%) 4 (17%) 2 (8%) 0 4 (17%)
Median response	4.0	2.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.238 0.46 (0.17,1.28) 0.136

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 785 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 14 of 16

Population: Intent-To-Treat

Table 90.58

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Gender

Gender: Male
Visit: Week 24

sit: week 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	24
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (4%) 6 (22%) 5 (19%) 4 (15%) 2 (7%) 1 (4%) 8 (30%)	7 (29%) 3 (13%) 3 (13%) 5 (21%) 1 (4%) 0 5 (21%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.313 0.54 (0.20,1.48) 0.230

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 786 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 15 of 16

Population: Intent-To-Treat

Table 90.58

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Gender

Gender: Male
Visit: Week 28

SIC. WEEK 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	24
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (11%) 4 (15%) 5 (19%) 6 (22%) 2 (7%) 0 7 (26%)	10 (42%) 2 (8%) 3 (13%) 3 (13%) 1 (4%) 1 (4%) 4 (17%)
Median response	4.0	2.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.250
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.45 (0.16,1.26) 0.128

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 787 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 16 of 16

Population: Intent-To-Treat

Table 90.58

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Gender

Gender: Male
Visit: Week 32

sic. week 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	24
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (4%) 5 (19%) 6 (22%) 5 (19%) 2 (7%) 0 8 (30%)	10 (42%) 1 (4%) 2 (8%) 3 (13%) 1 (4%) 1 (4%) 6 (25%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio		0.195 0.49
95% CI for inverse odds ratio p-value		(0.18,1.35) 0.169

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 788 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 1 of 16

Population: Intent-To-Treat

Table 90.59

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Region

Region: Europe Visit: Week 4

sit: week 4	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	33	31
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (3%) 4 (12%) 6 (18%) 17 (52%) 4 (12%) 0 1 (3%)	6 (19%) 5 (16%) 5 (16%) 13 (42%) 1 (3%) 1 (3%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.095 0.42 (0.17,1.07) 0.071

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 789 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 2 of 16

Population: Intent-To-Treat

Table 90.59

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Region

Region: Europe Visit: Week 8

sit: week o	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	33	31
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (15%) 2 (6%) 6 (18%) 14 (42%) 1 (3%) 2 (6%) 3 (9%)	8 (26%) 5 (16%) 4 (13%) 11 (35%) 2 (6%) 0 1 (3%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.167 0.49 (0.20,1.20) 0.117

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 790 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 3 of 16

Population: Intent-To-Treat

Table 90.59

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Region

Region: Europe Visit: Week 12

STO. HOUR IZ	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	33	31
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (15%) 7 (21%) 3 (9%) 9 (27%) 2 (6%) 1 (3%) 6 (18%)	10 (32%) 3 (10%) 7 (23%) 7 (23%) 3 (10%) 0 1 (3%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.139 0.46 (0.19,1.12) 0.087

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 791 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 4 of 16

Population: Intent-To-Treat

Table 90.59

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Region

Region: Europe Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	33	31
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (15%) 2 (6%) 5 (15%) 9 (27%) 4 (12%) 1 (3%) 7 (21%)	11 (35%) 2 (6%) 10 (32%) 5 (16%) 1 (3%) 0 2 (6%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.007 0.25 (0.10,0.63) 0.003

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 792 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 5 of 16

Population: Intent-To-Treat

Table 90.59

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Region

Region: Europe Visit: Week 20

sit: week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	33	31
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	4 (12%) 3 (9%) 3 (9%) 8 (24%) 4 (12%) 2 (6%) 9 (27%)	12 (39%) 5 (16%) 5 (16%) 6 (19%) 2 (6%) 0 1 (3%)
Median response	4.0	2.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		<0.001 0.17 (0.07,0.45) <0.001

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 793 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 6 of 16

Population: Intent-To-Treat

Table 90.59

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Region

Region: Europe Visit: Week 24

SIC: Week 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	33	31
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (9%) 4 (12%) 1 (3%) 10 (30%) 6 (18%) 1 (3%) 8 (24%)	11 (35%) 3 (10%) 6 (19%) 8 (26%) 2 (6%) 0 1 (3%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		<0.001 0.18 (0.07,0.46) <0.001

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 794 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 7 of 16

Population: Intent-To-Treat

Table 90.59

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Region

Region: Europe Visit: Week 28

sit: week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	33	31
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	6 (18%) 1 (3%) 4 (12%) 12 (36%) 1 (3%) 1 (3%) 8 (24%)	12 (39%) 6 (19%) 4 (13%) 6 (19%) 0 2 (6%) 1 (3%)
Median response	4.0	2.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.004 0.24 (0.09,0.60) 0.002

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 795 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 8 of 16

Population: Intent-To-Treat

Table 90.59

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Region

Region: Europe Visit: Week 32

sit: week 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	33	31
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (9%) 4 (12%) 4 (12%) 9 (27%) 4 (12%) 0 9 (27%)	14 (45%) 3 (10%) 4 (13%) 6 (19%) 1 (3%) 1 (3%) 2 (6%)
Median response	4.0	2.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.001 0.20 (0.08,0.52) <0.001

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 796 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 9 of 16

Population: Intent-To-Treat

Table 90.59

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Region

Region: Rest of World

Visit: Week 4

Placebo (N=54)	Mepolizumab 300mg SC (N=54)
21	23
1 (5%) 4 (19%) 2 (10%) 9 (43%) 1 (5%) 2 (10%) 2 (10%)	4 (17%) 4 (17%) 5 (22%) 5 (22%) 0 1 (4%) 4 (17%)
4.0	3.0
	0.151 0.37 (0.12,1.12) 0.078
	(N=54)  21  1 (5%) 4 (19%) 2 (10%) 9 (43%) 1 (5%) 2 (10%) 2 (10%)

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 797 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 10 of 16

Population: Intent-To-Treat

Table 90.59

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Region

Region: Rest of World

Visit: Week 8

sit: week o	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	21	23
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (5%) 4 (19%) 4 (19%) 6 (29%) 3 (14%) 1 (5%) 2 (10%)	4 (17%) 1 (4%) 3 (13%) 6 (26%) 1 (4%) 1 (4%) 7 (30%)
Median response	4.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.633
Inverse odds ratio 95% CI for inverse odds ratio p-value		1.05 (0.36,3.07) 0.928

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 798 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 11 of 16

Population: Intent-To-Treat

Table 90.59

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Region

Region: Rest of World

Visit: Week 12

sit: week 12	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	21	23
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 2 (10%) 3 (14%) 8 (38%) 5 (24%) 1 (5%) 2 (10%)	3 (13%) 3 (13%) 4 (17%) 4 (17%) 1 (4%) 0 8 (35%)
Median response	4.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.458 0.64 (0.22,1.89) 0.422

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 799 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 12 of 16

Population: Intent-To-Treat

Table 90.59

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Region

Region: Rest of World

Visit: Week 16

sit: week 10	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	21	23
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 2 (10%) 6 (29%) 6 (29%) 1 (5%) 3 (14%) 3 (14%)	4 (17%) 5 (22%) 1 (4%) 2 (9%) 2 (9%) 0 9 (39%)
Median response	4.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.580 0.69 (0.23,2.02) 0.497

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 800 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 13 of 16

Population: Intent-To-Treat

Table 90.59

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Region

Region: Rest of World

Visit: Week 20

SIC. WEEK 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	21	23
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (5%) 2 (10%) 5 (24%) 8 (38%) 1 (5%) 0 4 (19%)	0 5 (22%) 3 (13%) 3 (13%) 1 (4%) 0 11 (48%)
Median response	4.0	5.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.459 1.69 (0.57,5.06) 0.345

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 801 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 14 of 16

Population: Intent-To-Treat

Table 90.59

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Region

Region: Rest of World

Visit: Week 24

SIC. WEEK 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	21	23
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 7 (33%) 5 (24%) 4 (19%) 0 1 (5%) 4 (19%)	2 (9%) 4 (17%) 2 (9%) 1 (4%) 2 (9%) 0 12 (52%)
Median response	3.0	7.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.247 2.34 (0.77,7.10) 0.133

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 802 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 15 of 16

Population: Intent-To-Treat

Table 90.59

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Region

Mana a 1 - - - - - la

Region: Rest of World

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	21	23	-
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (10%) 3 (14%) 4 (19%) 5 (24%) 3 (14%) 0 4 (19%)	4 (17%) 2 (9%) 1 (4%) 2 (9%) 3 (13%) 1 (4%) 10 (43%)	
Median response	4.0	5.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.337	
Inverse odds ratio 95% CI for inverse odds ratio p-value		1.89 (0.64,5.60) 0.250	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 803 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 16 of 16

Population: Intent-To-Treat

Table 90.59

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Region

Region: Rest of World

Visit: Week 32

sit: week 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	21	23
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 4 (19%) 7 (33%) 3 (14%) 2 (10%) 0 5 (24%)	4 (17%) 0 3 (13%) 1 (4%) 2 (9%) 2 (9%) 11 (48%)
Median response	3.0	6.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.263 2.09 (0.70,6.30) 0.188

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 804 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 1 of 16

Population: Intent-To-Treat

Table 90.60

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: <2.76 Years

Visit: Week 4

SIL. WEEK 4	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	32	22
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (3%) 5 (16%) 7 (22%) 14 (44%) 2 (6%) 1 (3%) 2 (6%)	5 (23%) 3 (14%) 3 (14%) 7 (32%) 1 (5%) 0 3 (14%)
Median response	4.0	3.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.169 0.56 (0.20,1.52) 0.252

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 805 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 2 of 16

Population: Intent-To-Treat

Table 90.60

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Duration of Disease

Mass a 1 - - - - - la

Duration of disease: <2.76 Years

Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	32	22	
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	6 (19%) 1 (3%) 9 (28%) 7 (22%) 3 (9%) 2 (6%) 4 (13%)	4 (18%) 4 (18%) 2 (9%) 6 (27%) 2 (9%) 1 (5%) 3 (14%)	
Median response	3.5	4.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.760 0.84 (0.31,2.25) 0.730	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 806 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 3 of 16

Population: Intent-To-Treat

Table 90.60

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: <2.76 Years

Visit: Week 12

SIL. WEEK 12	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	32	22
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	4 (13%) 7 (22%) 2 (6%) 9 (28%) 4 (13%) 0 6 (19%)	5 (23%) 3 (14%) 3 (14%) 5 (23%) 3 (14%) 0
Median response	4.0	3.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.354 0.67 (0.25,1.79) 0.421

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 807 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 4 of 16

Population: Intent-To-Treat

Table 90.60

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: <2.76 Years

Visit: Week 16

SIC. WEEK IO	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	32	22
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (16%) 2 (6%) 7 (22%) 5 (16%) 4 (13%) 2 (6%) 7 (22%)	7 (32%) 3 (14%) 4 (18%) 4 (18%) 0 0 4 (18%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.091 0.41 (0.15,1.13) 0.085

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 808 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 5 of 16

Population: Intent-To-Treat

Table 90.60

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: <2.76 Years

Visit: Week 20

SIL: Week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	32	22
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	4 (13%) 3 (9%) 6 (19%) 6 (19%) 2 (6%) 1 (3%) 10 (31%)	6 (27%) 4 (18%) 3 (14%) 4 (18%) 1 (5%) 0 4 (18%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.095
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.42 (0.15,1.16) 0.093

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 809 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 6 of 16

Population: Intent-To-Treat

Table 90.60

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: <2.76 Years

Visit: Week 24

sit: week 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	32	22
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (9%) 10 (31%) 3 (9%) 5 (16%) 4 (13%) 0 7 (22%)	6 (27%) 3 (14%) 2 (9%) 5 (23%) 1 (5%) 0 5 (23%)
Median response	3.5	3.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.321 0.77 (0.28,2.06) 0.595

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 810 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 7 of 16

Population: Intent-To-Treat

Table 90.60

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: <2.76 Years

Visit: Week 28

sit: week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	32	22
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	8 (25%) 3 (9%) 7 (22%) 3 (9%) 3 (9%) 1 (3%) 7 (22%)	7 (32%) 4 (18%) 1 (5%) 5 (23%) 1 (5%) 0 4 (18%)
Median response	3.0	2.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.491 0.77 (0.28,2.07) 0.599

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 811 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 8 of 16

Population: Intent-To-Treat

Table 90.60

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: <2.76 Years

Visit: Week 32

sit: week 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	32	22
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (9%) 7 (22%) 6 (19%) 5 (16%) 3 (9%) 0 8 (25%)	6 (27%) 3 (14%) 3 (14%) 4 (18%) 1 (5%) 0 5 (23%)
Median response	3.5	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.315
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.66 (0.25,1.79) 0.416

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 812 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 9 of 16

Population: Intent-To-Treat

Table 90.60

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: >=2.76 Years

Visit: Week 4

SIL. WEEK 4	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	22	32
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (5%) 3 (14%) 1 (5%) 12 (55%) 3 (14%) 1 (5%) 1 (5%)	5 (16%) 6 (19%) 7 (22%) 11 (34%) 0 2 (6%) 1 (3%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.047
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.32 (0.11,0.91) 0.033

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 813 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 10 of 16

Population: Intent-To-Treat

Table 90.60

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: >=2.76 Years

Visit: Week 8

sit: week o	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	22	32
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 5 (23%) 1 (5%) 13 (59%) 1 (5%) 1 (5%)	8 (25%) 2 (6%) 5 (16%) 11 (34%) 1 (3%) 0 5 (16%)
Median response	4.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio		0.317 0.62
95% CI for inverse odds ratio p-value		(0.23,1.69) 0.349

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 814 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 11 of 16

Population: Intent-To-Treat

Table 90.60

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: >=2.76 Years

Visit: Week 12

sit: week 12	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	22	32
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (5%) 2 (9%) 4 (18%) 8 (36%) 3 (14%) 2 (9%) 2 (9%)	8 (25%) 3 (9%) 8 (25%) 6 (19%) 1 (3%) 0 6 (19%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.200 0.48 (0.18,1.30) 0.152

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 815 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 12 of 16

Population: Intent-To-Treat

Table 90.60

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: >=2.76 Years

Visit: Week 16

sit: week 10	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	22	32
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 2 (9%) 4 (18%) 10 (45%) 1 (5%) 2 (9%) 3 (14%)	8 (25%) 4 (13%) 7 (22%) 3 (9%) 3 (9%) 0 7 (22%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.056 0.41 (0.15,1.10) 0.078

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 816 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 13 of 16

Population: Intent-To-Treat

Table 90.60

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: >=2.76 Years

Visit: Week 20

sit: week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	22	32
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (5%) 2 (9%) 2 (9%) 10 (45%) 3 (14%) 1 (5%) 3 (14%)	6 (19%) 6 (19%) 5 (16%) 5 (16%) 2 (6%) 0 8 (25%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.169 0.53 (0.20,1.41) 0.205

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 817 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 14 of 16

Population: Intent-To-Treat

Table 90.60

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: >=2.76 Years

Visit: Week 24

SIC: Week 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	22	32
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 1 (5%) 3 (14%) 9 (41%) 2 (9%) 2 (9%) 5 (23%)	7 (22%) 4 (13%) 6 (19%) 4 (13%) 3 (9%) 0 8 (25%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.080
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.41 (0.15,1.11) 0.081

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 818 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 15 of 16

Population: Intent-To-Treat

Table 90.60

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: >=2.76 Years

Visit: Week 28

SIL: Week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	22	32
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 1 (5%) 1 (5%) 14 (64%) 1 (5%) 0 5 (23%)	9 (28%) 4 (13%) 4 (13%) 3 (9%) 2 (6%) 3 (9%) 7 (22%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.066 0.38 (0.14,1.04) 0.059

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 819 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 16 of 16

Population: Intent-To-Treat

Table 90.60

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: >=2.76 Years

Visit: Week 32

SIL: Week 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	22	32
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 1 (5%) 5 (23%) 7 (32%) 3 (14%) 0 6 (27%)	12 (38%) 0 4 (13%) 3 (9%) 2 (6%) 3 (9%) 8 (25%)
Median response	4.0	3.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.110 0.44 (0.16,1.19) 0.107

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 820 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 1 of 16

Population: Intent-To-Treat

Table 90.61

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: <1.5 10^9/L

Visit: Week 4

SIL. WEEK 4	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	30	26
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 4 (13%) 3 (10%) 15 (50%) 4 (13%) 2 (7%) 2 (7%)	4 (15%) 2 (8%) 5 (19%) 10 (38%) 1 (4%) 1 (4%) 3 (12%)
Median response	4.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.123 0.41 (0.15,1.12) 0.083

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 821 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 2 of 16

Population: Intent-To-Treat

Table 90.61

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: <1.5 10^9/L

Visit: Week 8

ster neek o	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	30	26
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 3 (10%) 7 (23%) 13 (43%) 2 (7%) 1 (3%) 2 (7%)	3 (12%) 2 (8%) 5 (19%) 9 (35%) 1 (4%) 1 (4%) 5 (19%)
Median response	4.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.829
Inverse odds ratio 95% CI for inverse odds ratio p-value		1.11 (0.43,2.92) 0.826

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 822 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 3 of 16

Population: Intent-To-Treat

Table 90.61

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: <1.5 10^9/L

Visit: Week 12

sit: week iz	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	30	26
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 4 (13%) 5 (17%) 13 (43%) 2 (7%) 2 (7%) 2 (7%)	3 (12%) 2 (8%) 8 (31%) 4 (15%) 4 (15%) 0 5 (19%)
Median response	4.0	3.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.951
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.89 (0.34,2.30) 0.807

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 823 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 4 of 16

Population: Intent-To-Treat

Table 90.61

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: <1.5 10^9/L

Visit: Week 16

SIC. WEEK 10	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	30	26
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (3%) 2 (7%) 7 (23%) 14 (47%) 3 (10%) 1 (3%) 2 (7%)	4 (15%) 3 (12%) 8 (31%) 4 (15%) 1 (4%) 0 6 (23%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.184 0.46 (0.17,1.22) 0.117

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 824 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 5 of 16

Population: Intent-To-Treat

Table 90.61

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: <1.5 10^9/L

Visit: Week 20

SIC. WEEK 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	30	26
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 3 (10%) 4 (13%) 14 (47%) 3 (10%) 1 (3%) 3 (10%)	5 (19%) 2 (8%) 5 (19%) 6 (23%) 2 (8%) 0 6 (23%)
Median response	4.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.615 0.80 (0.31,2.10) 0.656

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 825 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 6 of 16

Population: Intent-To-Treat

Table 90.61

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Mass a 1 - - - - - la

Baseline blood eosinophils: <1.5 10^9/L

Visit: Week 24

Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
30	26	-
1 (3%) 6 (20%) 4 (13%) 10 (33%) 5 (17%) 1 (3%) 3 (10%)	4 (15%) 3 (12%) 5 (19%) 5 (19%) 2 (8%) 0 7 (27%)	
4.0	4.0	
	0.637 0.89 (0.34,2.29) 0.802	
	(N=54)  30  1 (3%) 6 (20%) 4 (13%) 10 (33%) 5 (17%) 1 (3%) 3 (10%)	Placebo (N=54) (N=54)  30 26  1 (3%) 4 (15%) 6 (20%) 3 (12%) 4 (13%) 5 (19%) 10 (33%) 5 (19%) 5 (17%) 2 (8%) 1 (3%) 7 (27%) 4.0  4.0 4.0  0.637  0.89 (0.34,2.29)

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 826 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 7 of 16

Population: Intent-To-Treat

Table 90.61

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: <1.5 10^9/L

Visit: Week 28

sit: week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	30	26
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	4 (13%) 2 (7%) 6 (20%) 12 (40%) 2 (7%) 1 (3%) 3 (10%)	5 (19%) 5 (19%) 2 (8%) 6 (23%) 2 (8%) 0 6 (23%)
Median response	4.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.882
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.91 (0.35,2.38) 0.848

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 827 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 8 of 16

Population: Intent-To-Treat

Table 90.61

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Mass a 1 - - - - - la

Baseline blood eosinophils: <1.5 10^9/L

Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	30	26	
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (3%) 4 (13%) 10 (33%) 8 (27%) 3 (10%) 0 4 (13%)	5 (19%) 2 (8%) 3 (12%) 5 (19%) 2 (8%) 1 (4%) 8 (31%)	
Median response	3.5	4.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio		0.561 1.35 (0.52,3.48)	
p-value		0.537	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 828 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 9 of 16

Population: Intent-To-Treat

Table 90.61

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: >=1.5 10^9/L

Visit: Week 4

sit: week 4	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	24	28
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (8%) 4 (17%) 5 (21%) 11 (46%) 1 (4%) 0 1 (4%)	6 (21%) 7 (25%) 5 (18%) 8 (29%) 0 1 (4%) 1 (4%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio		0.094
95% CI for inverse odds ratio p-value		(0.16,1.25) 0.127

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 829 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 10 of 16

Population: Intent-To-Treat

Table 90.61

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Mass a 1 - - - - - la

Baseline blood eosinophils: >=1.5 10^9/L

Visit: Week 8

Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
24	28	-
4 (17%) 3 (13%) 3 (13%) 7 (29%) 2 (8%) 2 (8%) 3 (13%)	9 (32%) 4 (14%) 2 (7%) 8 (29%) 2 (7%) 0 3 (11%)	
4.0	3.0	
	0.282 0.55 (0.20,1.47)	
	(N=54)  24  4 (17%) 3 (13%) 3 (13%) 7 (29%) 2 (8%) 2 (8%) 3 (13%)	Placebo (N=54) (N=54)  24 28  4 (17%) 9 (32%) 3 (13%) 4 (14%) 3 (13%) 2 (7%) 7 (29%) 8 (29%) 2 (8%) 2 (7%) 2 (8%) 0 3 (13%) 3 (11%)  4.0 3.0  0.282  0.55

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 830 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 11 of 16

Population: Intent-To-Treat

Table 90.61

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: >=1.5 10^9/L

Visit: Week 12

SIC. WEEK 12	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	24	28
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (13%) 5 (21%) 1 (4%) 4 (17%) 5 (21%) 0 6 (25%)	10 (36%) 4 (14%) 3 (11%) 7 (25%) 0 0 4 (14%)
Median response	4.0	2.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.090 0.36 (0.13,1.00) 0.049

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 831 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 12 of 16

Population: Intent-To-Treat

Table 90.61

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: >=1.5 10^9/L

Visit: Week 16

SIC. WEEK 10	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	24	28
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	4 (17%) 2 (8%) 4 (17%) 1 (4%) 2 (8%) 3 (13%) 8 (33%)	11 (39%) 4 (14%) 3 (11%) 3 (11%) 2 (7%) 0 5 (18%)
Median response	5.0	2.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.070 0.34 (0.12,0.93) 0.036

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 832 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 13 of 16

Population: Intent-To-Treat

Table 90.61

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: >=1.5 10^9/L

Visit: Week 20

SIC. Week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	24	28
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (13%) 2 (8%) 4 (17%) 2 (8%) 2 (8%) 1 (4%) 10 (42%)	7 (25%) 8 (29%) 3 (11%) 3 (11%) 1 (4%) 0 6 (21%)
Median response	5.0	2.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.042 0.32 (0.11,0.89) 0.029

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 833 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 14 of 16

Population: Intent-To-Treat

Table 90.61

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Mara a 1 d mara a la

Baseline blood eosinophils: >=1.5 10^9/L

Visit: Week 24

Placebo (N=54)	Mepolizumab 300mg SC (N=54)
24	28
2 (8%) 5 (21%) 2 (8%) 4 (17%) 1 (4%) 1 (4%) 9 (38%)	9 (32%) 4 (14%) 3 (11%) 4 (14%) 2 (7%) 0 6 (21%)
4.0	3.0
	0.088 0.40 (0.15,1.09) 0.073
	(N=54)  24  2 (8%) 5 (21%) 2 (8%) 4 (17%) 1 (4%) 1 (4%) 9 (38%)

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 834 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 15 of 16

Population: Intent-To-Treat

Table 90.61

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: >=1.5 10^9/L

Visit: Week 28

SIC. Week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	24	28
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	4 (17%) 2 (8%) 2 (8%) 5 (21%) 2 (8%) 0 9 (38%)	11 (39%) 3 (11%) 3 (11%) 2 (7%) 1 (4%) 3 (11%) 5 (18%)
Median response	4.0	2.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.061 0.37 (0.13,1.02) 0.054

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 835 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 16 of 16

Population: Intent-To-Treat

Table 90.61

Subgroup Analysis of Clinician-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: >=1.5 10^9/L

Visit: Week 32

sit: week 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	24	28
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (8%) 4 (17%) 1 (4%) 4 (17%) 3 (13%) 0 10 (42%)	13 (46%) 1 (4%) 4 (14%) 2 (7%) 1 (4%) 2 (7%) 5 (18%)
Median response	5.0	2.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.004 0.21 (0.07,0.62) 0.005

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 836 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 1 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: 12-<18 Years Visit: Week 4

SIC. WEEK 4	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	3	1
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 2 (67%) 1 (33%) 0 0	0 0 0 0 0 0 1 (100%)
Median response	2.0	7.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		Non-estimable
Inverse odds ratio 95% CI for inverse odds ratio p-value		Non-estimable Non-estimable Non-estimable

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 837 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 2 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: 12-<18 Years Visit: Week 8

sit: week 8	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	3	1
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (33%) 1 (33%) 1 (33%) 0 0	0 0 0 0 0 0 1 (100%)
Median response	2.0	7.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		Non-estimable Non-estimable Non-estimable Non-estimable

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 838 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 3 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: 12-<18 Years Visit: Week 12

SIL. WEEK 12	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	3	1
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (33%) 1 (33%) 0 0 0 0 1 (33%)	0 0 0 0 0 0 0 1 (100%)
Median response	2.0	7.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		Non-estimable
Inverse odds ratio 95% CI for inverse odds ratio p-value		Non-estimable Non-estimable Non-estimable

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 839 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 4 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: 12-<18 Years Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	3	1
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 1 (33%) 0 1 (33%) 0 0 1 (33%)	0 0 0 0 0 0 1 (100%)
Median response	4.0	7.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		Non-estimable
Inverse odds ratio 95% CI for inverse odds ratio p-value		Non-estimable Non-estimable Non-estimable

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 840 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 5 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: 12-<18 Years Visit: Week 20

SIL. WEEK 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	3	1
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 1 (33%) 1 (33%) 0 0 0 1 (33%)	0 0 0 0 0 0 1 (100%)
Median response	3.0	7.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		Non-estimable
Inverse odds ratio 95% CI for inverse odds ratio p-value		Non-estimable Non-estimable Non-estimable

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 841 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 6 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: 12-<18 Years Visit: Week 24

SIL. WEEK 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	3	1
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 1 (33%) 1 (33%) 0 0 0 1 (33%)	0 0 0 0 0 0 1 (100%)
Median response	3.0	7.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		Non-estimable
Inverse odds ratio 95% CI for inverse odds ratio p-value		Non-estimable Non-estimable Non-estimable

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 842 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 7 of 24

Population: Intent-To-Treat

Table 90.64 Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: 12-<18 Years Visit: Week 28

SIL. WEEK 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	3	1
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 0 1 (33%) 1 (33%) 0 0 1 (33%)	0 0 0 0 0 0 1 (100%)
Median response	4.0	7.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		Non-estimable
Inverse odds ratio 95% CI for inverse odds ratio p-value		Non-estimable Non-estimable Non-estimable

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 843 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 8 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: 12-<18 Years Visit: Week 32

SIC. WEEK 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	3	1
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 1 (33%) 1 (33%) 0 0 0 1 (33%)	0 0 0 0 0 0 0 1 (100%)
Median response	3.0	7.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		Non-estimable
Inverse odds ratio 95% CI for inverse odds ratio p-value		Non-estimable Non-estimable Non-estimable

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 844 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 9 of 24

Population: Intent-To-Treat

Table 90.64 Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: 18-64 Years Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	41	49
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (5%) 6 (15%) 13 (32%) 14 (34%) 0 1 (2%) 5 (12%)	12 (24%) 4 (8%) 9 (18%) 17 (35%) 4 (8%) 1 (2%) 2 (4%)
Median response	3.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.204 0.67 (0.32,1.41) 0.288

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 845 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 10 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: 18-64 Years Visit: Week 8

sit: week o	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	41	49
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (12%) 7 (17%) 6 (15%) 16 (39%) 2 (5%) 1 (2%) 4 (10%)	13 (27%) 6 (12%) 7 (14%) 15 (31%) 1 (2%) 0 7 (14%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.276 0.68 (0.32,1.44) 0.318

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 846 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 11 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: 18-64 Years Visit: Week 12

SIC. WEEK 12	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	41	49
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (12%) 3 (7%) 10 (24%) 13 (32%) 3 (7%) 1 (2%) 6 (15%)	12 (24%) 7 (14%) 7 (14%) 13 (27%) 1 (2%) 1 (2%) 8 (16%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.120 0.62 (0.29,1.30) 0.202

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 847 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 12 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: 18-64 Years Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	41	49
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (12%) 9 (22%) 4 (10%) 15 (37%) 1 (2%) 0 7 (17%)	12 (24%) 4 (8%) 14 (29%) 9 (18%) 2 (4%) 0 8 (16%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.219 0.67 (0.32,1.40) 0.286

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 848 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 13 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: 18-64 Years Visit: Week 20

SIC. WEEK 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	41	49
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	4 (10%) 7 (17%) 9 (22%) 11 (27%) 1 (2%) 2 (5%) 7 (17%)	13 (27%) 4 (8%) 13 (27%) 7 (14%) 2 (4%) 0 10 (20%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.155 0.66 (0.31,1.38) 0.265

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 849 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 14 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: 18-64 Years Visit: Week 24

SIC. WEEK 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	41	49
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	4 (10%) 8 (20%) 5 (12%) 12 (29%) 2 (5%) 2 (5%) 8 (20%)	15 (31%) 5 (10%) 7 (14%) 11 (22%) 1 (2%) 0 10 (20%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.107 0.57 (0.27,1.21) 0.142

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 850 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 15 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: 18-64 Years Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	41	49
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (7%) 7 (17%) 7 (17%) 13 (32%) 1 (2%) 2 (5%) 8 (20%)	12 (24%) 10 (20%) 7 (14%) 8 (16%) 1 (2%) 1 (2%) 10 (20%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.040 0.52 (0.24,1.09) 0.082

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 851 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 16 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: 18-64 Years Visit: Week 32

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	41	49
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	7 (17%) 6 (15%) 4 (10%) 10 (24%) 4 (10%) 1 (2%) 9 (22%)	11 (22%) 9 (18%) 10 (20%) 8 (16%) 1 (2%) 0 10 (20%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.106 0.60 (0.29,1.26) 0.177

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 852 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622
Population: Intent-To-Treat
Page 17 of 24

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: >=65 Years Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	10	4
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 1 (10%) 2 (20%) 4 (40%) 3 (30%) 0	0 1 (25%) 2 (50%) 0 0 1 (25%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.416
Inverse odds ratio 95% CI for inverse odds ratio p-value		1.18 (0.03,48.68) 0.931

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 853 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622
Population: Intent-To-Treat
Page 18 of 24

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: >=65 Years Visit: Week 8

sit: week o	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	10	4
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 1 (10%) 1 (10%) 6 (60%) 1 (10%) 0	0 0 1 (25%) 2 (50%) 0 1 (25%)
Median response	4.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio		0.683 2.99 (0.05,177.50)
p-value		0.599

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 854 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 19 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: >=65 Years Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	10	4
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (10%) 1 (10%) 2 (20%) 3 (30%) 1 (10%) 0 2 (20%)	1 (25%) 0 1 (25%) 0 1 (25%) 0 1 (25%)
Median response	4.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio		0.614 3.05
95% CI for inverse odds ratio p-value		(0.08,112.63) 0.545

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 855 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 20 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: >=65 Years Visit: Week 16

SIC. WEEK IO	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	10	4
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 3 (30%) 2 (20%) 3 (30%) 0 0 2 (20%)	0 1 (25%) 2 (50%) 0 0 0 1 (25%)
Median response	3.5	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.942 0.39 (0.01,15.47) 0.612

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 856 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622
Population: Intent-To-Treat
Page 21 of 24

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: >=65 Years Visit: Week 20

SIC. Week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	10	4
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (10%) 2 (20%) 2 (20%) 3 (30%) 0 0 2 (20%)	0 2 (50%) 0 1 (25%) 0 0 1 (25%)
Median response	3.5	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.940 1.63 (0.04,60.87) 0.790

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 857 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 22 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: >=65 Years Visit: Week 24

SIC. WEEK 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	10	4
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (10%) 2 (20%) 1 (10%) 4 (40%) 0 0 2 (20%)	0 2 (50%) 0 1 (25%) 0 0 1 (25%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.709 2.01 (0.05,79.85) 0.709

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 858 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 23 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: >=65 Years Visit: Week 28

SIC. WEEK 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	10	4
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 1 (10%) 1 (10%) 6 (60%) 0 0 2 (20%)	1 (25%) 1 (25%) 0 1 (25%) 0 0 0 1 (25%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.698 1.87 (0.04,90.11) 0.752

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 859 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 24 of 24

Population: Intent-To-Treat

Table 90.64

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Age

Age: >=65 Years Visit: Week 32

SIL. WEEK 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	10	4
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 0 4 (40%) 3 (30%) 0 0 3 (30%)	1 (25%) 0 2 (50%) 0 0 0 1 (25%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.369 0.67 (0.01,42.15) 0.852

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 860 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 1 of 16

Population: Intent-To-Treat

Table 90.65

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Gender

Gender: Female
Visit: Week 4

SIC. WEER 4	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	30
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (4%) 2 (7%) 7 (26%) 11 (41%) 3 (11%) 1 (4%) 2 (7%)	11 (37%) 2 (7%) 3 (10%) 9 (30%) 2 (7%) 0 3 (10%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.017
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.31 (0.12,0.85) 0.023

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 861 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 2 of 16

Population: Intent-To-Treat

Table 90.65

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Gender

Gender: Female
Visit: Week 8

ste. Heek c	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	30
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (11%) 5 (19%) 3 (11%) 11 (41%) 2 (7%) 1 (4%) 2 (7%)	8 (27%) 1 (3%) 3 (10%) 11 (37%) 0 0 7 (23%)
Median response	4.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.704 0.83 (0.32,2.19) 0.711

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 862 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 3 of 16

Population: Intent-To-Treat

Table 90.65
Subgroup Analysis of Subject-Rated Overall Response to Therapy by Gender

Gender: Female
Visit: Week 12

SIC. WEEK 12	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	30
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (11%) 3 (11%) 3 (11%) 11 (41%) 2 (7%) 1 (4%) 4 (15%)	7 (23%) 2 (7%) 4 (13%) 8 (27%) 1 (3%) 0 8 (27%)
Median response	4.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.354 0.68 (0.26,1.77) 0.425

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 863 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 4 of 16

Population: Intent-To-Treat

Table 90.65

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Gender

Gender: Female
Visit: Week 16

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	30
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (11%) 5 (19%) 3 (11%) 12 (44%) 0 0 4 (15%)	8 (27%) 2 (7%) 7 (23%) 4 (13%) 2 (7%) 0 7 (23%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.205 0.59 (0.22,1.54) 0.279

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 864 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 5 of 16

Population: Intent-To-Treat

Table 90.65

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Gender

Gender: Female
Visit: Week 20

sit: week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	30
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 5 (19%) 3 (11%) 10 (37%) 1 (4%) 2 (7%) 4 (15%)	7 (23%) 3 (10%) 7 (23%) 4 (13%) 1 (3%) 0 8 (27%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.115 0.53 (0.20,1.40) 0.200

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 865 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 6 of 16

Population: Intent-To-Treat

Table 90.65

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Gender

Gender: Female
Visit: Week 24

SIC. WEEK 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	30
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 6 (22%) 3 (11%) 9 (33%) 1 (4%) 2 (7%) 4 (15%)	8 (27%) 3 (10%) 4 (13%) 7 (23%) 0 0 8 (27%)
Median response	4.0	3.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.241 0.62 (0.24,1.62) 0.330

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 866 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 7 of 16

Population: Intent-To-Treat

Table 90.65

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Gender

Gender: Female
Visit: Week 28

30
7 (23%) 6 (20%) 3 (10%) 5 (17%) 1 (3%) 0 8 (27%)
3.0
0.046 0.43 (0.16,1.13) 0.086

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 867 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 8 of 16

Population: Intent-To-Treat

Table 90.65

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Gender

Gender: Female
Visit: Week 32

SIL. WEEK 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	30
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 3 (11%) 4 (15%) 8 (30%) 4 (15%) 1 (4%) 5 (19%)	7 (23%) 3 (10%) 8 (27%) 4 (13%) 1 (3%) 0 7 (23%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio		0.016 0.34
95% CI for inverse odds ratio p-value		(0.13,0.92) 0.034

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 868 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 9 of 16

Population: Intent-To-Treat

Table 90.65

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Gender

Gender: Male
Visit: Week 4

sit: week 4	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	24
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (4%) 7 (26%) 9 (33%) 7 (26%) 0 0 3 (11%)	1 (4%) 3 (13%) 8 (33%) 8 (33%) 2 (8%) 2 (8%)
Median response	3.0	3.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.355 1.67 (0.60,4.66) 0.327

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 869 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 10 of 16

Population: Intent-To-Treat

Table 90.65

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Gender

Mana a 1 - - - - - la

Gender: Male
Visit: Week 8

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	27	24	
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (11%) 4 (15%) 5 (19%) 11 (41%) 1 (4%) 0 3 (11%)	5 (21%) 5 (21%) 5 (21%) 6 (25%) 1 (4%) 1 (4%) 1 (4%)	
Median response	4.0	3.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.302 0.52 (0.19,1.43) 0.204	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 870 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 11 of 16

Population: Intent-To-Treat

Table 90.65

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Gender

Gender: Male
Visit: Week 12

sic. week iz	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	24
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	4 (15%) 2 (7%) 9 (33%) 5 (19%) 2 (7%) 0 5 (19%)	6 (25%) 5 (21%) 4 (17%) 5 (21%) 1 (4%) 1 (4%) 2 (8%)
Median response	3.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio		0.338
95% CI for inverse odds ratio p-value		(0.21,1.61) 0.300

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 871 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 12 of 16

Population: Intent-To-Treat

Table 90.65

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Gender

Gender: Male
Visit: Week 16

sit: week io	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	24
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 8 (30%) 3 (11%) 7 (26%) 1 (4%) 0 6 (22%)	4 (17%) 3 (13%) 9 (38%) 5 (21%) 0 0 3 (13%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.481 0.64 (0.23,1.76) 0.388

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 872 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 13 of 16

Population: Intent-To-Treat

Table 90.65

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Gender

Mass a 1 - - - - - la

Gender: Male
Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	27	24	
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (11%) 5 (19%) 9 (33%) 4 (15%) 0 0 6 (22%)	6 (25%) 3 (13%) 6 (25%) 4 (17%) 1 (4%) 0 4 (17%)	
Median response	3.0	3.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.579 0.79 (0.29,2.16) 0.648	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 873 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 14 of 16

Population: Intent-To-Treat

Table 90.65

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Gender

Mana a 1 - - - - - la

Gender: Male
Visit: Week 24

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	27	24	
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (11%) 5 (19%) 4 (15%) 7 (26%) 1 (4%) 0 7 (26%)	7 (29%) 4 (17%) 3 (13%) 5 (21%) 1 (4%) 0 4 (17%)	
Median response	4.0	3.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio		0.586 0.60 (0.22,1.64) 0.320	
p-value		0.320	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 874 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 15 of 16

Population: Intent-To-Treat

Table 90.65

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Gender

Gender: Male
Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	27	24	
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 4 (15%) 5 (19%) 9 (33%) 0 0 7 (26%)	6 (25%) 5 (21%) 4 (17%) 4 (17%) 0 1 (4%) 4 (17%)	
Median response	4.0	3.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.283	
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.49 (0.18,1.35) 0.167	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 875 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 16 of 16

Population: Intent-To-Treat

Table 90.65

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Gender

Gender: Male
Visit: Week 32

sic. week 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	27	24
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (19%) 4 (15%) 5 (19%) 5 (19%) 0 0 8 (30%)	5 (21%) 6 (25%) 4 (17%) 4 (17%) 0 0 5 (21%)
Median response	3.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio		0.733 0.74 (0.27,2.03)
p-value		0.564

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 876 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 1 of 16

Population: Intent-To-Treat

Table 90.66
Subgroup Analysis of Subject-Rated Overall Response to Therapy by Region

Region: Europe Visit: Week 4

SIC. WEEK 4	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	33	31
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (3%) 4 (12%) 9 (27%) 14 (42%) 1 (3%) 1 (3%) 3 (9%)	7 (23%) 3 (10%) 7 (23%) 10 (32%) 3 (10%) 1 (3%) 0
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.237 0.53 (0.22,1.31) 0.168

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 877 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 2 of 16

Population: Intent-To-Treat

Table 90.66

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Region

Region: Europe Visit: Week 8

sit: week o	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	33	31
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (15%) 3 (9%) 5 (15%) 14 (42%) 2 (6%) 1 (3%) 3 (9%)	9 (29%) 5 (16%) 5 (16%) 10 (32%) 1 (3%) 0 1 (3%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.060 0.39 (0.16,0.96) 0.041

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 878 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 3 of 16

Population: Intent-To-Treat

Table 90.66

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Region

Mass a 1 - - - - - la

Region: Europe Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	33	31	
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	7 (21%) 1 (3%) 5 (15%) 12 (36%) 1 (3%) 1 (3%) 6 (18%)	10 (32%) 4 (13%) 6 (19%) 9 (29%) 1 (3%) 0 1 (3%)	
Median response	4.0	3.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.049 0.37 (0.15,0.91) 0.030	
		· · · · · · · · · · · · · · · · · · ·	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 879 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 4 of 16

Population: Intent-To-Treat

Table 90.66

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Region

Region: Europe Visit: Week 16

SIC. WEEK 10	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	33	31
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (15%) 8 (24%) 2 (6%) 10 (30%) 1 (3%) 0 7 (21%)	8 (26%) 2 (6%) 14 (45%) 6 (19%) 0 0 1 (3%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.076 0.41 (0.17,1.01) 0.052

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 880 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 5 of 16

Population: Intent-To-Treat

Table 90.66
Subgroup Analysis of Subject-Rated Overall Response to Therapy by Region

Region: Europe Visit: Week 20

SIC. Week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	33	31
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (15%) 2 (6%) 7 (21%) 10 (30%) 0 2 (6%) 7 (21%)	10 (32%) 2 (6%) 12 (39%) 5 (16%) 1 (3%) 0 1 (3%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.008 0.26 (0.10,0.66) 0.005

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 881 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 6 of 16

Population: Intent-To-Treat

Table 90.66

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Region

Region: Europe Visit: Week 24

Placebo (N=54)	Mepolizumab 300mg SC (N=54)
33	31
5 (15%) 4 (12%) 4 (12%) 9 (27%) 2 (6%) 1 (3%) 8 (24%)	10 (32%) 6 (19%) 6 (19%) 8 (26%) 0 0 1 (3%)
4.0	2.0
	0.006 0.25 (0.10,0.64) 0.004
	(N=54)  33  5 (15%) 4 (12%) 4 (12%) 9 (27%) 2 (6%) 1 (3%) 8 (24%)

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 882 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 7 of 16

Population: Intent-To-Treat

Table 90.66
Subgroup Analysis of Subject-Rated Overall Response to Therapy by Region

Region: Europe Visit: Week 28

sit: week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	33	31
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (6%) 5 (15%) 4 (12%) 12 (36%) 1 (3%) 1 (3%) 8 (24%)	11 (35%) 6 (19%) 6 (19%) 7 (23%) 0 0 1 (3%)
Median response	4.0	2.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		<0.001 0.16 (0.06,0.43) <0.001

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 883 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 8 of 16

Population: Intent-To-Treat

Table 90.66

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Region

Region: Europe Visit: Week 32

SIC. WEEK 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	33	31
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	6 (18%) 2 (6%) 4 (12%) 9 (27%) 3 (9%) 1 (3%) 8 (24%)	8 (26%) 8 (26%) 8 (26%) 5 (16%) 0 0 2 (6%)
Median response	4.0	2.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.006 0.25 (0.10,0.63) 0.003

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 884 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 9 of 16

Population: Intent-To-Treat

Table 90.66

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Region

Region: Rest of World

Visit: Week 4

SIC. WEEK 4	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	21	23
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (5%) 5 (24%) 7 (33%) 4 (19%) 2 (10%) 0 2 (10%)	5 (22%) 2 (9%) 4 (17%) 7 (30%) 1 (4%) 1 (4%) 3 (13%)
Median response	3.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.794 0.79 (0.27,2.32) 0.670

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 885 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 10 of 16

Population: Intent-To-Treat

Table 90.66

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Region

Region: Rest of World

Visit: Week 8

sit: week o	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	21	23
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (5%) 6 (29%) 3 (14%) 8 (38%) 1 (5%) 0 2 (10%)	4 (17%) 1 (4%) 3 (13%) 7 (30%) 0 1 (4%) 7 (30%)
Median response	4.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.346
Inverse odds ratio 95% CI for inverse odds ratio p-value		1.42 (0.48,4.22) 0.527

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 886 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 11 of 16

Population: Intent-To-Treat

Table 90.66

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Region

Mass a 1 - - - - - la

Region: Rest of World

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	21	23	
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 4 (19%) 7 (33%) 4 (19%) 3 (14%) 0 3 (14%)	3 (13%) 3 (13%) 2 (9%) 4 (17%) 1 (4%) 1 (4%) 9 (39%)	
Median response	3.0	4.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.496 1.27 (0.43,3.72) 0.665	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 887 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 12 of 16

Population: Intent-To-Treat

Table 90.66
Subgroup Analysis of Subject-Rated Overall Response to Therapy by Region

Region: Rest of World

Visit: Week 16

SIC. WEEK 10	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	21	23
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 5 (24%) 4 (19%) 9 (43%) 0 0 3 (14%)	4 (17%) 3 (13%) 2 (9%) 3 (13%) 2 (9%) 0 9 (39%)
Median response	4.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.781 1.23 (0.42,3.61) 0.712

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 888 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 13 of 16

Population: Intent-To-Treat

Table 90.66

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Region

Region: Rest of World

Visit: Week 20

sit: week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	21	23
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 8 (38%) 5 (24%) 4 (19%) 1 (5%) 0 3 (14%)	3 (13%) 4 (17%) 1 (4%) 3 (13%) 1 (4%) 0
Median response	3.0	5.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.299 2.00 (0.67,5.98) 0.217

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 889 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 14 of 16

Population: Intent-To-Treat

Table 90.66

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Region

Region: Rest of World

Visit: Week 24

sit: week 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	21	23
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 7 (33%) 3 (14%) 7 (33%) 0 1 (5%) 3 (14%)	5 (22%) 1 (4%) 1 (4%) 4 (17%) 1 (4%) 0
Median response	4.0	5.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.307 2.00 (0.67,5.98) 0.217

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 890 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 15 of 16

Population: Intent-To-Treat

Table 90.66

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Region

Mass a 1 - - - - - la

Region: Rest of World

Visit: Week 28

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	21	23	
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (5%) 3 (14%) 5 (24%) 8 (38%) 0 1 (5%) 3 (14%)	2 (9%) 5 (22%) 1 (4%) 2 (9%) 1 (4%) 1 (4%) 11 (48%)	
Median response	4.0	6.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.384 1.87 (0.63,5.58) 0.260	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 891 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 16 of 16

Population: Intent-To-Treat

Table 90.66

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Region

Region: Rest of World

Visit: Week 32

sit: week 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	21	23
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (5%) 5 (24%) 5 (24%) 4 (19%) 1 (5%) 0 5 (24%)	4 (17%) 1 (4%) 4 (17%) 3 (13%) 1 (4%) 0 10 (43%)
Median response	3.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.602 1.38 (0.47,4.07) 0.562

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 892 von 1069

<sup>[1]</sup>  $\dot{\text{Wilcoxon}}$  Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 1 of 16

Population: Intent-To-Treat

Table 90.67

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: <2.76 Years

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	32	22
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (6%) 5 (16%) 10 (31%) 8 (25%) 3 (9%) 0 4 (13%)	3 (14%) 2 (9%) 6 (27%) 5 (23%) 3 (14%) 1 (5%) 2 (9%)
Median response	3.0	3.5
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.657
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.94 (0.35,2.51) 0.897

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 893 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 2 of 16

Population: Intent-To-Treat

Table 90.67

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: <2.76 Years

Visit: Week 8

sie. Week e	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	32	22
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	4 (13%) 8 (25%) 6 (19%) 8 (25%) 2 (6%) 0 4 (13%)	5 (23%) 4 (18%) 3 (14%) 5 (23%) 1 (5%) 1 (5%) 3 (14%)
Median response	3.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.615
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.68 (0.25,1.83) 0.448

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 894 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 3 of 16

Population: Intent-To-Treat

Table 90.67

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: <2.76 Years

Visit: Week 12

sit: week 12	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	32	22
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (16%) 4 (13%) 7 (22%) 6 (19%) 2 (6%) 1 (3%) 7 (22%)	5 (23%) 4 (18%) 1 (5%) 6 (27%) 2 (9%) 1 (5%) 3 (14%)
Median response	3.5	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.576
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.69 (0.26,1.86) 0.463

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 895 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 4 of 16

Population: Intent-To-Treat

Table 90.67

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: <2.76 Years

Visit: Week 16

SIL. WEEK 10	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	32	22
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	4 (13%) 9 (28%) 4 (13%) 8 (25%) 0 0 7 (22%)	2 (9%) 5 (23%) 8 (36%) 3 (14%) 1 (5%) 0 3 (14%)
Median response	3.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.564 0.77 (0.29,2.08) 0.610

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 896 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 5 of 16

Population: Intent-To-Treat

Table 90.67

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: <2.76 Years

Visit: Week 20

sit: week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	32	22
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (16%) 6 (19%) 7 (22%) 5 (16%) 0 2 (6%) 7 (22%)	5 (23%) 5 (23%) 5 (23%) 3 (14%) 0 0 4 (18%)
Median response	3.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.189
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.60 (0.22,1.63) 0.318

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 897 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 6 of 16

Population: Intent-To-Treat

Table 90.67

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: <2.76 Years

Visit: Week 24

sit: week 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	32	22
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (16%) 8 (25%) 4 (13%) 7 (22%) 0 1 (3%) 7 (22%)	6 (27%) 3 (14%) 3 (14%) 5 (23%) 1 (5%) 0 4 (18%)
Median response	3.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.658 0.77 (0.29,2.08) 0.610

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 898 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 7 of 16

Population: Intent-To-Treat

Table 90.67

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: <2.76 Years

Visit: Week 28

SIL. WEEK 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	32	22
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (9%) 7 (22%) 4 (13%) 10 (31%) 0 1 (3%) 7 (22%)	5 (23%) 7 (32%) 2 (9%) 3 (14%) 0 1 (5%) 4 (18%)
Median response	4.0	2.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.122 0.46 (0.17,1.26) 0.131

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 899 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 8 of 16

Population: Intent-To-Treat

Table 90.67

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: <2.76 Years

Visit: Week 32

SIC. WEEK 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	32	22
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	7 (22%) 3 (9%) 7 (22%) 6 (19%) 1 (3%) 0 8 (25%)	5 (23%) 5 (23%) 5 (23%) 3 (14%) 0 0 4 (18%)
Median response	3.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.290 0.60 (0.22,1.64) 0.324

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 900 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 9 of 16

Population: Intent-To-Treat

Table 90.67

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: >=2.76 Years

Visit: Week 4

SIL: Week 4	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	22	32	-
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 4 (18%) 6 (27%) 10 (45%) 0 1 (5%) 1 (5%)	9 (28%) 3 (9%) 5 (16%) 12 (38%) 1 (3%) 1 (3%)	
Median response	4.0	3.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.209	
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.49 (0.18,1.34) 0.166	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 901 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 10 of 16

Population: Intent-To-Treat

Table 90.67

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Duration of Disease

Mass a 1 - - - - - la

Duration of disease: >=2.76 Years

Visit: Week 8

Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
22	32	-
2 (9%) 1 (5%) 2 (9%) 14 (64%) 1 (5%) 1 (5%)	8 (25%) 2 (6%) 5 (16%) 12 (38%) 0 0 5 (16%)	
4.0	4.0	
	0.206 0.55 (0.20,1.55) 0.257	
	(N=54)  22  2 (9%) 1 (5%) 2 (9%) 14 (64%) 1 (5%) 1 (5%) 1 (5%)	Placebo (N=54) (N=54)  22 32  2 (9%) 8 (25%) 1 (5%) 2 (6%) 2 (9%) 5 (16%) 14 (64%) 12 (38%) 1 (5%) 0 1 (5%) 0 1 (5%) 5 (16%) 4.0 4.0  0.206  0.55

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 902 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 11 of 16

Population: Intent-To-Treat

Table 90.67

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: >=2.76 Years

Visit: Week 12

SIC. WEEK 12	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	22	32
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (9%) 1 (5%) 5 (23%) 10 (45%) 2 (9%) 0 2 (9%)	8 (25%) 3 (9%) 7 (22%) 7 (22%) 0 0 7 (22%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.267 0.60 (0.22,1.60) 0.308

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 903 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 12 of 16

Population: Intent-To-Treat

Table 90.67

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: >=2.76 Years

Visit: Week 16

SIC. WEEK IO	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	22	32
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (5%) 4 (18%) 2 (9%) 11 (50%) 1 (5%) 0 3 (14%)	10 (31%) 0 8 (25%) 6 (19%) 1 (3%) 0 7 (22%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.361 0.57 (0.21,1.52) 0.259

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 904 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 13 of 16

Population: Intent-To-Treat

Table 90.67

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: >=2.76 Years

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	22	32	
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 4 (18%) 5 (23%) 9 (41%) 1 (5%) 0 3 (14%)	8 (25%) 1 (3%) 8 (25%) 5 (16%) 2 (6%) 0 8 (25%)	
Median response	4.0	3.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.442	
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.75 (0.28,1.99) 0.565	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 905 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 14 of 16

Population: Intent-To-Treat

Table 90.67

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: >=2.76 Years

Visit: Week 24

SIL. WEEK 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	22	32
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 3 (14%) 3 (14%) 9 (41%) 2 (9%) 1 (5%) 4 (18%)	9 (28%) 4 (13%) 4 (13%) 7 (22%) 0 0 8 (25%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.111 0.44 (0.16,1.18) 0.102

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 906 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 15 of 16

Population: Intent-To-Treat

Table 90.67

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: >=2.76 Years

Visit: Week 28

SIC. Week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	22	32
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 1 (5%) 5 (23%) 10 (45%) 1 (5%) 1 (5%) 4 (18%)	8 (25%) 4 (13%) 5 (16%) 6 (19%) 1 (3%) 0 8 (25%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.084 0.45 (0.17,1.21) 0.115

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 907 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 16 of 16

Population: Intent-To-Treat

Table 90.67

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Duration of Disease

Duration of disease: >=2.76 Years

Visit: Week 32

sit: week 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	22	32
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 4 (18%) 2 (9%) 7 (32%) 3 (14%) 1 (5%) 5 (23%)	7 (22%) 4 (13%) 7 (22%) 5 (16%) 1 (3%) 0 8 (25%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.058
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.44 (0.16,1.18) 0.102

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 908 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 1 of 16

Population: Intent-To-Treat

Table 90.68

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Mana a 1 - - - - - la

Baseline blood eosinophils: <1.5 10^9/L

Visit: Week 4

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	30	26	
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	0 3 (10%) 11 (37%) 10 (33%) 2 (7%) 1 (3%) 3 (10%)	5 (19%) 1 (4%) 4 (15%) 11 (42%) 1 (4%) 2 (8%) 2 (8%)	
Median response	4.0	4.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.532	
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.69 (0.26,1.80) 0.445	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 909 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 2 of 16

Population: Intent-To-Treat

Table 90.68

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: <1.5 10^9/L

Visit: Week 8

SIC. Week o	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	30	26
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 6 (20%) 6 (20%) 12 (40%) 1 (3%) 1 (3%) 2 (7%)	4 (15%) 5 (19%) 2 (8%) 9 (35%) 0 1 (4%) 5 (19%)
Median response	4.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.913
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.89 (0.34,2.32) 0.813

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 910 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 3 of 16

Population: Intent-To-Treat

Table 90.68

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Mana a 1 - - - - - la

Baseline blood eosinophils: <1.5 10^9/L

Visit: Week 12

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	30	26	
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (10%) 4 (13%) 9 (30%) 10 (33%) 1 (3%) 1 (3%) 2 (7%)	4 (15%) 4 (15%) 3 (12%) 7 (27%) 1 (4%) 1 (4%) 6 (23%)	
Median response	3.0	4.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.573	
Inverse odds ratio 95% CI for inverse odds ratio p-value		1.27 (0.49,3.30) 0.620	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 911 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 4 of 16

Population: Intent-To-Treat

Table 90.68

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: <1.5 10^9/L

Visit: Week 16

STOP MOOK TO	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	30	26
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (3%) 10 (33%) 5 (17%) 11 (37%) 1 (3%) 0 2 (7%)	4 (15%) 3 (12%) 7 (27%) 5 (19%) 2 (8%) 0 5 (19%)
Median response	3.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.788
Inverse odds ratio 95% CI for inverse odds ratio p-value		1.10 (0.42,2.85) 0.849

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 912 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 5 of 16

Population: Intent-To-Treat

Table 90.68

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Mass a 1 - - - - - la

Baseline blood eosinophils: <1.5 10^9/L

Visit: Week 20

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	30	26	
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 8 (27%) 5 (17%) 12 (40%) 0 1 (3%) 2 (7%)	6 (23%) 2 (8%) 6 (23%) 6 (23%) 0 0 6 (23%)	
Median response	3.5	3.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.838 0.98 (0.38,2.55) 0.968	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 913 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 6 of 16

Population: Intent-To-Treat

Table 90.68

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: <1.5 10^9/L

Visit: Week 24

sit: week 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	30	26
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 9 (30%) 5 (17%) 10 (33%) 1 (3%) 1 (3%) 2 (7%)	7 (27%) 3 (12%) 2 (8%) 7 (27%) 0 0 7 (27%)
Median response	3.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio		0.939
95% CI for inverse odds ratio p-value		(0.39,2.60) 0.997

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 914 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 7 of 16

Population: Intent-To-Treat

Table 90.68

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: <1.5 10^9/L

Visit: Week 28

SIC. Week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	30	26
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 4 (13%) 9 (30%) 12 (40%) 0 1 (3%) 2 (7%)	5 (19%) 4 (15%) 3 (12%) 6 (23%) 0 1 (4%) 7 (27%)
Median response	3.5	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.986 1.12 (0.43,2.89) 0.822

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 915 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 8 of 16

Population: Intent-To-Treat

Table 90.68

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: <1.5 10^9/L

Visit: Week 32

ster meek 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	30	26
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (7%) 7 (23%) 7 (23%) 8 (27%) 3 (10%) 0	3 (12%) 5 (19%) 6 (23%) 5 (19%) 0 0 7 (27%)
Median response	3.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.910
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.97 (0.38,2.50) 0.946

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 916 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 9 of 16

Population: Intent-To-Treat

Table 90.68

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: >=1.5 10^9/L

Visit: Week 4

sit: week 4	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	24	28
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	2 (8%) 6 (25%) 5 (21%) 8 (33%) 1 (4%) 0 2 (8%)	7 (25%) 4 (14%) 7 (25%) 6 (21%) 3 (11%) 0 1 (4%)
Median response	3.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.341
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.67 (0.25,1.78) 0.420

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 917 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 10 of 16

Population: Intent-To-Treat

Table 90.68

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: >=1.5 10^9/L

Visit: Week 8

SIC. Week o	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	24	28
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	4 (17%) 3 (13%) 2 (8%) 10 (42%) 2 (8%) 0 3 (13%)	9 (32%) 1 (4%) 6 (21%) 8 (29%) 1 (4%) 0 3 (11%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.304 0.56 (0.21,1.52) 0.254

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 918 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 11 of 16

Population: Intent-To-Treat

Table 90.68

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: >=1.5 10^9/L

Visit: Week 12

SIC. WEEK 12	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	24	28
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	4 (17%) 1 (4%) 3 (13%) 6 (25%) 3 (13%) 0 7 (29%)	9 (32%) 3 (11%) 5 (18%) 6 (21%) 1 (4%) 0 4 (14%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.066 0.36 (0.13,0.99) 0.048

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 919 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 12 of 16

Population: Intent-To-Treat

Table 90.68

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: >=1.5 10^9/L

Visit: Week 16

SIC. WEEK 10	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	24	28
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	4 (17%) 3 (13%) 1 (4%) 8 (33%) 0 0	8 (29%) 2 (7%) 9 (32%) 4 (14%) 0 0 5 (18%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.135 0.39 (0.14,1.06) 0.066

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 920 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 13 of 16

Population: Intent-To-Treat

Table 90.68

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: >=1.5 10^9/L

Visit: Week 20

sit: week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	24	28
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (13%) 2 (8%) 7 (29%) 2 (8%) 1 (4%) 1 (4%) 8 (33%)	7 (25%) 4 (14%) 7 (25%) 2 (7%) 2 (7%) 0 6 (21%)
Median response	3.5	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.111
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.46 (0.17,1.24) 0.126

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 921 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 14 of 16

Population: Intent-To-Treat

Table 90.68

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: >=1.5 10^9/L

Visit: Week 24

SIL. WEEK 24	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	24	28
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	3 (13%) 2 (8%) 2 (8%) 6 (25%) 1 (4%) 1 (4%) 9 (38%)	8 (29%) 4 (14%) 5 (18%) 5 (18%) 1 (4%) 0 5 (18%)
Median response	4.0	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.062 0.33 (0.12,0.91) 0.032

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 922 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 15 of 16

Population: Intent-To-Treat

Table 90.68

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: >=1.5 10^9/L

Visit: Week 28

sit: week 20	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	24	28
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	1 (4%) 4 (17%) 0 8 (33%) 1 (4%) 1 (4%) 9 (38%)	8 (29%) 7 (25%) 4 (14%) 3 (11%) 1 (4%) 0 5 (18%)
Median response	4.0	2.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.004 0.22 (0.08,0.63) 0.005

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 923 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 16 of 16

Population: Intent-To-Treat

Table 90.68

Subgroup Analysis of Subject-Rated Overall Response to Therapy by Baseline Blood Eosinophils

Baseline blood eosinophils: >=1.5 10^9/L

Visit: Week 32

sit: week 32	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	24	28
Significantly improved (1) Moderately improved (2) Mildly improved (3) No change (4) Mildly worse (5) Moderately worse (6) Significantly worse (7)	5 (21%) 0 2 (8%) 5 (21%) 1 (4%) 1 (4%) 10 (42%)	9 (32%) 4 (14%) 6 (21%) 3 (11%) 1 (4%) 0 5 (18%)
Median response	4.5	3.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.021
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.28 (0.10,0.80) 0.017

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 924 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Table 90.70

Subgroup Analysis of Subject-Rated Symptom Severity at Week 32 by Age

Age: 12-<18 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	3	1
4 point improvement (-4) 3 point improvement (-3) 2 point improvement (-2) 1 point improvement (-1) No change (0) 1 point worsening (1) 2 point worsening (2) 3 point worsening (3) 4 point worsening (4)	0 0 1 (33%) 0 1 (33%) 0 0 0	0 0 0 0 0 0 0 0 0 1 (100%)
Median response	0.0	4.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		Non-estimable Non-estimable Non-estimable Non-estimable

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 925 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Table 90.70

Subgroup Analysis of Subject-Rated Symptom Severity at Week 32 by Age

Age: 18-64 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	41	49	_
<pre>4 point improvement (-4) 3 point improvement (-3) 2 point improvement (-2) 1 point improvement (-1) No change (0) 1 point worsening (1) 2 point worsening (2) 3 point worsening (3) 4 point worsening (4)</pre>	0 1 (2%) 3 (7%) 13 (32%) 9 (22%) 4 (10%) 2 (5%) 0 9 (22%)	0 7 (14%) 1 (2%) 13 (27%) 8 (16%) 9 (18%) 1 (2%) 0 10 (20%)	
Median response	0.0	0.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.667 0.86 (0.41,1.80) 0.683	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 926 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 3 of 3

Population: Intent-To-Treat

Table 90.70

Subgroup Analysis of Subject-Rated Symptom Severity at Week 32 by Age

M - - - 1 - - - - 1-

Age: >=65 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	10	4
4 point improvement (-4) 3 point improvement (-3) 2 point improvement (-2) 1 point improvement (-1) No change (0) 1 point worsening (1) 2 point worsening (2) 3 point worsening (3) 4 point worsening (4)	0 0 1 (10%) 3 (30%) 3 (30%) 0 0 0 3 (30%)	0 0 1 (25%) 2 (50%) 0 0 1 (25%)
Median response	0.0	0.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.850 0.33 (0.01,15.08) 0.568

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 927 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo. PPD

Table 90.71

Subgroup Analysis of Subject-Rated Symptom Severity at Week 32 by Gender

Gender: Female

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	27	30	
4 point improvement (-4) 3 point improvement (-3) 2 point improvement (-2) 1 point improvement (-1) No change (0) 1 point worsening (1) 2 point worsening (2) 3 point worsening (3) 4 point worsening (4)	0 1 (4%) 3 (11%) 7 (26%) 6 (22%) 4 (15%) 1 (4%) 0 5 (19%)	0 5 (17%) 0 5 (17%) 8 (27%) 4 (13%) 1 (3%) 0 7 (23%)	
Median response	0.0	0.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.828 0.90 (0.35,2.34) 0.833	
<del>-</del>			

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 928 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo. PPD

Table 90.71

Subgroup Analysis of Subject-Rated Symptom Severity at Week 32 by Gender

Gender: Male

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	27	24	
4 point improvement (-4) 3 point improvement (-3) 2 point improvement (-2) 1 point improvement (-1) No change (0) 1 point worsening (1) 2 point worsening (2) 3 point worsening (3) 4 point worsening (4)	0 0 2 (7%) 9 (33%) 7 (26%) 0 1 (4%) 0 8 (30%)	0 2 (8%) 1 (4%) 9 (38%) 2 (8%) 5 (21%) 0 0 5 (21%)	
Median response	0.0	-0.5	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.464 0.77 (0.28,2.12) 0.608	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 929 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo. PPD

Table 90.72 Subgroup Analysis of Subject-Rated Symptom Severity at Week 32 by Region

Region: Europe

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	33	31	
4 point improvement (-4) 3 point improvement (-3) 2 point improvement (-2) 1 point improvement (-1) No change (0) 1 point worsening (1) 2 point worsening (2) 3 point worsening (3) 4 point worsening (4)	0 1 (3%) 3 (9%) 8 (24%) 8 (24%) 3 (9%) 2 (6%) 0 8 (24%)	0 6 (19%) 1 (3%) 11 (35%) 5 (16%) 6 (19%) 0 0 2 (6%)	
Median response	0.0	-1.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.031 0.36 (0.15,0.90) 0.028	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 930 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Table 90.72

Subgroup Analysis of Subject-Rated Symptom Severity at Week 32 by Region

Region: Rest of World

Placebo (N=54)	Mepolizumab 300mg SC (N=54)
21	23
0 0 2 (10%) 8 (38%) 5 (24%) 1 (5%) 0 0 5 (24%)	0 1 (4%) 0 3 (13%) 5 (22%) 3 (13%) 1 (4%) 0
0.0	1.0
	0.050 3.17 (1.02,9.82) 0.045
	(N=54)  21  0 0 2 (10%) 8 (38%) 5 (24%) 1 (5%) 0 0 5 (24%)

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 931 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 1 of 2

Population: Intent-To-Treat

Table 90.73

Subgroup Analysis of Subject-Rated Symptom Severity at Week 32 by Duration of Disease

Duration of disease: <2.76 Years

Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
32	22	
0 1 (3%) 3 (9%) 10 (31%) 8 (25%) 2 (6%) 0 0	0 3 (14%) 0 5 (23%) 5 (23%) 5 (23%) 0 0 4 (18%)	
0.0	0.0	
	0.938 1.01 (0.38,2.74)	
	(N=54)  32  0 1 (3%) 3 (9%) 10 (31%) 8 (25%) 2 (6%) 0 0 8 (25%)	Placebo (N=54) (N=54)  32 22  0 0 0 1 (3%) 3 (14%) 3 (9%) 0 10 (31%) 5 (23%) 8 (25%) 5 (23%) 2 (6%) 5 (23%) 0 0 0 0 0 0 0 0 8 (25%) 4 (18%)  0.0 0.0 0.0  0.938  1.01

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 932 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 2 of 2

Population: Intent-To-Treat

Table 90.73

Subgroup Analysis of Subject-Rated Symptom Severity at Week 32 by Duration of Disease

Duration of disease: >=2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	22	32	
4 point improvement (-4) 3 point improvement (-3) 2 point improvement (-2) 1 point improvement (-1) No change (0) 1 point worsening (1) 2 point worsening (2) 3 point worsening (3) 4 point worsening (4)	0 0 2 (9%) 6 (27%) 5 (23%) 2 (9%) 2 (9%) 0 5 (23%)	0 4 (13%) 1 (3%) 9 (28%) 5 (16%) 4 (13%) 1 (3%) 0 8 (25%)	
Median response	0.0	0.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.664	
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.76 (0.29,2.02) 0.589	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 933 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 1 of 2

Population: Intent-To-Treat

Table 90.74

Subgroup Analysis of Subject-Rated Symptom Severity at Week 32 by Baseline Blood Eosinophils

Baseline blood eosinophils: <1.5 10^9/L

Serine brook cosmophine. (1.5 10 3/1	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n	30	26
4 point improvement (-4) 3 point improvement (-3) 2 point improvement (-2) 1 point improvement (-1) No change (0) 1 point worsening (1) 2 point worsening (2) 3 point worsening (3) 4 point worsening (4)	0 0 5 (17%) 9 (30%) 9 (30%) 3 (10%) 1 (3%) 0 3 (10%)	0 3 (12%) 1 (4%) 6 (23%) 4 (15%) 4 (15%) 1 (4%) 0 7 (27%)
Median response	0.0	0.0
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2] Inverse odds ratio 95% CI for inverse odds ratio p-value		0.331 1.67 (0.64,4.35) 0.291

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 934 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo. PPD

Protocol: 200622 Page 2 of 2

Population: Intent-To-Treat

Table 90.74

Subgroup Analysis of Subject-Rated Symptom Severity at Week 32 by Baseline Blood Eosinophils

Baseline blood eosinophils: >=1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
n	24	28	
4 point improvement (-4) 3 point improvement (-3) 2 point improvement (-2) 1 point improvement (-1) No change (0) 1 point worsening (1) 2 point worsening (2) 3 point worsening (3) 4 point worsening (4)	0 1 (4%) 0 7 (29%) 4 (17%) 1 (4%) 1 (4%) 0	0 4 (14%) 0 8 (29%) 6 (21%) 5 (18%) 0 0	
Median response	0.5	0.0	
Comparison Mepolizumab 300mg vs Placebo Wilcoxon Rank Sum Test p-value [1] Logistic regression [2]		0.107	
Inverse odds ratio 95% CI for inverse odds ratio p-value		0.41 (0.15,1.13) 0.084	

Note: Subjects with missing response at Week 32 are included with the largest (i.e., worst) change observed for any subject.

Mepolizumab (Nucala) - HES Seite 935 von 1069

<sup>[1]</sup> Wilcoxon Rank Sum test stratified by baseline OCS (0-<=20mg/day and >20mg/day) prednisone or equivalent and region.

<sup>[2]</sup> Ordinal logistic regression analysis adjusted for baseline OCS and region. Inverse odds ratio <1 indicates higher odds of a lower score (more favourable response) with Mepolizumab compared with Placebo.

Protocol: 200622 Page 1 of 3

Population: Intent-to-Treat

Table 90.77

Subgroup Analysis of Change from Baseline in MSAS-SF Total Score at Week 32 by Age (Mixed Model Repeated Measures)

Age (years): 12-<18 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	3	1
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	3 2 Non-estimable Non-estimable	0 0 Non-estimable Non-estimable

[1] Number of subjects with analysable data for one or more time points.

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 936 von 1069

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.77

Subgroup Analysis of Change from Baseline in MSAS-SF Total Score at Week 32 by Age (Mixed Model Repeated Measures)

Menolizumah

Age (years): 18-64 Years

	Placebo (N=54)	300mg SC (N=54)
Number of subjects in subgroup	41	49
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	39 32 0.84 (0.077) -0.13 (0.077)	47 39 0.58 (0.070) -0.39 (0.070)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.25 (-0.46, -0.05) 0.017
Corrected Hedges g [3] 95% CI		-0.58 (-1.05, -0.10)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 937 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.77

Subgroup Analysis of Change from Baseline in MSAS-SF Total Score at Week 32 by Age (Mixed Model Repeated Measures)

Age (years): >=65 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	10	4
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	10 7 0.55 (0.159) -0.42 (0.159)	4 3 1.17 (0.279) 0.20 (0.279)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.62 (-0.14, 1.39) 0.103
Corrected Hedges g [3] 95% CI		1.29 (-0.18, 2.76)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 938 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.78 Subgroup Analysis of Change from Baseline in MSAS-SF Total Score at Week 32 by Gender (Mixed Model Repeated Measures)

Gender: Female

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	27	30
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	27 22 0.95 (0.101) -0.16 (0.101)	27 23 0.79 (0.101) -0.31 (0.101)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.15 (-0.44, 0.14) 0.297
Corrected Hedges g [3] 95% CI		-0.31 (-0.90, 0.28)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 939 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.78 Subgroup Analysis of Change from Baseline in MSAS-SF Total Score at Week 32 by Gender (Mixed Model Repeated Measures)

Gender: Male

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	27	24
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	25 19 0.56 (0.096) -0.27 (0.096)	24 19 0.54 (0.097) -0.30 (0.097)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.02 (-0.31, 0.26) 0.870
Corrected Hedges g [3] 95% CI		-0.05 (-0.69, 0.58)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 940 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.79 Subgroup Analysis of Change from Baseline in MSAS-SF Total Score at Week 32 by Region (Mixed Model Repeated Measures)

Region: Europe

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	33	31
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	32 25 0.90 (0.092) -0.09 (0.092)	31 29 0.60 (0.089) -0.39 (0.089)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.30 (-0.56, -0.04) 0.024
Corrected Hedges g [3] 95% CI		-0.62 (-1.17, -0.08)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 941 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.79 Subgroup Analysis of Change from Baseline in MSAS-SF Total Score at Week 32 by Region (Mixed Model Repeated Measures)

Manalizumah

Region: Rest of World

	Placebo (N=54)	300mg SC (N=54)	
Number of subjects in subgroup	21	23	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	20 16 0.67 (0.107) -0.30 (0.107)	20 13 0.72 (0.116) -0.25 (0.116)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.05 (-0.27, 0.37) 0.750	
Corrected Hedges g [3] 95% CI		0.12 (-0.62, 0.85)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 942 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.80

Subgroup Analysis of Change from Baseline in MSAS-SF Total Score at Week 32 by Duration of Disease (Mixed Model Repeated Measures)

Menolizumah

Duration of disease: <2.76 Years

	Placebo (N=54)	300mg SC (N=54)
Number of subjects in subgroup	32	22
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	31 24 0.71 (0.080) -0.19 (0.080)	20 18 0.60 (0.096) -0.29 (0.096)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.11 (-0.36, 0.15) 0.403
Corrected Hedges g [3] 95% CI		-0.26 (-0.87, 0.35)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 943 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.80

Subgroup Analysis of Change from Baseline in MSAS-SF Total Score at Week 32 by Duration of Disease (Mixed Model Repeated Measures)

Duration of disease: >=2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	22	32
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	21 17 0.94 (0.125) -0.12 (0.125)	31 24 0.68 (0.106) -0.38 (0.106)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.26 (-0.59, 0.08) 0.128
Corrected Hedges g [3] 95% CI		-0.48 (-1.11, 0.15)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 944 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.81
Subgroup Analysis of Change from Baseline in MSAS-SF Total Score at Week 32
by Baseline Blood Eosinophils
(Mixed Model Repeated Measures)

Baseline blood eosinophils: <1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	30	26	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	29 27 0.79 (0.093) -0.17 (0.093)	24 19 0.69 (0.108) -0.27 (0.108)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.10 (-0.39, 0.19) 0.490	
Corrected Hedges g [3] 95% CI		-0.20 (-0.79, 0.38)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or

bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 945 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.81

Subgroup Analysis of Change from Baseline in MSAS-SF Total Score at Week 32 by Baseline Blood Eosinophils

(Mixed Model Repeated Measures)

Baseline blood eosinophils: >=1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	24	28	-
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	23 14 0.75 (0.101) -0.24 (0.101)	27 23 0.63 (0.085) -0.36 (0.085)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.12 (-0.39, 0.15) 0.385	
Corrected Hedges g [3] 95% CI		-0.29 (-0.95, 0.38)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 0 = Not at all distressed or bothered/No symptoms to 4 = Very much distressed or bothered/Almost constant symptoms.

Mepolizumab (Nucala) - HES Seite 946 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.85

Subgroup Analysis of Change from Baseline in PROMIS Physical Function Score at Week 32 by Age (Mixed Model Repeated Measures)

Age (years): 12-<18 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	3	1
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	3 2 Non-estimable Non-estimable	0 0 Non-estimable Non-estimable

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

Mepolizumab (Nucala) - HES Seite 947 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.85

Subgroup Analysis of Change from Baseline in PROMIS Physical Function Score at Week 32 by Age (Mixed Model Repeated Measures)

Age (years): 18-64 Years

. 10 01 10010	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	41	49
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	38 32 3.93 (0.111) 0.35 (0.111)	47 39 4.10 (0.100) 0.52 (0.100)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.17 (-0.13, 0.47) 0.263
Corrected Hedges g [3] 95% CI		0.27 (-0.20, 0.74)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

Mepolizumab (Nucala) - HES Seite 948 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.85

Subgroup Analysis of Change from Baseline in PROMIS Physical Function Score at Week 32 by Age (Mixed Model Repeated Measures)

Mana a 1 d ------ a la

Age (years): >=65 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	10	4
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	10 7 3.34 (0.358) 0.27 (0.358)	4 3 2.70 (0.688) -0.37 (0.688)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.64 (-2.61, 1.33) 0.495
Corrected Hedges g [3] 95% CI		-0.57 (-1.95, 0.80)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

Mepolizumab (Nucala) - HES Seite 949 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.86

Subgroup Analysis of Change from Baseline in PROMIS Physical Function Score at Week 32 by Gender (Mixed Model Repeated Measures)

Gender: Female

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	27	30
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	27 22 3.51 (0.166) 0.26 (0.166)	27 23 3.87 (0.166) 0.63 (0.166)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.36 (-0.11, 0.84) 0.128
Corrected Hedges g [3] 95% CI		0.46 (-0.14, 1.05)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

Mepolizumab (Nucala) - HES Seite 950 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.86

Subgroup Analysis of Change from Baseline in PROMIS Physical Function Score at Week 32 by Gender (Mixed Model Repeated Measures)

Gender: Male

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	27	24
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	24 19 4.27 (0.117) 0.42 (0.117)	24 19 4.15 (0.117) 0.30 (0.117)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.12 (-0.46, 0.22) 0.496
Corrected Hedges g [3] 95% CI		-0.22 (-0.86, 0.42)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

Mepolizumab (Nucala) - HES Seite 951 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.87

Subgroup Analysis of Change from Baseline in PROMIS Physical Function Score at Week 32 by Region (Mixed Model Repeated Measures)

Mana all i muna ala

Region: Europe

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	33	31	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	32 25 3.81 (0.131) 0.21 (0.131)	31 29 4.19 (0.128) 0.59 (0.128)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.38 (0.02, 0.75) 0.040	
Corrected Hedges g [3] 95% CI		0.56 (0.02, 1.11)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

Mepolizumab (Nucala) - HES Seite 952 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.87

Subgroup Analysis of Change from Baseline in PROMIS Physical Function Score at Week 32 by Region (Mixed Model Repeated Measures)

Region: Rest of World

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	21	23
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	19 16 3.93 (0.128) 0.52 (0.128)	20 13 3.77 (0.135) 0.35 (0.135)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.17 (-0.55, 0.22) 0.380
Corrected Hedges g [3] 95% CI		-0.33 (-1.06, 0.41)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

Mepolizumab (Nucala) - HES Seite 953 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.88

Subgroup Analysis of Change from Baseline in PROMIS Physical Function Score at Week 32

by Duration of Disease (Mixed Model Repeated Measures)

Duration of disease: <2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	32	22	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	30 24 3.97 (0.128) 0.41 (0.128)	20 18 3.95 (0.151) 0.39 (0.151)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.02 (-0.42, 0.39) 0.936	
Corrected Hedges g [3] 95% CI		-0.03 (-0.64, 0.59)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

Mepolizumab (Nucala) - HES Seite 954 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.88

Subgroup Analysis of Change from Baseline in PROMIS Physical Function Score at Week 32

by Duration of Disease (Mixed Model Repeated Measures)

Duration of disease: >=2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	22	32	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	21 17 3.71 (0.171) 0.21 (0.171)	31 24 4.05 (0.142) 0.56 (0.142)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.35 (-0.11, 0.80) 0.130	
Corrected Hedges g [3] 95% CI		0.48 (-0.15, 1.11)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

Mepolizumab (Nucala) - HES Seite 955 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.89

Subgroup Analysis of Change from Baseline in PROMIS Physical Function Score at Week 32

by Baseline Blood Eosinophils (Mixed Model Repeated Measures)

Baseline blood eosinophils: <1.5 10^9/L

ood coolinophilio. XI.O IO 37E	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	30	26
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	28 27 3.84 (0.135) 0.32 (0.135)	24 19 3.94 (0.153) 0.41 (0.153)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.10 (-0.32, 0.51) 0.640
Corrected Hedges g [3] 95% CI		0.14 (-0.45, 0.73)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

Mepolizumab (Nucala) - HES Seite 956 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.89

Subgroup Analysis of Change from Baseline in PROMIS Physical Function Score at Week 32

by Baseline Blood Eosinophils (Mixed Model Repeated Measures)

Baseline blood eosinophils: >=1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	24	28	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	23 14 3.90 (0.156) 0.37 (0.156)	27 23 4.10 (0.136) 0.56 (0.136)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		0.19 (-0.23, 0.61) 0.360	
Corrected Hedges g [3] 95% CI		0.30 (-0.37, 0.97)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Cannot do/unable to do to 5 = Not at all/Without any difficulty.

Mepolizumab (Nucala) - HES Seite 957 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.93

Subgroup Analysis of Change from Baseline in PROMIS Sleep Score at Week 32 by Age (Mixed Model Repeated Measures)

Age (years): 12-<18 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	3	1
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	3 2 Non-estimable Non-estimable	0 0 Non-estimable Non-estimable

[1] Number of subjects with analysable data for one or more time points.

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

Mepolizumab (Nucala) - HES Seite 958 von 1069

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.93 Subgroup Analysis of Change from Baseline in PROMIS Sleep Score at Week 32 by Age (Mixed Model Repeated Measures)

Age (years): 18-64 Years

: 18-64 Years	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	41	49
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	38 32 2.46 (0.129) -0.04 (0.129)	47 39 2.18 (0.118) -0.32 (0.118)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.28 (-0.63, 0.07) 0.120
Corrected Hedges g [3] 95% CI		-0.37 (-0.85, 0.10)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

Mepolizumab (Nucala) - HES Seite 959 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.93 Subgroup Analysis of Change from Baseline in PROMIS Sleep Score at Week 32 by Age (Mixed Model Repeated Measures)

Age (years): >=65 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	10	4
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	10 7 2.10 (0.328) -0.55 (0.328)	4 3 3.58 (0.551) 0.92 (0.551)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		1.47 (-0.01, 2.96) 0.052
Corrected Hedges g [3] 95% CI		1.49 (-0.01, 2.99)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

Seite 960 von 1069

Mepolizumab (Nucala) - HES

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.94 Subgroup Analysis of Change from Baseline in PROMIS Sleep Score at Week 32 by Gender (Mixed Model Repeated Measures)

Gender: Female

naie	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	27	30
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	27 22 2.75 (0.171) 0.15 (0.171)	27 23 2.37 (0.168) -0.24 (0.168)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.38 (-0.88, 0.11) 0.127
Corrected Hedges g [3] 95% CI		-0.47 (-1.06, 0.12)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

Mepolizumab (Nucala) - HES Seite 961 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.94
Subgroup Analysis of Change from Baseline in PROMIS Sleep Score at Week 32 by Gender
(Mixed Model Repeated Measures)

Mara a 1 d - . . . . . . la

Gender: Male

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	27	24	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	24 19 2.11 (0.126) -0.27 (0.126)	24 19 2.03 (0.127) -0.35 (0.127)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.07 (-0.44, 0.29) 0.689	
Corrected Hedges g [3] 95% CI		-0.13 (-0.77, 0.51)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

Mepolizumab (Nucala) - HES Seite 962 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.95 Subgroup Analysis of Change from Baseline in PROMIS Sleep Score at Week 32 by Region

(Mixed Model Repeated Measures)

Region: Europe

-ope	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	33	31
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	32 25 2.59 (0.154) 0.04 (0.154)	31 29 2.19 (0.148) -0.36 (0.148)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.41 (-0.84, 0.03) 0.065
Corrected Hedges g [3] 95% CI		-0.51 (-1.05, 0.03)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

Mepolizumab (Nucala) - HES Seite 963 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.95

Subgroup Analysis of Change from Baseline in PROMIS Sleep Score at Week 32 by Region (Mixed Model Repeated Measures)

Region: Rest of World

0 01 10114	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	21	23
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	19 16 2.26 (0.135) -0.14 (0.135)	20 13 2.20 (0.151) -0.21 (0.151)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.06 (-0.48, 0.35) 0.760
Corrected Hedges g [3] 95% CI		-0.11 (-0.85, 0.62)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

Mepolizumab (Nucala) - HES Seite 964 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.96

Subgroup Analysis of Change from Baseline in PROMIS Sleep Score at Week 32

Monoligumah

by Duration of Disease (Mixed Model Repeated Measures)

Duration of disease: <2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	32	22	_
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	30 24 2.42 (0.141) 0.04 (0.141)	20 18 2.14 (0.164) -0.23 (0.164)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.27 (-0.72, 0.17) 0.218	
Corrected Hedges g [3] 95% CI		-0.39 (-1.00, 0.23)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

Mepolizumab (Nucala) - HES Seite 965 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.96

Subgroup Analysis of Change from Baseline in PROMIS Sleep Score at Week 32

by Duration of Disease (Mixed Model Repeated Measures)

Monoligumah

Duration of disease: >=2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	22	32	-
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	21 17 2.55 (0.175) -0.06 (0.175)	31 24 2.19 (0.148) -0.42 (0.148)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.36 (-0.83, 0.11) 0.131	
Corrected Hedges g [3] 95% CI		-0.49 (-1.12, 0.14)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

Mepolizumab (Nucala) - HES Seite 966 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.97

Subgroup Analysis of Change from Baseline in PROMIS Sleep Score at Week 32

Menolizumah

by Baseline Blood Eosinophils (Mixed Model Repeated Measures)

Baseline blood eosinophils: <1.5 10^9/L

	Placebo (N=54)	300mg SC (N=54)	
Number of subjects in subgroup	30	26	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	28 27 2.59 (0.150) 0.00 (0.150)	24 19 2.15 (0.176) -0.44 (0.176)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.44 (-0.92, 0.03) 0.064	
Corrected Hedges g [3] 95% CI		-0.56 (-1.16, 0.04)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

Mepolizumab (Nucala) - HES Seite 967 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.97

Subgroup Analysis of Change from Baseline in PROMIS Sleep Score at Week 32

Menolizumah

by Baseline Blood Eosinophils (Mixed Model Repeated Measures)

Baseline blood eosinophils: >=1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	24	28	_
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	23 14 2.33 (0.175) -0.06 (0.175)	27 23 2.17 (0.141) -0.22 (0.141)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.16 (-0.62, 0.30) 0.493	
Corrected Hedges g [3] 95% CI		-0.23 (-0.90, 0.43)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Scale 1 = Not at all difficulty in falling asleep/Never trouble staying asleep to 5 = Very much difficulty in falling asleep/Always trouble staying asleep.

Mepolizumab (Nucala) - HES Seite 968 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.102

Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Physical Component Summary Score at Week 32 by Age

Age: 12-<18 Years

12-\10 Tears	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	3 2 (67%) 1 (33%) 0	1 0 1 (100%) 1 (100%)
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		Non-estimable Non-estimable 1.00 (0.05,>999.99) >999.99 (0.24,>999.99) 0.67 (-0.59,0.99) 1.000

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

Mepolizumab (Nucala) - HES Seite 969 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score

Population: Intent-to-Treat

Table 90.102

Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Physical Component Summary Score at Week 32 by Age

Age: 18-64 Years

TO OI ICUID	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder	41 15 (37%) 26 (63%)	49 22 (45%) 27 (55%)
Missing response	3 (7%)	2 (4%)
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2]		
Inverse odds ratio (95% CI)		0.70 (0.27,1.81)
p-value		0.461
Inverse unadjusted odds ratio (95% CI) [3]		0.71 (0.28,1.79)
Inverse relative risk (95% CI) [4]		0.81 (0.45,1.36)
Risk difference (95% CI) [4]		-0.08 (-0.28,0.12)
Fisher's Exact p-value (2-sided)		0.520

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

Mepolizumab (Nucala) - HES Seite 970 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.102

Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Physical Component Summary Score at Week 32 by Age

Age: >=65 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	10 3 (30%) 7 (70%) 1 (10%)	4 1 (25%) 3 (75%) 1 (25%)
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		0.19 (<0.01,100.89) 0.607 1.26 (0.06,89.70) 1.20 (0.18,31.21) 0.05 (-0.56,0.51) 1.000

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

Mepolizumab (Nucala) - HES Seite 971 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.103

Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in Physical Component Summary Score at Week 32 by Gender

Gender: Female

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	27 13 (48%) 14 (52%) 2 (7%)	
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		0.94 (0.31,2.89) 0.913 0.82 (0.25,2.60) 0.90 (0.50,1.58) -0.05 (-0.31,0.21) 0.793

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

Mepolizumab (Nucala) - HES Seite 972 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.103
Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in Physical Component Summary Score at Week 32 by Gender

Gender: Male

r. Male	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	20 (74%)	24 7 (29%) 17 (71%) 3 (13%)
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		0.66 (0.13,3.42) 0.624 0.85 (0.21,3.50) 0.89 (0.32,2.47) -0.03 (-0.29,0.22) 1.000

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

PPD

PPD

Mepolizumab (Nucala) - HES Seite 973 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.104

Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Physical Component Summary Score at Week 32 by Region

Region: Europe

n. Europe	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	33 12 (36%) 21 (64%) 2 (6%)	` ,
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		0.68 (0.23,1.98) 0.481 0.70 (0.23,2.12) 0.81 (0.41,1.49) -0.09 (-0.33,0.16) 0.611

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

PPD

PPD

Mepolizumab (Nucala) - HES Seite 974 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.104

Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Physical Component Summary Score at Week 32 by Region

Region: Rest of World

n. Rest of world	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	21 8 (38%) 13 (62%) 2 (10%)	, ,
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		1.31 (0.28,6.05) 0.729 0.96 (0.24,3.80) 0.97 (0.41,2.16) -0.01 (-0.31,0.28) 1.000

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

Mepolizumab (Nucala) - HES Seite 975 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.105

Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Physical Component Summary Score at Week 32 by Duration of Disease

Duration of disease: <2.76 Years

cion of disease. <2.70 leafs	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	32 12 (38%) 20 (63%) 2 (6%)	( )
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		0.99 (0.25,3.97) 0.990 1.28 (0.36,4.84) 1.18 (0.55,2.85) 0.06 (-0.21,0.31) 0.775

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

Mepolizumab (Nucala) - HES Seite 976 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

## Table 90.105

Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Physical Component Summary Score at Week 32 by Duration of Disease

Duration of disease: >=2.76 Years

ion of disease. >-2.70 feats	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	22 8 (36%) 14 (64%) 2 (9%)	` ,
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		0.73 (0.22,2.46) 0.617 0.58 (0.16,1.98) 0.73 (0.34,1.37) -0.14 (-0.39,0.14) 0.407

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

Mepolizumab (Nucala) - HES Seite 977 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.106

Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Physical Component Summary Score at Week 32 by Baseline Blood Eosinophils

Baseline blood eosinophils: <1.5 10^9/L

2100	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	30 13 (43%) 17 (57%) 1 (3%)	` ,
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		0.84 (0.25,2.88) 0.785 1.04 (0.32,3.44) 1.02 (0.54,2.08) 0.01 (-0.25,0.27) 1.000

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

Mepolizumab (Nucala) - HES Seite 978 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.106

Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Physical Component Summary Score at Week 32 by Baseline Blood Eosinophils

Baseline blood eosinophils: >=1.5 10^9/L

ine brook cobinophiris. / 1.3 to 3/E	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	24 7 (29%) 17 (71%) 3 (13%)	, ,
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		0.61 (0.17,2.28) 0.466 0.56 (0.15,2.00) 0.68 (0.28,1.45) -0.14 (-0.40,0.15) 0.391

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

Mepolizumab (Nucala) - HES Seite 979 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.111
Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Mental Component Summary Score at Week 32 by Age

Age: 12-<18 Years

	Mepolizumab Placebo 300mg SC (N=54) (N=54)
n	3 1
Responder	1 (33%) 0
Non-Responder	2 (67%) 1 (100%)
Missing response	0 1 (100%)
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2]	
Inverse odds ratio (95% CI)	Non-estimable
p-value	Non-estimable
Inverse unadjusted odds ratio (95% CI) [3]	0.33 (0.02,>999.99)
Inverse relative risk (95% CI) [4]	>999.99 (0.03,>999.99)
Risk difference (95% CI) [4]	0.33 (-0.81,0.91)
Fisher's Exact p-value (2-sided)	1.000

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

Mepolizumab (Nucala) - HES Seite 980 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.111
Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Mental Component Summary Score at Week 32 by Age

Age: 18-64 Years

To of fearb	Mepolizumab Placebo 300mg SC (N=54) (N=54)
n	41 49
Responder	12 (29%) 23 (47%)
Non-Responder	29 (71%) 26 (53%)
Missing response	3 (7%) 2 (4%)
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3]	0.36 (0.13,1.01) 0.051 0.47 (0.18,1.22)
Inverse relative risk (95% CI) [4]	0.62 (0.33,1.09)
Risk difference (95% CI) [4]	-0.18 (-0.37,0.04)
Fisher's Exact p-value (2-sided)	0.128

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

Mepolizumab (Nucala) - HES Seite 981 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.111
Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Mental Component Summary Score at Week 32 by Age

Age: >=65 Years

· / 03 leals	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder	10 4 (40%)	4 2 (50%)
Non-Responder	6 (60%)	2 (50%)
Missing response	1 (10%)	1 (25%)
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2]		
Inverse odds ratio (95% CI)		11.29 (0.02,>999.99)
p-value		0.472
Inverse unadjusted odds ratio (95% CI) [3]		0.69 (0.03,13.30)
Inverse relative risk (95% CI) [4]		0.80 (0.22,5.70)
Risk difference (95% CI) [4]		-0.10 (-0.64,0.45)
Fisher's Exact p-value (2-sided)		1.000

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

Mepolizumab (Nucala) - HES Seite 982 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.112

Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Mental Component Summary Score at Week 32 by Gender

Gender: Female

er. remare	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	27 10 (37%) 17 (63%) 2 (7%)	` ,
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		1.26 (0.38,4.19) 0.709 0.88 (0.26,2.92) 0.93 (0.42,1.85) -0.03 (-0.29,0.23) 1.000

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

PPD

PPD

Mepolizumab (Nucala) - HES Seite 983 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.112

Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Mental Component Summary Score at Week 32 by Gender

Gender: Male

er. Male	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	, ,	24 13 (54%) 11 (46%) 3 (13%)
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		0.08 (0.01,0.51) 0.007 0.30 (0.08,1.11) 0.48 (0.21,1.01) -0.28 (-0.53,0.00) 0.049

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

PPD

PPD

Mepolizumab (Nucala) - HES Seite 984 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.113

Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Mental Component Summary Score at Week 32 by Region

Region: Europe

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	, ,	31 16 (52%) 15 (48%) 1 (3%)
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		0.29 (0.09,0.90) 0.032 0.31 (0.09,0.97) 0.47 (0.21,0.93) -0.27 (-0.49,-0.03) 0.038

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

PPD

PPD

Mepolizumab (Nucala) - HES Seite 985 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.113

Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Mental Component Summary Score at Week 32 by Region

Region: Rest of World

m. Rest of World	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	21 9 (43%) 12 (57%) 2 (10%)	` ,
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		1.31 (0.32,5.39) 0.704 1.16 (0.30,4.58) 1.10 (0.50,2.39) 0.04 (-0.27,0.33) 1.000

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

PPD

PPD

Mepolizumab (Nucala) - HES Seite 986 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.114

Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Mental Component Summary Score at Week 32 by Duration of Disease

Duration of disease: <2.76 Years

ion of disease. N2.70 feats	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	32 13 (41%) 19 (59%) 2 (6%)	
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		0.33 (0.07,1.59) 0.168 0.69 (0.20,2.34) 0.81 (0.44,1.63) -0.09 (-0.36,0.18) 0.582

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

Mepolizumab (Nucala) - HES Seite 987 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.114

Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Mental Component Summary Score at Week 32 by Duration of Disease

Duration of disease: >=2.76 Years

ion of disease. 7-2.70 feats	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	22 4 (18%) 18 (82%) 2 (9%)	
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		0.31 (0.08,1.18) 0.085 0.29 (0.06,1.17) 0.42 (0.10,1.06) -0.26 (-0.48,0.01) 0.078

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

Mepolizumab (Nucala) - HES Seite 988 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

## Table 90.115

Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Mental Component Summary Score at Week 32 by Baseline Blood Eosinophils

Baseline blood eosinophils: <1.5 10^9/L

The blood edsinophilis. (1.5 to 5/ b	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	30 10 (33%) 20 (67%) 1 (3%)	,
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		0.79 (0.20,3.15) 0.742 0.80 (0.23,2.75) 0.87 (0.41,1.84) -0.05 (-0.32,0.21) 0.783

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

Mepolizumab (Nucala) - HES Seite 989 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.115

Subgroup Analysis of Proportion of Subjects with an Improvement of >=5 in SF-36 Mental Component Summary Score at Week 32 by Baseline Blood Eosinophils

Baseline blood eosinophils: >=1.5 10^9/L

Time Brook Coolinophilis. 7 1.0 10 3/1	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
n Responder Non-Responder Missing response	24 7 (29%) 17 (71%) 3 (13%)	13 (46%)
Comparison Mepolizumab 300mg vs Placebo [1] Logistic regression [2] Inverse odds ratio (95% CI) p-value Inverse unadjusted odds ratio (95% CI) [3] Inverse relative risk (95% CI) [4] Risk difference (95% CI) [4] Fisher's Exact p-value (2-sided)		0.44 (0.12,1.58) 0.206 0.36 (0.09,1.29) 0.54 (0.22,1.08) -0.24 (-0.49,0.03) 0.096

Note: Inverse odds ratio and inverse relative risk <1 and risk difference <0 indicate benefit for Mepolizumab over Placebo.

Mepolizumab (Nucala) - HES Seite 990 von 1069

<sup>[1]</sup> Analysis compares the number of responders. Subjects with missing response are categorised as non-responders.

<sup>[2]</sup> Logistic regression analysis adjusted for baseline OCS dose, region and baseline score.

<sup>[3]</sup> Exact method.

<sup>[4]</sup> Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Population: Intent-to-Treat

Table 90.127

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Work Time Missed Due to Health (%) by Age (Mixed Model Repeated Measures)

Age (years): 12-<18 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	3	1
n [1] n [2]	0 0	0 0

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 991 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.127

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Work Time Missed Due to Health (%) by Age (Mixed Model Repeated Measures)

Age (years): 18-64 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	41	49
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	25 17 12.46 (6.676) -6.04 (6.676)	28 19 19.79 (6.348) 1.28 (6.348)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		7.33 (-11.56, 26.21) 0.432
Corrected Hedges g [3] 95% CI		0.26 (-0.40, 0.92)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

. . \_

Mepolizumab (Nucala) - HES Seite 992 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.127

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Work Time Missed Due to Health (%) by Age (Mixed Model Repeated Measures)

Age (years): >=65 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	10	4	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	4 1 Non-estimable Non-estimable	0 0 Non-estimable Non-estimable	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 993 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.128

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Work Time Missed Due to Health (%) by Gender (Mixed Model Repeated Measures)

Gender: Female

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	27	30
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	14 8 14.64 (11.442) -11.44 (11.442)	14 10 22.79 (11.284) -3.28 (11.284)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		8.15 (-25.96, 42.26) 0.619
Corrected Hedges g [3] 95% CI		0.23 (-0.71, 1.16)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 994 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.128

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Work Time Missed Due to Health (%) by Gender (Mixed Model Repeated Measures)

Gender: Male

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	27	24	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	15 10 Non-estimable Non-estimable	14 9 Non-estimable Non-estimable	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 995 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.129

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Work Time Missed Due to Health (%) by Region (Mixed Model Repeated Measures)

Region: Europe

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	33	31	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	17 11 8.92 (6.787) -10.19 (6.787)	17 13 8.72 (6.360) -10.39 (6.360)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-0.20 (-19.82, 19.41) 0.983	
Corrected Hedges g [3] 95% CI		-0.01 (-0.81, 0.79)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 996 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.129

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Work Time Missed Due to Health (%) by Region (Mixed Model Repeated Measures)

Region: Rest of World

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	21	23
n [1] n [2] LS Mean (SE)	12 7 Non-estimable	11 6 Non-estimable
LS Mean Change (SE)	Non-estimable	Non-estimable

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 997 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.130

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Work Time Missed Due to Health (%) by Duration of Disease (Mixed Model Repeated Measures)

Duration of disease: <2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	32	22
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	16 9 12.55 (22.491) -3.30 (22.454)	11 9 -0.13 (25.684) -15.99 (25.680)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-12.68 (-90.07, 64.71) 0.719
Corrected Hedges g [3] 95% CI		-0.17 (-1.09, 0.76)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 998 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.130

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Work Time Missed Due to Health (%) by Duration of Disease (Mixed Model Repeated Measures)

Duration of disease: >=2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	22	32	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	13 9 10.16 (8.503) -9.80 (8.503)	17 10 17.01 (7.841) -2.95 (7.848)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		6.85 (-17.68, 31.38) 0.564	
Corrected Hedges g [3] 95% CI		0.26 (-0.64, 1.16)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 999 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.131

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Work Time Missed Due to Health (%) by Baseline Blood Eosinophils (Mixed Model Repeated Measures)

Baseline blood eosinophils: <1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	30	26
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	16 14 -6.09 (13.983) -20.95 (14.006)	14 10 43.34 (15.532) 28.49 (15.537)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		49.44 (4.72, 94.16) 0.033
Corrected Hedges g [3] 95% CI		0.93 (0.08, 1.79)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1000 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.131

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Work Time Missed Due to Health (%) by Baseline Blood Eosinophils (Mixed Model Repeated Measures)

Baseline blood eosinophils: >=1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	24	28
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	13 4 Non-estimable Non-estimable	14 9 Non-estimable Non-estimable

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

FFD

Mepolizumab (Nucala) - HES Seite 1001 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.134

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Impairment While Working Due to Health (%) by Age (Mixed Model Repeated Measures)

Age (years): 12-<18 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	3	1
n [1] n [2]	O O	0 0

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1002 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.134

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Impairment While Working Due to Health (%) by Age (Mixed Model Repeated Measures)

Age (years): 18-64 Years

· 10 01 10d10	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	41	49
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	21 16 29.42 (4.517) -5.64 (4.517)	25 16 20.53 (4.314) -14.53 (4.314)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-8.89 (-21.79, 4.01) 0.170
Corrected Hedges g [3] 95% CI		-0.49 (-1.19, 0.21)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1003 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.134

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Impairment While Working Due to Health (%) by Age (Mixed Model Repeated Measures)

Age (years): >=65 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	10	4
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	4 1 Non-estimable Non-estimable	0 0 Non-estimable Non-estimable

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1004 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.135

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Impairment While Working Due to Health (%) by Gender (Mixed Model Repeated Measures)

Gender: Female

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	27	30
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	11 7 Non-estimable Non-estimable	12 7 Non-estimable Non-estimable

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of treatment and visit, plus interaction terms for visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1005 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.135

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Impairment While Working Due to Health (%) by Gender (Mixed Model Repeated Measures)

Gender: Male

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	27	24
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	14 10 19.09 (5.651) 1.14 (5.051)	13 9 17.96 (5.832) -10.87 (5.317)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-12.02 (-27.37, 3.34) 0.118
Corrected Hedges g [3] 95% CI		-0.72 (-1.65, 0.21)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of treatment and visit, plus interaction terms for visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1006 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.136

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Impairment While Working Due to Health (%) by Region (Mixed Model Repeated Measures)

Region: Europe

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	33	31
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	14 10 27.21 (4.566) -4.43 (4.566)	14 12 15.32 (4.271) -16.32 (4.271)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-11.89 (-24.95, 1.16) 0.072
Corrected Hedges g [3] 95% CI		-0.78 (-1.65, 0.09)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1007 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.136

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Impairment While Working Due to Health (%) by Region (Mixed Model Repeated Measures)

Region: Rest of World

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	21	23
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	11 7 Non-estimable Non-estimable	11 4 Non-estimable Non-estimable

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1008 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.137

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Impairment While Working Due to Health (%) by Duration of Disease (Mixed Model Repeated Measures)

Duration of disease: <2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	32	22
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	13 8 Non-estimable Non-estimable	10 8 Non-estimable Non-estimable

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Seite 1009 von 1069

Mepolizumab (Nucala) - HES

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.137

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Impairment While Working Due to Health (%) by Duration of Disease (Mixed Model Repeated Measures)

Duration of disease: >=2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	22	32
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	12 9 Non-estimable Non-estimable	15 8 Non-estimable Non-estimable

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1010 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.138

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Impairment While Working Due to Health (%)

by Baseline Blood Eosinophils (Mixed Model Repeated Measures)

Baseline blood eosinophils: <1.5 10^9/L

ood coolinophilis. (1.6 10 3/1	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	30	26
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	16 14 Non-estimable Non-estimable	12 8 Non-estimable Non-estimable

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1011 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.138

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Impairment While Working Due to Health (%) by Baseline Blood Eosinophils

Manaligumah

(Mixed Model Repeated Measures)

Baseline blood eosinophils: >=1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	24	28
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	9 3 Non-estimable Non-estimable	13 8 Non-estimable Non-estimable

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Б

Mepolizumab (Nucala) - HES Seite 1012 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.141

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Overall Work Impairment Due to Health (%) by Age (Mixed Model Repeated Measures)

Age (years): 12-<18 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	3	1
n [1] n [2]	O O	0 0

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1013 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.141

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Overall Work Impairment Due to Health (%) by Age (Mixed Model Repeated Measures)

Age (years): 18-64 Years

· 10 01 10d10	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	41	49
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	25 17 39.37 (6.960) -6.63 (6.960)	28 19 31.79 (6.577) -14.21 (6.577)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-7.58 (-27.15, 11.98) 0.436
Corrected Hedges g [3] 95% CI		-0.26 (-0.92, 0.40)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1014 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.141

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Overall Work Impairment Due to Health (%) by Age (Mixed Model Repeated Measures)

Age (years): >=65 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	10	4	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	4 1 Non-estimable Non-estimable	0 0 Non-estimable Non-estimable	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1015 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.142

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Overall Work Impairment Due to Health (%) by Gender (Mixed Model Repeated Measures)

Gender: Female

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	27	30
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	14 8 45.33 (11.773) -14.23 (11.773)	14 10 36.66 (11.028) -22.90 (11.028)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-8.67 (-42.98, 25.64) 0.603
Corrected Hedges g [3] 95% CI		-0.24 (-1.17, 0.69)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1016 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.142

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Overall Work Impairment Due to Health (%) by Gender (Mixed Model Repeated Measures)

Gender: Male

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	27	24
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	15 10 32.33 (10.092) 0.81 (10.092)	14 9 11.74 (10.328) -19.78 (10.328)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-20.59 (-54.38, 13.20) 0.196
Corrected Hedges g [3] 95% CI		-0.62 (-1.55, 0.30)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1017 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.143

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Overall Work Impairment Due to Health (%) by Region (Mixed Model Repeated Measures)

Region: Europe

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	33	31	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	17 11 39.55 (8.038) -4.13 (8.038)	17 13 21.29 (7.356) -22.40 (7.356)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-18.27 (-41.40, 4.86) 0.114	
Corrected Hedges g [3] 95% CI		-0.66 (-1.49, 0.16)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1018 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.143

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Overall Work Impairment Due to Health (%) by Region (Mixed Model Repeated Measures)

Region: Rest of World

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	21	23
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	12 7 Non-estimable Non-estimable	11 6 Non-estimable Non-estimable

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1019 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.144

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Overall Work Impairment Due to Health (%) by Duration of Disease (Mixed Model Repeated Measures)

Duration of disease: <2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	32	22
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	16 9 28.08 (10.615) -10.50 (10.163)	11 9 47.91 (11.465) -5.64 (10.745)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		4.86 (-26.39, 36.11) 0.747
Corrected Hedges g [3] 95% CI		0.15 (-0.78, 1.07)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of treatment and visit, plus interaction terms for visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1020 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.144

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Overall Work Impairment Due to Health (%) by Duration of Disease (Mixed Model Repeated Measures)

Duration of disease: >=2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	22	32	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	13 9 42.75 (8.834) 3.56 (10.691)	17 10 22.25 (8.176) -25.63 (9.908)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-29.18 (-59.50, 1.13) 0.058	
Corrected Hedges g [3] 95% CI		-0.88 (-1.82, 0.06)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of treatment and visit, plus interaction terms for visit-by-treatment group. LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1021 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.145

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Overall Work Impairment Due to Health (%) by Baseline Blood Eosinophils (Mixed Model Repeated Measures)

Manaligumah

Baseline blood eosinophils: <1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	30	26
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	16 14 30.23 (7.385) -14.22 (7.385)	14 10 47.82 (8.640) 3.37 (8.640)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		17.59 (-6.68, 41.86) 0.145
Corrected Hedges g [3] 95% CI		0.62 (-0.21, 1.45)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1022 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.145

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Overall Work Impairment Due to Health (%) by Baseline Blood Eosinophils

(Mixed Model Repeated Measures)

Baseline blood eosinophils: >=1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	24	28
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	13 4 Non-estimable Non-estimable	14 9 Non-estimable Non-estimable

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

FFD

Mepolizumab (Nucala) - HES Seite 1023 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.148

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Activity Impairment Due to Health (%) by Age (Mixed Model Repeated Measures)

Age (years): 12-<18 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	3	1	_
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	3 2 Non-estimable Non-estimable	0 0 Non-estimable Non-estimable	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

FFD

Mepolizumab (Nucala) - HES Seite 1024 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.148

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Activity Impairment Due to Health (%) by Age (Mixed Model Repeated Measures)

Age (years): 18-64 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	41	49
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	39 32 39.21 (4.042) -2.94 (4.042)	47 39 20.77 (3.693) -21.39 (3.693)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-18.44 (-29.40, -7.49) 0.001
Corrected Hedges g [3] 95% CI		-0.79 (-1.28, -0.31)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1025 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.148

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Activity Impairment Due to Health (%) by Age (Mixed Model Repeated Measures)

Age (years): >=65 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	10	4	•
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	10 7 Non-estimable Non-estimable	4 3 Non-estimable Non-estimable	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1026 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.149

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Activity Impairment Due to Health (%) by Gender (Mixed Model Repeated Measures)

Gender: Female

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	27	30	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	27 22 42.21 (5.394) -7.87 (5.394)	27 23 30.28 (5.387) -19.80 (5.387)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-11.93 (-27.32, 3.46) 0.126	
Corrected Hedges g [3] 95% CI		-0.46 (-1.05, 0.13)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1027 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.149

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Activity Impairment Due to Health (%) by Gender (Mixed Model Repeated Measures)

Gender: Male

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	27	24	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	25 19 32.24 (4.287) -1.07 (4.287)	24 19 12.76 (4.248) -20.54 (4.248)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-19.47 (-31.87, -7.07) 0.003	
Corrected Hedges g [3] 95% CI		-1.02 (-1.70, -0.35)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1028 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.150

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Activity Impairment Due to Health (%) by Region (Mixed Model Repeated Measures)

Region: Europe

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	33	31
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	32 25 39.11 (4.680) -3.01 (4.680)	31 29 20.24 (4.444) -21.88 (4.444)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-18.87 (-31.85, -5.89) 0.005
Corrected Hedges g [3] 95% CI		-0.78 (-1.34, -0.23)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1029 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.150

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Activity Impairment Due to Health (%) by Region (Mixed Model Repeated Measures)

Region: Rest of World

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	21	23
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	20 16 38.97 (5.196) -3.13 (5.196)	20 13 25.32 (5.846) -16.78 (5.846)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-13.65 (-29.69, 2.39) 0.092
Corrected Hedges g [3] 95% CI		-0.63 (-1.38, 0.12)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1030 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.151

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Activity Impairment Due to Health (%) by Duration of Disease (Mixed Model Repeated Measures)

Duration of disease: <2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	32	22	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	31 24 29.00 (4.223) -8.08 (4.223)	20 18 23.99 (5.061) -13.09 (5.061)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-5.01 (-18.37, 8.34) 0.454	
Corrected Hedges g [3] 95% CI		-0.23 (-0.85, 0.38)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1031 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.151

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Activity Impairment Due to Health (%) by Duration of Disease (Mixed Model Repeated Measures)

Duration of disease: >=2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	22	32
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	21 17 49.72 (5.865) 2.58 (5.865)	31 24 22.02 (4.963) -25.12 (4.963)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-27.70 (-43.40, -12.01) <0.001
Corrected Hedges g [3] 95% CI		-1.12 (-1.79, -0.45)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

FFD

Mepolizumab (Nucala) - HES Seite 1032 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.152

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Activity Impairment Due to Health (%)

> by Baseline Blood Eosinophils (Mixed Model Repeated Measures)

> > Manaligumah

Baseline blood eosinophils: <1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)
Number of subjects in subgroup	30	26
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	29 27 35.74 (4.469) -5.64 (4.469)	24 19 20.81 (5.289) -20.57 (5.289)
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-14.93 (-29.00, -0.86) 0.038
Corrected Hedges g [3] 95% CI		-0.63 (-1.23, -0.03)

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1033 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Population: Intent-to-Treat

Table 90.152

Subgroup Analysis of Change from Baseline in Work Productivity and Activity Impairment Questionnaire (WPAI) at Week 32: Activity Impairment Due to Health (%)

> by Baseline Blood Eosinophils (Mixed Model Repeated Measures)

> > Manaligumah

Baseline blood eosinophils: >=1.5 10^9/L

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	
Number of subjects in subgroup	24	28	
n [1] n [2] LS Mean (SE) LS Mean Change (SE)	23 14 42.21 (5.668) -0.76 (5.668)	27 23 23.61 (4.793) -19.36 (4.793)	
Mepolizumab 300mg SC vs Placebo Difference (Mepo - Placebo) 95% CI p-value		-18.59 (-33.65, -3.53) 0.017	
Corrected Hedges g [3] 95% CI		-0.81 (-1.50, -0.12)	

Note: Analysis performed separately for each subgroup using mixed model repeated measures with covariates of baseline, baseline OCS dose, region, treatment and visit, plus interaction terms for visit-by-baseline and visit-by-treatment group.

LS mean estimates are weighted according to the observed proportion of each categorical covariate in the study data.

Mepolizumab (Nucala) - HES Seite 1034 von 1069

<sup>[1]</sup> Number of subjects with analysable data for one or more time points.

<sup>[2]</sup> Number of subjects with analysable data at the given time point.

<sup>[3]</sup> Derived from LS means and associated SE.

Protocol: 200622 Page 1 of 1 Population: Safety

Table 100.1 Summary and Analysis of Proportion of Subjects with On-Treatment Adverse Events Overall and by Subgroup

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [1]	Risk Difference (Exact 95% CI) [1]	p-value [2]
All Subjects	47 (87%)	48 (89%)	1.19 (0.32,4.63)	1.02 (0.87,1.20)	0.02 (-0.11,0.15)	>0.999
Subgroups Age (Years) 12-<18 18-64 >=65	2/3 (67%) 36/41 (88%) 9/10 (90%)	0/1 44/49 (90%) 4/4 (>99%)	0.00 (0.00,19.00) 1.22 (0.26,5.75) Inf (0.02,Inf)	0.00 (0.00,4.24) 1.02 (0.87,1.24) 1.11 (0.41,1.80)	-0.67 (-0.99,0.59) 0.02 (-0.12,0.17) 0.10 (-0.47,0.47)	>0.999 >0.999 >0.999
Gender Male Female	23/27 (85%) 24/27 (89%)	21/24 (88%) 27/30 (90%)	1.22 (0.18,9.27) 1.13 (0.14,9.20)	1.03 (0.77,1.34) 1.01 (0.81,1.30)	0.02 (-0.20,0.24) 0.01 (-0.17,0.20)	>0.999 >0.999
Region Europe Rest of World	29/33 (88%) 18/21 (86%)	28/31 (90%) 20/23 (87%)	1.29 (0.20,9.55) 1.11 (0.13,9.37)	1.03 (0.83,1.27) 1.01 (0.76,1.38)	0.02 (-0.15,0.20) 0.01 (-0.23,0.25)	>0.999 >0.999
Duration of Disease (Years) <2.76 >=2.76	26/32 (81%) 21/22 (95%)	19/22 (86%) 29/32 (91%)	1.46 (0.27,10.11) 0.46 (0.01,6.28)	1.06 (0.76,1.39) 0.95 (0.78,1.19)	0.05 (-0.19,0.26) -0.05 (-0.21,0.16)	0.723 0.638
Baseline Blood Eosinophils <1.5 10^9/L >=1.5 10^9/L	25/30 (83%) 22/24 (92%)	22/26 (85%) 26/28 (93%)	1.10 (0.21,6.27) 1.18 (0.08,17.50)	1.02 (0.76,1.34) 1.01 (0.82,1.29)	0.01 (-0.21,0.22) 0.01 (-0.16,0.21)	>0.999 >0.999

Note: Information presented as number of subjects with event / number subjects in the subgroup. [1] Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Mepolizumab (Nucala) - HES Seite 1035 von 1069

<sup>[2] 2-</sup>sided Fisher's Exact p-value.

Protocol: 200622 Page 1 of 1 Population: Safety

Table 100.8 Summary and Analysis of Proportion of Subjects with On-Treatment Non-Fatal Serious Adverse Events Overall and by Subgroup

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [1]	Risk Difference (Exact 95% CI) [1]	p-value [2]
All Subjects	8 (15%)	9 (17%)	1.15 (0.36,3.76)	1.13 (0.45,3.22)	0.02 (-0.13,0.16)	>0.999
Subgroups Age (Years) 12-<18 18-64 >=65	2/3 (67%) 5/41 (12%) 1/10 (10%)	0/1 8/49 (16%) 1/4 (25%)	0.00 (0.00,19.00) 1.40 (0.36,5.95) 3.00 (0.03,261.12)	0.00 (0.00,4.24) 1.34 (0.47,4.57) 2.50 (0.08,78.55)	-0.67 (-0.99,0.59) 0.04 (-0.12,0.19) 0.15 (-0.30,0.69)	>0.999 0.765 0.505
Gender Male Female	2/27 (7%) 6/27 (22%)	4/24 (17%) 5/30 (17%)	2.50 (0.31,29.77) 0.70 (0.15,3.22)	2.25 (0.42,16.63) 0.75 (0.23,2.42)	0.09 (-0.10,0.31) -0.06 (-0.28,0.16)	0.402 0.740
Region Europe Rest of World	5/33 (15%) 3/21 (14%)	5/31 (16%) 4/23 (17%)	1.08 (0.22,5.27) 1.26 (0.18,9.80)	1.06 (0.31,3.68) 1.22 (0.28,7.62)	0.01 (-0.18,0.20) 0.03 (-0.23,0.27)	>0.999 >0.999
Duration of Disease (Years) <2.76 >=2.76	6/32 (19%) 2/22 (9%)	6/22 (27%) 3/32 (9%)	1.63 (0.36,7.22) 1.03 (0.11,13.43)	1.45 (0.46,4.55) 1.03 (0.18,10.20)	0.09 (-0.15,0.33) 0.00 (-0.20,0.18)	0.517 >0.999
Baseline Blood Eosinophils <1.5 10^9/L >=1.5 10^9/L	3/30 (10%) 5/24 (21%)	5/26 (19%) 4/28 (14%)	2.14 (0.36,15.18) 0.63 (0.11,3.43)	1.92 (0.47,16.67) 0.69 (0.18,2.69)	0.09 (-0.11,0.31) -0.07 (-0.29,0.15)	0.451 0.716

Note: Information presented as number of subjects with event / number subjects in the subgroup. [1] Exact unconditional CI calculated by inverting two separate one-sided tests based on the score statistic.

Mepolizumab (Nucala) - HES Seite 1036 von 1069

<sup>[2] 2-</sup>sided Fisher's Exact p-value.

Protocol: 200622 Page 1 of 9
Population: Safety

Table 100.14

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Age

Age: 12-<18 Years

Age: 12-\10 rears	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Number of Subjects in Subgroup	3	1				
Risks						
Serious Adverse Events	2 (67%)	0	0.00 (0.00,19.00)	0.00 (0.00,4.24)	-0.67 (-0.99,0.59)	>0.999
Systemic Reactions [1]	0	0				
Anaphylaxis [2]	0	0				
Allergic (Type I) Hypersensit ivity	0	0				

- [1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.
- [2] Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.
- [3] Identified by the investigator in eCRF designed for collecting data on local injection site reactions.
- [4] Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Mepolizumab (Nucala) - HES Seite 1037 von 1069

Protocol: 200622 Page 2 of 9
Population: Safety

Table 100.14

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Age

Age: 12-<18 Years

₁qe:	12-<18 rears					
<i>y</i>		Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Risk Difference (Exact 95% CI) [8]	p-value [9]
	Other Systemic	0	0		 	
I	ocal njection Site eactions [3]	0	0			
	ll Infections 4]	0	0			
	Serious Infections	0	0			
0	otential pportunistic nfections [5]	0	0			
N	eoplasms [4]	0	0			
	alignancies 6]	0	0			

- [1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.
- [2] Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.
- [3] Identified by the investigator in eCRF designed for collecting data on local injection site reactions.
- [4] Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Mepolizumab (Nucala) - HES Seite 1038 von 1069

Protocol: 200622
Population: Safety
Page 3 of 9

Table 100.14

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Age

Age: 12-<18 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Cardiac Disorders [	0	0				
Serious Cardiac Disorder	0 s	0				
Serious CVT Events [6]	0	0				
Serious Ischemic Events [		0				

- [1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.
- [2] Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.
- [3] Identified by the investigator in eCRF designed for collecting data on local injection site reactions.
- [4] Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Mepolizumab (Nucala) - HES Seite 1039 von 1069

Protocol: 200622 Page 4 of 9
Population: Safety

Table 100.14

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Age

Age: 18-64 Years

Age: 18-64 Years	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Number of Subjects in Subgroup	41	49				
Risks						
Serious Adverse Events	5 (12%)	8 (16%)	1.40 (0.36,5.95)	1.34 (0.47,4.57)	0.04 (-0.12,0.19)	0.765
Systemic Reactions [1]	0	1 (2%)	Inf (0.04,Inf)	Inf (0.06,Inf)	0.02 (-0.07,0.11)	>0.999
Anaphylaxis	0	0				
Allergic (Type I) Hypersensit ivity	0	0				

- [1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.
- [2] Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.
- [3] Identified by the investigator in eCRF designed for collecting data on local injection site reactions.
- [4] Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Mepolizumab (Nucala) - HES Seite 1040 von 1069

Protocol: 200622 Page 5 of 9
Population: Safety

Table 100.14
Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Age

Age: 18-64 Years

		Place (N=5		300	oolizumab Omg SC =54)		Odds Ratio kact 95% CI)		ative Risk act 95% CI) [8]	(Exact	oifference 2 95% CI) 8]	p-value [9]
_	Other Systemic	0		1	(2%)	Inf	(0.04,Inf)	Inf	(0.06,Inf)	0.02	(-0.07,0.11)	>0.999
	Local Injection Site Reactions [3]	1 (2	2%)	4	(8%)	3.56	(0.33,179.40)	3.35	(0.47,84.62)	0.06	(-0.06,0.18)	0.371
	All Infections [4]	23 (	56%)	35	(71%)	1.96	(0.75,5.15)	1.27	(0.92,1.87)	0.15	(-0.05,0.35)	0.185
	Serious Infections	0		5	(10%)	Inf	(1.07,Inf)	Inf	(1.01,Inf)	0.10	(0.01,0.22)	0.060
	Potential Opportunistic Infections [5]	3 (	7%)	2	(4%)	0.54	(0.04,4.99)	0.56	(0.06,3.36)	-0.03	(-0.17,0.08)	0.656
	Neoplasms [4]	2 (	5응)	0		0.00	(0.00,2.88)	0.00	(0.00,2.23)	-0.05	(-0.17,0.03)	0.205
	Malignancies [6]	1 (2	2응)	0		0.00	(0.00,15.90)	0.00	(0.00,12.19)	-0.02	(-0.13,0.06)	0.456

- [1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.
- [2] Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.
- [3] Identified by the investigator in eCRF designed for collecting data on local injection site reactions.

Mepolizumab (Nucala) - HES Seite 1041 von 1069

<sup>[4]</sup> Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Protocol: 200622 Page 6 of 9
Population: Safety

Table 100.14

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Age

Age: 18-64 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	(	Odds Ratio kact 95% CI)	_	Lative Risk kact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Cardiac Disorders [4]	1 (2%)	4 (8%)	3.56	(0.33,179.40)	3.35	(0.47,84.62)	0.06 (-0.06,0.18)	0.371
Serious Cardiac Disorders	0	1 (2%)	Inf	(0.04,Inf)	Inf	(0.06,Inf)	0.02 (-0.07,0.11)	>0.999
Serious CVT Events [6]	1 (2%)	2 (4%)	1.70	(0.09,102.89)	1.67	(0.15,45.44)	0.02 (-0.09,0.12)	>0.999
Serious Ischemic Events [7]	0	0						

Mepolizumab (Nucala) - HES Seite 1042 von 1069

<sup>[1]</sup> Identified by the investigator in eCRF designed for collecting data on systemic reactions.

<sup>[2]</sup> Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.

<sup>[3]</sup> Identified by the investigator in eCRF designed for collecting data on local injection site reactions.

<sup>[4]</sup> Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Protocol: 200622 Page 7 of 9
Population: Safety

Table 100.14

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Age

Age: >=65 Years

Age: 7-03 rears	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Number of Subjects in Subgroup	10	4				
Risks						
Serious Adverse Events	1 (10%)	2 (50%)	9.00 (0.27,587.99)	5.00 (0.52,136.38)	0.40 (-0.13,0.85)	0.176
Systemic Reactions [1]	0	0				
Anaphylaxis [2]	0	0				
Allergic (Type I) Hypersensit ivity	0	0				

- [1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.
- [2] Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.
- [3] Identified by the investigator in eCRF designed for collecting data on local injection site reactions.
- [4] Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Mepolizumab (Nucala) - HES Seite 1043 von 1069

Protocol: 200622 Page 8 of 9
Population: Safety

Table 100.14

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Age

Age: >=65 Years

age -	: >=05 rears	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
	Other Systemic	0	0				
	Local Injection Site Reactions [3]	1 (10%)	0	0.00 (0.00,47.50)	0.00 (0.00,33.15)	-0.10 (-0.47,0.47)	>0.999
	All Infections [4]	5 (50%)	2 (50%)	1.00 (0.05,19.26)	1.00 (0.17,3.18)	0.00 (-0.55,0.55)	>0.999
	Serious Infections	0	2 (50%)	Inf (0.83, Inf)	Inf (0.96, Inf)	0.50 (-0.01,0.93)	0.066
	Potential Opportunistic Infections [5]	1 (10%)	1 (25%)	3.00 (0.03,261.12)	2.50 (0.08,78.55)	0.15 (-0.30,0.69)	0.505
	Neoplasms [4]	0	0				
	Malignancies [6]	0	0				

- [1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.
- [2] Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.
- [3] Identified by the investigator in eCRF designed for collecting data on local injection site reactions.
- [4] Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Mepolizumab (Nucala) - HES Seite 1044 von 1069

Protocol: 200622 Page 9 of 9
Population: Safety

Table 100.14
Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Age

Age: >=65 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Cardiac Disorders [4]	1 (10%)	0	0.00 (0.00,47.50)	0.00 (0.00,33.15)	-0.10 (-0.47,0.47)	>0.999
Serious Cardiac Disorders	1 (10%)	0	0.00 (0.00,47.50)	0.00 (0.00,33.15)	-0.10 (-0.47,0.47)	>0.999
Serious CVT Events [6]	1 (10%)	0	0.00 (0.00,47.50)	0.00 (0.00,33.15)	-0.10 (-0.47,0.47)	>0.999
Serious Ischemic Events [7]	0	0				

Mepolizumab (Nucala) - HES Seite 1045 von 1069

<sup>[1]</sup> Identified by the investigator in eCRF designed for collecting data on systemic reactions.

<sup>[2]</sup> Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.

<sup>[3]</sup> Identified by the investigator in eCRF designed for collecting data on local injection site reactions.

<sup>[4]</sup> Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Protocol: 200622 Page 1 of 6
Population: Safety

Table 100.15

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Gender

Gender: Male

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Number of Subjects in Subgroup	27	24				
Risks						
Serious Adverse Events	2 (7%)	5 (21%)	3.29 (0.46,37.24)	2.81 (0.59,20.77)	0.13 (-0.07,0.35)	0.232
Systemic Reactions [1]	0	1 (4%)	Inf (0.06, Inf)	Inf (0.08,Inf)	0.04 (-0.09,0.21)	0.471
Anaphylaxis [2]	0	0				
Allergic (Type I) Hypersensit ivity	0	0				

[1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.

Mepolizumab (Nucala) - HES Seite 1046 von 1069

<sup>[2]</sup> Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.

<sup>[3]</sup> Identified by the investigator in eCRF designed for collecting data on local injection site reactions.

<sup>[4]</sup> Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Protocol: 200622 Page 2 of 6
Population: Safety

Table 100.15
Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Gender

Gender: Male

	Placebo (N=54)	Mepolizuma 300mg SC (N=54)	nb Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Other Syste		1 (4%)	Inf (0.06,Inf)	Inf (0.08,Inf)	0.04 (-0.09,0.21)	0.471
Local Injection Reaction		1 (4%)	Inf (0.06,Inf)	Inf (0.08,Inf)	0.04 (-0.09,0.21)	0.471
All Infe	ctions 12 (44%)	17 (71%)	3.04 (0.83,11.54)	1.59 (0.97,2.97)	0.26 (-0.02,0.52)	0.089
Serio Infec		4 (17%)	Inf (1.08, Inf)	Inf (1.11, Inf)	0.17 (0.02,0.37)	0.043
Potentia Opportun Infectio	istic	1 (4%)	0.54 (0.01,11.23)	0.56 (0.02,6.01)	-0.03 (-0.21,0.15)	>0.999
Neoplasm	s [4] 0	0				
Malignan [6]	cies 0	0				

- [1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.
- [2] Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.
- [3] Identified by the investigator in eCRF designed for collecting data on local injection site reactions.
- [4] Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Mepolizumab (Nucala) - HES Seite 1047 von 1069

Protocol: 200622 Page 3 of 6 Population: Safety

Table 100.15

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Gender

Gender: Male

	Placebo (N=54)	Mepolizumak 300mg SC (N=54)		Odds Ratio xact 95% CI)	_	lative Risk xact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Cardiac Disorders [4]	0	2 (8%)	Inf	(0.33,Inf)	Inf	(0.43,Inf)	0.08 (-0.05,0.27)	0.216
Serious Cardiac Disorders	0	1 (4%)	Inf	(0.06,Inf)	Inf	(0.08,Inf)	0.04 (-0.09,0.21)	0.471
Serious CVT Events [6]	0	1 (4%)	Inf	(0.06,Inf)	Inf	(0.08,Inf)	0.04 (-0.09,0.21)	0.471
Serious Ischemic Events [7]	0	0						

Mepolizumab (Nucala) - HES Seite 1048 von 1069

<sup>[1]</sup> Identified by the investigator in eCRF designed for collecting data on systemic reactions.

<sup>[2]</sup> Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.

<sup>[3]</sup> Identified by the investigator in eCRF designed for collecting data on local injection site reactions.

<sup>[4]</sup> Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Protocol: 200622 Page 4 of 6 Population: Safety

Table 100.15

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Gender

Gender: Female

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Number of Subjects in Subgroup	27	30				
Risks						
Serious Adverse Events	6 (22%)	5 (17%)	0.70 (0.15,3.22)	0.75 (0.23,2.42)	-0.06 (-0.28,0.16)	0.740
Systemic Reactions [1]	0	0				
Anaphylaxis [2]	0	0				
Allergic (Type I) Hypersensit ivity	0	0				

- [1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.
- [2] Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.
- [3] Identified by the investigator in eCRF designed for collecting data on local injection site reactions.
- [4] Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Mepolizumab (Nucala) - HES Seite 1049 von 1069

Protocol: 200622 Page 5 of 6
Population: Safety

Table 100.15
Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Gender

Gender: Female

		Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
_	Other Systemic	0	0				
	Local Injection Site Reactions [3]	2 (7%)	3 (10%)	1.39 (0.15,17.82)	1.35 (0.23,13.34)	0.03 (-0.16,0.20)	>0.999
	All Infections [4]	16 (59%)	20 (67%)	1.38 (0.41,4.64)	1.13 (0.74,1.78)	0.07 (-0.19,0.33)	0.594
	Serious Infections	0	3 (10%)	Inf (0.54, Inf)	Inf (0.63,Inf)	0.10 (-0.03,0.27)	0.239
	Potential Opportunistic Infections [5]	2 (7%)	2 (7%)	0.89 (0.06,13.20)	0.90 (0.06,13.26)	-0.01 (-0.19,0.16)	>0.999
	Neoplasms [4]	2 (7%)	0	0.00 (0.00,3.09)	0.00 (0.00,2.36)	-0.07 (-0.24,0.05)	0.220
	Malignancies [6]	1 (4%)	0	0.00 (0.00,17.10)	0.00 (0.00,13.03)	-0.04 (-0.19,0.09)	0.474

<sup>[1]</sup> Identified by the investigator in eCRF designed for collecting data on systemic reactions.

Mepolizumab (Nucala) - HES Seite 1050 von 1069

<sup>[2]</sup> Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.

<sup>[3]</sup> Identified by the investigator in eCRF designed for collecting data on local injection site reactions.

<sup>[4]</sup> Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Protocol: 200622 Page 6 of 6 Population: Safety

Table 100.15

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Gender

Gender: Female

	Placebo (N=54)	Mepolizumak 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Cardiac Disorders [4]	2 (7%)	2 (7%)	0.89 (0.06,13.20)	0.90 (0.06,13.26)	-0.01 (-0.19,0.16)	>0.999
Serious Cardiac Disorders	1 (4%)	0	0.00 (0.00,17.10)	0.00 (0.00,13.03)	-0.04 (-0.19,0.09)	0.474
Serious CVT Events [6]	2 (7%)	1 (3%)	0.43 (0.01,8.87)	0.45 (0.02,4.84)	-0.04 (-0.21,0.11)	0.599
Serious Ischemic Events [7]	0	0				

Mepolizumab (Nucala) - HES Seite 1051 von 1069

<sup>[1]</sup> Identified by the investigator in eCRF designed for collecting data on systemic reactions.

<sup>[2]</sup> Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.

<sup>[3]</sup> Identified by the investigator in eCRF designed for collecting data on local injection site reactions.

<sup>[4]</sup> Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Protocol: 200622 Page 1 of 6
Population: Safety

Table 100.16

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Region

Region: Europe

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Number of Subjects in Subgroup	33	31				
Risks						
Serious Adverse Events	5 (15%)	5 (16%)	1.08 (0.22,5.27)	1.06 (0.31,3.68)	0.01 (-0.18,0.20)	>0.999
Systemic Reactions [1]	0	1 (3%)	Inf (0.06, Inf)	<pre>Inf (0.07,Inf)</pre>	0.03 (-0.08,0.17)	0.484
Anaphylaxis [2]	0	0				
Allergic (Type I) Hypersensit ivity	0	0				

[1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.

Mepolizumab (Nucala) - HES Seite 1052 von 1069

<sup>[2]</sup> Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.

<sup>[3]</sup> Identified by the investigator in eCRF designed for collecting data on local injection site reactions.

<sup>[4]</sup> Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Protocol: 200622 Page 2 of 6
Population: Safety

Table 100.16
Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Region

Region: Europe

Region: Europe	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Other Systemic	0	1 (3%)	Inf (0.06,Inf)	Inf (0.07,Inf)	0.03 (-0.08,0.17)	0.484
Local Injection Site Reactions [3]	1 (3%)	2 (6%)	2.21 (0.11,134.20)	2.13 (0.20,57.73)	0.03 (-0.11,0.19)	0.607
All Infections [4]	18 (55%)	22 (71%)	2.04 (0.65,6.58)	1.30 (0.88,2.08)	0.16 (-0.08,0.40)	0.205
Serious Infections	0	4 (13%)	Inf (1.00,Inf)	Inf (1.06, Inf)	0.13 (0.01,0.30)	0.050
Potential Opportunistic Infections [5]	3 (9%)	1 (3%)	0.33 (0.01,4.49)	0.35 (0.01,3.36)	-0.06 (-0.22,0.09)	0.614
Neoplasms [4]	2 (6%)	0	0.00 (0.00,3.67)	0.00 (0.00,2.81)	-0.06 (-0.20,0.06)	0.493
Malignancies [6]	1 (3%)	0	0.00 (0.00,20.23)	0.00 (0.00,15.42)	-0.03 (-0.16,0.08)	>0.999

<sup>[1]</sup> Identified by the investigator in eCRF designed for collecting data on systemic reactions.

Mepolizumab (Nucala) - HES Seite 1053 von 1069

<sup>[2]</sup> Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.

<sup>[3]</sup> Identified by the investigator in eCRF designed for collecting data on local injection site reactions.

<sup>[4]</sup> Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Protocol: 200622 Page 3 of 6
Population: Safety

Table 100.16
Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Region

Region: Europe

-	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Cardiac Disorders [4]	2 (6%)	3 (10%)	1.66 (0.18,21.08)	1.60 (0.27,15.79)	0.04 (-0.12,0.20)	0.667
Serious Cardiac Disorders	1 (3%)	1 (3%)	1.07 (0.01,86.31)	1.06 (0.03,35.34)	0.00 (-0.14,0.14)	>0.999
Serious CVT Events [6]	1 (3%)	1 (3%)	1.07 (0.01,86.31)	1.06 (0.03,35.34)	0.00 (-0.14,0.14)	>0.999
Serious Ischemic Events [7]	0	0				

Mepolizumab (Nucala) - HES Seite 1054 von 1069

<sup>[1]</sup> Identified by the investigator in eCRF designed for collecting data on systemic reactions.

<sup>[2]</sup> Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.

<sup>[3]</sup> Identified by the investigator in eCRF designed for collecting data on local injection site reactions.

<sup>[4]</sup> Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Protocol: 200622 Page 4 of 6 Population: Safety

Table 100.16

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Region

Region: Rest of World

kegion: kest oi wo	rıa					
J	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Number of Subjects in Subgroup	21	23				
Risks						
Serious Adverse Events	3 (14%)	5 (22%)	1.67 (0.27,12.22)	1.52 (0.39,13.16)	0.07 (-0.18,0.31)	0.701
Systemic Reactions [1]	0	0				
Anaphylaxis [2]	0	0				
Allergic (Type I) Hypersensit ivity	0	0				

- [1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.
- [2] Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.
- [3] Identified by the investigator in eCRF designed for collecting data on local injection site reactions.
- [4] Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Mepolizumab (Nucala) - HES Seite 1055 von 1069

Protocol: 200622 Page 5 of 6 Population: Safety

Table 100.16

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Region

Region: Rest of World

Regi	on: Rest of Wo	rla				-1 1 -1 66	
		Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
	Other Systemic	0	0				
	Local Injection Site Reactions [3]	1 (5%)	2 (9%)	1.90 (0.09,117.90)	1.83 (0.17,49.46)	0.04 (-0.16,0.24)	>0.999
	All Infections [4]	10 (48%	) 15 (65%)	2.06 (0.52,8.24)	1.37 (0.80,2.83)	0.18 (-0.14,0.46)	0.361
	Serious Infections	0	3 (13%)	Inf (0.55,Inf)	Inf (0.64, Inf)	0.13 (-0.05,0.34)	0.234
	Potential Opportunistic Infections [5]	1 (5%)	2 (9%)	1.90 (0.09,117.90)	1.83 (0.17,49.46)	0.04 (-0.16,0.24)	>0.999
	Neoplasms [4]	0	0				
	Malignancies [6]	0	0				

- [1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.
- [2] Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.
- [3] Identified by the investigator in eCRF designed for collecting data on local injection site reactions.
- [4] Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Mepolizumab (Nucala) - HES Seite 1056 von 1069

Protocol: 200622 Page 6 of 6 Population: Safety

Table 100.16

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Region

Region: Rest of World

-	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	(	Odds Ratio xact 95% CI)	_	lative Risk act 95% CI) [8]		Difference 5 95% CI) [8]	p-value [9]
Cardiac Disorders [4]	0	1 (4%)	Inf	(0.05,Inf)	Inf	(0.06,Inf)	0.04	(-0.13,0.23)	>0.999
Serious Cardiac Disorders	0	0							
Serious CVT Events [6]	1 (5%)	1 (4%)	0.91	(0.01,74.89)	0.91	(0.03,30.20)	0.00	(-0.20,0.18)	>0.999
Serious Ischemic Events [7]	0	0							

Mepolizumab (Nucala) - HES Seite 1057 von 1069

<sup>[1]</sup> Identified by the investigator in eCRF designed for collecting data on systemic reactions.

<sup>[2]</sup> Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.

<sup>[3]</sup> Identified by the investigator in eCRF designed for collecting data on local injection site reactions.

<sup>[4]</sup> Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Protocol: 200622 Page 1 of 6
Population: Safety

## Table 100.17

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Duration of Disease

Duration of Disease: <2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Number of Subjects in Subgroup	32	22				
Risks						
Serious Adverse Events	6 (19%)	7 (32%)	2.02 (0.47,8.71)	1.70 (0.58,4.74)	0.13 (-0.11,0.38)	0.338
Systemic Reactions [1]	0	1 (5%)	Inf (0.08, Inf)	Inf (0.10, Inf)	0.05 (-0.08,0.23)	0.407
Anaphylaxis [2]	0	0				
Allergic (Type I) Hypersensit ivity	0	0				

- [1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.
- [2] Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.
- [3] Identified by the investigator in eCRF designed for collecting data on local injection site reactions.
- [4] Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Mepolizumab (Nucala) - HES Seite 1058 von 1069

Protocol: 200622 Page 2 of 6
Population: Safety

## Table 100.17

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Duration of Disease

Duration of Disease: <2.76 Years

		Placebo (N=54)	30	polizumak Omg SC =54)	(	Odds Ratio kact 95% CI)	_	lative Risk kact 95% CI) [8]	(Exact	Difference 5 95% CI) [8]	p-value [9]
	Other Systemic	0	1	(5%)	Inf	(0.08,Inf)	Inf	(0.10,Inf)	0.05	(-0.08, 0.23)	0.407
]	Cocal Injection Site Reactions [3]	1 (3%)	0		0.00	(0.00,27.64)	0.00	(0.00,20.94)	-0.03	(-0.16,0.13)	>0.999
	All Infections [4]	12 (38%)	14	(64%)	2.92	(0.83,10.51)	1.70	(0.96,3.14)	0.26	(-0.02,0.51)	0.096
	Serious Infections	0	5	(23%)	Inf	(2.01,Inf)	Inf	(1.78,Inf)	0.23	(0.07,0.45)	0.008
	Potential Opportunistic Infections [5]	1 (3%)	1	(5%)	1.48	(0.02,119.56)	1.45	(0.04,48.09)	0.01	(-0.13,0.20)	>0.999
1	Neoplasms [4]	1 (3%)	0		0.00	(0.00,27.64)	0.00	(0.00,20.94)	-0.03	(-0.16,0.13)	>0.999
	Malignancies [6]	1 (3%)	0		0.00	(0.00,27.64)	0.00	(0.00,20.94)	-0.03	(-0.16,0.13)	>0.999

- [1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.
- [2] Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.
- [3] Identified by the investigator in eCRF designed for collecting data on local injection site reactions.

Mepolizumab (Nucala) - HES Seite 1059 von 1069

<sup>[4]</sup> Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Protocol: 200622 Page 3 of 6 Population: Safety

Table 100.17

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Duration of Disease

Duration of Disease: <2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Cardiac Disorders [4]	1 (3%)	3 (14%)	4.89 (0.35,265.05)	4.36 (0.46,112.28)	0.11 (-0.05,0.32)	0.293
Serious Cardiac Disorders	1 (3%)	1 (5%)	1.48 (0.02,119.56)	1.45 (0.04,48.09)	0.01 (-0.13,0.20)	>0.999
Serious CVT Events [6]	2 (6%)	2 (9%)	1.50 (0.10,22.11)	1.45 (0.10,21.29)	0.03 (-0.13,0.23)	>0.999
Serious Ischemic Events [7]	0	0				

Mepolizumab (Nucala) - HES Seite 1060 von 1069

<sup>[1]</sup> Identified by the investigator in eCRF designed for collecting data on systemic reactions.

<sup>[2]</sup> Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.

<sup>[3]</sup> Identified by the investigator in eCRF designed for collecting data on local injection site reactions.

<sup>[4]</sup> Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Protocol: 200622 Page 4 of 6 Population: Safety

Table 100.17

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Duration of Disease

Duration of Disease: >=2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Number of Subjects in Subgroup	22	32				
Risks						
Serious Adverse Events	2 (9%)	3 (9%)	1.03 (0.11,13.43)	1.03 (0.18,10.20)	0.00 (-0.20,0.18)	>0.999
Systemic Reactions [1]	0	0				
Anaphylaxis [2]	0	0				
Allergic (Type I) Hypersensit ivity	0	0				

- [1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.
- [2] Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.
- [3] Identified by the investigator in eCRF designed for collecting data on local injection site reactions.
- [4] Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Mepolizumab (Nucala) - HES Seite 1061 von 1069

Protocol: 200622 Page 5 of 6 Population: Safety

## Table 100.17

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Duration of Disease

Duration of Disease: >=2.76 Years

	Placebo (N=54)	Mepolizuma 300mg SC (N=54)	b Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]	
Other Systemi	0 C	0					
Local Injection Reactions		4 (13%)	3.00 (0.27,154.66)	2.75 (0.40,69.72)	0.08 (-0.12,0.26)	0.638	
All Infect [4]	ions 16 (73%	5) 23 (72%)	0.96 (0.23,3.75)	0.99 (0.70,1.51)	-0.01 (-0.25,0.25)	>0.999	
Serious Infecti		2 (6%)	Inf (0.20,Inf)	Inf (0.26,Inf)	0.06 (-0.10,0.21)	0.508	
Potential Opportunis Infections		5) 2 (6%)	0.42 (0.03,4.11)	0.46 (0.05,2.69)	-0.07 (-0.30,0.10)	0.388	
Neoplasms	[4] 1 (5%)	0	0.00 (0.00,13.06)	0.00 (0.00,9.96)	-0.05 (-0.23,0.08)	0.407	
Malignanci [6]	es 0	0					

- [1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.
- [2] Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.
- [3] Identified by the investigator in eCRF designed for collecting data on local injection site reactions.

Mepolizumab (Nucala) - HES Seite 1062 von 1069

<sup>[4]</sup> Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Protocol: 200622 Page 6 of 6 Population: Safety

Table 100.17

Summary and Analysis of Proportion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Duration of Disease

Duration of Disease: >=2.76 Years

	Placebo (N=54)	Mepolizumab 300mg SC (N=54)	Odds Ratio (Exact 95% CI)	Relative Risk (Exact 95% CI) [8]	Risk Difference (Exact 95% CI) [8]	p-value [9]
Cardiac Disorders [4]	1 (5%)	1 (3%)	0.68 (0.01,55.68)	0.69 (0.02,22.83)	-0.01 (-0.20,0.13)	>0.999
Serious Cardiac Disorders	0	0				
Serious CVT Events [6]	0	0				
Serious Ischemic Events [7]	0	0				

Mepolizumab (Nucala) - HES Seite 1063 von 1069

<sup>[1]</sup> Identified by the investigator in eCRF designed for collecting data on systemic reactions.

<sup>[2]</sup> Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.

<sup>[3]</sup> Identified by the investigator in eCRF designed for collecting data on local injection site reactions.

<sup>[4]</sup> Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Protocol: 200622 Page 1 of 6
Population: Safety

Table 100.18

Summary and Analysis of Proporion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Baseline Blood Eosinophils

Baseline Blood Eosi	nophils:	<1.5 10^9/L Mepolizumab		Relative Risk	Risk Difference		
	Placebo (N=54)	300mg SC (N=54)	Odds Ratio (Exact 95% CI)		(Exact 95% CI) [8]	p-value [9]	
Number of Subjects in Subgroup	30	26					
Risks							
Serious Adverse Events	3 (10%)	6 (23%)	2.70 (0.49,18.39)	2.31 (0.64,16.95)	0.13 (-0.07,0.35)	0.277	
Systemic Reactions [1]	0	0					
Anaphylaxis [2]	0	0					
Allergic (Type I) Hypersensit ivity	0	0					

- [1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.
- [2] Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.
- [3] Identified by the investigator in eCRF designed for collecting data on local injection site reactions.
- [4] Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Mepolizumab (Nucala) - HES Seite 1064 von 1069

Protocol: 200622 Page 2 of 6
Population: Safety

Table 100.18

Summary and Analysis of Proporion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Baseline Blood Eosinophils

Basel	ine Blood Eos	inophils:	<1.5 10^9/L Mepolizumak		D	elative Risk	Risk Difference	
		Placebo (N=54)	300mg SC (N=54)	Odds Ra (Exact 95	atio (	Exact 95% CI) [8]		p-value [9]
	Other Systemic	0	0					
I	ocal Injection Site Reactions [3]	1 (3%)	2 (8%)	2.42 (0.12,	147.40) 2.3	1 (0.21,62.53)	0.04 (-0.11,0.22)	0.592
	all Infections	16 (53%)	17 (65%)	1.65 (0.49,	5.63) 1.2	3 (0.76,2.00)	0.12 (-0.15, 0.37)	0.422
	Serious Infections	0	3 (12%)	Inf (0.70,	Inf) Inf	(0.81,Inf)	0.12 (-0.02,0.30)	0.094
0	Potential Opportunistic Infections [5]	1 (3%)	1 (4%)	1.16 (0.01,	94.15) 1.1	5 (0.03,38.23)	0.01 (-0.15,0.17)	>0.999
N	Meoplasms [4]	0	0					
	Malignancies 6]	0	0					

- [1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.
- [2] Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.
- [3] Identified by the investigator in eCRF designed for collecting data on local injection site reactions.
- [4] Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Mepolizumab (Nucala) - HES Seite 1065 von 1069

Protocol: 200622 Page 3 of 6 Population: Safety

Table 100.18

Summary and Analysis of Proporion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Baseline Blood Eosinophils

Baseline Blood Eosinophils: <1.5 10^9/L Risk Difference Mepolizumab Relative Risk Odds Ratio Placebo 300mg SC (Exact 95% CI) (Exact 95% CI) p-value (Exact 95% CI) (N=54)(N=54)[8] [8] [9] 3 (12%) 1.83 (0.19,23.36) 1.73 (0.29,17.06) 0.05 (-0.12,0.25) 0.655 Cardiac 2 (7%) Disorders [4] 1.16 (0.01,94.15) 1.15 (0.03,38.23) 0.01 (-0.15,0.17) >0.999 Serious 1 (3%) 1 (4%) Cardiac Disorders Serious CVT 1 (3%) 2 (8%) 2.42 (0.12,147.40) 2.31 (0.21,62.53) 0.04 (-0.11,0.22) 0.592 Events [6] Serious 0 Ischemic Events [7]

Mepolizumab (Nucala) - HES Seite 1066 von 1069

<sup>[1]</sup> Identified by the investigator in eCRF designed for collecting data on systemic reactions.

<sup>[2]</sup> Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.

<sup>[3]</sup> Identified by the investigator in eCRF designed for collecting data on local injection site reactions.

<sup>[4]</sup> Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Protocol: 200622 Page 4 of 6 Population: Safety

## Table 100.18

Summary and Analysis of Proporion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Baseline Blood Eosinophils

Baseline Blood Eos	inophils:	>=1.5 10^9/L Mepolizumab		Relative Risk	Risk Difference		
	Placebo (N=54)	300mg SC (N=54)	Odds Ratio (Exact 95% CI)		(Exact 95% CI) [8]	p-value [9]	
Number of Subjects in Subgroup	24	28					
Risks							
Serious Adverse Events	5 (21%)	4 (14%)	0.63 (0.11,3.43)	0.69 (0.18,2.69)	-0.07 (-0.29,0.15)	0.716	
Systemic Reactions [1]	0	1 (4%)	Inf (0.05, Inf)	Inf (0.06,Inf)	0.04 (-0.11,0.18)	>0.999	
Anaphylaxis [2]	0	0					
Allergic (Type I) Hypersensit ivity	0	0					

- [1] Identified by the investigator in eCRF designed for collecting data on systemic reactions.
- [2] Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.
- [3] Identified by the investigator in eCRF designed for collecting data on local injection site reactions.
- [4] Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Mepolizumab (Nucala) - HES Seite 1067 von 1069

Protocol: 200622 Page 5 of 6 Population: Safety

Table 100.18
Summary and Analysis of Proporion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Baseline Blood Eosinophils

Bas	eline Blood Eos:	Pla	phils: acebo =54)	Mer 300	.5 10^9/L polizumab Dmg SC =54)	C	Odds Ratio Eact 95% CI)	_	Lative Risk Kact 95% CI) [8]	(Exact	Difference 5 95% CI) [8]	p-value [9]
_	Other Systemic	0		1	(4응)	Inf	(0.05,Inf)	Inf	(0.06,Inf)	0.04	(-0.11,0.18)	>0.999
	Local Injection Site Reactions [3]		(4%)	2	(7%)	1.77	(0.09,108.85)	1.71	(0.16,46.47)	0.03	(-0.15,0.20)	>0.999
	All Infections [4]	12	(50%)	20	(71%)	2.50	(0.69,9.22)	1.43	(0.90,2.68)	0.21	(-0.07,0.47)	0.156
	Serious Infections	0		4	(14%)	Inf	(0.81,Inf)	Inf	(0.89,Inf)	0.14	(-0.02,0.33)	0.115
	Potential Opportunistic Infections [5]	3	(13%)	2	(7%)	0.54	(0.04,5.22)	0.57	(0.06,3.35)	-0.05	(-0.26,0.13)	0.652
	Neoplasms [4]	2	(8%)	0		0.00	(0.00,2.94)	0.00	(0.00,2.24)	-0.08	(-0.27,0.05)	0.208
	Malignancies [6]	1	(4%)	0		0.00	(0.00,16.29)	0.00	(0.00,12.40)	-0.04	(-0.22,0.09)	0.462

<sup>[1]</sup> Identified by the investigator in eCRF designed for collecting data on systemic reactions.

Mepolizumab (Nucala) - HES Seite 1068 von 1069

<sup>[2]</sup> Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.

<sup>[3]</sup> Identified by the investigator in eCRF designed for collecting data on local injection site reactions.

<sup>[4]</sup> Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.

Ischemic Events [7]

Protocol: 200622 Page 6 of 6 Population: Safety

Table 100.18

Summary and Analysis of Proporion of Subjects with On-Treatment Serious Adverse Events and Adverse Events of Special Interest by Baseline Blood Eosinophils

Baseline Blood Eosinophils: >=1.5 10^9/L Risk Difference Mepolizumab Relative Risk Odds Ratio Placebo 300mg SC (Exact 95% CI) (Exact 95% CI) p-value (Exact 95% CI) [8] (N=54) (N=54)[8] [9] 1 (4%) Inf (0.05, Inf) Inf (0.06, Inf) 0.04 (-0.11, 0.18) >0.999 Cardiac Disorders [4] Serious 0 Cardiac Disorders Serious CVT 1 (4%) 0 0.00 (0.00, 16.29) 0.00 (0.00, 12.40) -0.04 (-0.22, 0.09) 0.462Events [6] Serious 0

Mepolizumab (Nucala) - HES Seite 1069 von 1069

<sup>[1]</sup> Identified by the investigator in eCRF designed for collecting data on systemic reactions.

<sup>[2]</sup> Considered by the investigator to represent systemic reactions meeting Sampson's anaphylaxis criteria.

<sup>[3]</sup> Identified by the investigator in eCRF designed for collecting data on local injection site reactions.

<sup>[4]</sup> Infections from Infections and Infestations SOC; Neoplasms from Neoplasms Benign, Malignant and Unspecified (Including Cysts and Polyps) SOC; Cardiac disorders from Cardiac Disorders SOC. [5] Identified based on published list of pathogens and/or presentations of specific pathogens to be considered as potential opportunistic infections in the setting of biologic therapy (Winthrop, 2015). [6] Identified from prespecified standardised MedDRA queries (SMQs). [7] Subset of serious CVT events identified from prespecified standardised MedDRA queries (SMQs). [8] Score method, [9] 2-sided Fisher's Exact p-value.